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, 2020

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.)**

30 Winter Street
Boston, Massachusetts 02108
(Address of Principal Executive Offices) (zip code)

Registrant's telephone number, including area code: (857) 400-0101

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

Title of each class	Trading Symbol(s)	Name of each exchange on which registered
Common Stock, $0.001 par value	AVEO	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 every Interactive Data File required to be submitted 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 such files). Yes ☒ No ☐

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.

Large accelerated filer	☐	Accelerated filer	☐
Non-accelerated filer	☒	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 has filed a report on and attestation to its management's assessment of the effectiveness of its internal control over financial reporting under Section 404(b) of the Sarbanes-Oxley Act (15 U.S.C. 7262(b)) by the registered public accounting firm that prepared or issued its audit report. ☒

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, 2020, was $105.7 million.

The number of shares outstanding of the registrant's Common Stock as of March 15, 2021 was 27,130,087.

Documents incorporated by reference:

Portions of our definitive proxy statement for our 2021 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.

Presentation of our Common Stock

On February 19, 2020, we effected a 1-for-10 reverse stock split of our common stock. All references to shares of common stock outstanding and per share amounts in this Annual Report on Form 10-K give effect to the reverse stock split unless otherwise indicated.

Cautionary Note Regarding Forward-Looking Statements and Industry Data

This Annual Report on Form 10-K contains forward-looking statements within the meaning of the U.S. Private Securities Litigation Reform Act of 1995, which involve risks and uncertainties. All statements other than statements of historical fact contained in this report are statements that could be deemed forward-looking statements, including without limitation statements with respect to the plans, strategies and objectives of management for future operations; statements concerning product research, development and commercialization plans, timelines and anticipated results; statements of expectation or belief; statements with respect to clinical trials and studies; statements with respect to the therapeutic potential of product candidates; any expectations of revenue, expenses, earnings or losses from operations, or other financial results; and statements of assumptions underlying any of the foregoing. Without limiting the foregoing, the words “anticipates”, “believes”, “could”, “estimates”, “expects”, “intends”, “may”, “plans”, “seeks”, “will”, “strategy”, “potential”, “should”, “would” and other similar language, whether in the negative or affirmative, are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words. Forward-looking statements may include, but are not limited to, statements about:

- our plans to launch and commercialize FOTIVDA;
- our plans to develop our clinical stage assets and commercialize our product candidates;
- our manufacturing, marketing and sales capabilities and strategy;
- the rate and degree of market acceptance and clinical utility of our products;
- the initiation, timing, progress and results of future clinical trials, and our development programs;
- our ability to secure new collaborations, maintain existing collaborations or obtain additional funding;
- our intellectual property position;
- the potential of ficlatuzumab, AV-380 or other product candidates that we in-license, or may elect to in-license, or may acquire in the future;
- 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 competitive position;
- developments and projections relating to our competitors and our industry;
- impacts resulting from the COVID-19 pandemic and responsive actions relating thereto;
- 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; and
- our estimates regarding expenses, future revenue, capital requirements and needs for additional financing.

Our actual results may differ materially from those indicated by these forward-looking statements as a result of various important factors. We therefore caution you against relying on any of these forward-looking statements. Important factors that could cause actual results to differ materially from those in these forward-looking statements include the factors discussed below under the heading “Risk Factor Summary,” and the risk factors detailed further in Item 1A., “Risk Factors” of Part I of this report and in our U.S. Securities and Exchange Commission reports filed after this report.

This report also includes statistical and other industry and market data that we obtained from industry publications and research, surveys, and studies conducted by third parties as well as our own estimates. All of the market data used in this report involve a

number of assumptions and limitations, and you are cautioned not to give undue weight to such data. Industry publications and third-party research, surveys, and studies generally indicate that their information has been obtained from sources believed to be reliable, although they do not guarantee the accuracy or completeness of such information. Our estimates of the potential market opportunities for our product candidates include several key assumptions based on our industry knowledge, industry publications, third-party research, and other surveys, which may be based on a small sample size and may fail to accurately reflect market opportunities. While we believe that our internal assumptions are reasonable, no independent source has verified such assumptions.

The forward-looking statements included in this annual report represent our estimates as of the filing date of this annual report. We specifically disclaim any obligation to update these forward-looking statements in the future. These forward-looking statements should not be relied upon as representing our estimates or views as of any date subsequent to the date of this annual report.

Risk Factor Summary

Investment in our securities involves risk. You should carefully consider the following summary of what we believe to be the principle risks facing our business, in addition to the risks described more fully in Item 1A., "Risk Factors" of Part I of this Annual Report on Form 10-K and other information included in this report. The risks and uncertainties described below are not the only risks and uncertainties we face. Additional risks and uncertainties not presently known to us or that we presently deem less significant may also impair our business operations.

If any of the following risks occur, our business, financial condition and results of operations and future growth prospects could be materially and adversely affected, and the actual outcomes of matters as to which forward-looking statements are made in this report could be materially different from those anticipated in such forward-looking statements.

- We have incurred significant operating losses, anticipate that we will continue to incur significant operating expenses for the foreseeable future and may never generate significant revenue or achieve or sustain profitability.
- We may require substantial additional funding to advance our pipeline of clinical stage assets, and if we are unable to obtain this necessary capital when needed, we could be forced to delay, limit, reduce or terminate our research, product development or commercialization efforts.
- We have only recently transitioned from a development stage biopharmaceutical company to a commercial and clinical development stage biopharmaceutical company, which may make it difficult for you to evaluate the success of our business to date and to assess our future viability.
- We depend heavily on the success of our product, FOTIVDA, and on our clinical stage assets, including tivozanib (in other indications), ficlatuzumab and AV-380. If we are unable to complete the clinical development of, obtain marketing approval for or successfully commercialize our product candidates, our business will be materially harmed.
- 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.
- If clinical trials of any product candidates that we, or any collaborators, may develop fail to satisfactorily demonstrate safety and efficacy to the FDA and other regulators, we may incur additional costs or experience delays in completing, or ultimately be unable to complete, the development and commercialization of these product candidates.
- We face substantial competition from existing approved products and our competitors may also discover, develop or commercialize new competing products before, or more successfully, than we do.
- Adverse events or undesirable side effects caused by, or other unexpected properties of, product candidates that we develop may be identified during development and could delay or prevent their marketing approval or limit their use.
- We rely in part on third parties to produce our preclinical and clinical product candidate supplies and to conduct clinical trials of our internally-developed product candidates, and those third parties may not perform satisfactorily, including by failing to deliver supplies on time or to meet deadlines for the completion of such trials, research or testing.
- We rely on our licensee EUSA, over whom we have little control, for the sales, marketing and distribution efforts associated with the commercialization of FOTIVDA in certain European countries and any failure by EUSA to devote the necessary resources and attention to market and sell FOTIVDA effectively and successfully may materially impact our ability to generate revenue.

- 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 and, such failures or terminations could have a material adverse effect on our operations and business.

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

PART I

ITEM 1. Business

Overview

We are an oncology-focused biopharmaceutical company committed to delivering medicines that provide a better life for cancer patients. Our strategy is to focus our resources toward the development and commercialization of our product candidates in North America, while leveraging partnerships to support development and commercialization in other geographies. With the approval of our first commercial product, FOTIVDA® (tivozanib), in the United States, we have transitioned from a clinical development stage biopharmaceutical company to a commercial and clinical development stage biopharmaceutical company.

On March 10, 2021, the U.S. Food and Drug Administration, or FDA, approved FOTIVDA in the United States for the treatment of adult patients with relapsed or refractory advanced renal cell carcinoma following two or more prior systemic therapies. FOTIVDA is an oral, next-generation vascular endothelial growth factor receptor, or VEGFR, tyrosine kinase inhibitor, or TKI. The approval of FOTIVDA is based on our pivotal phase 3 randomized, controlled, multi-center, open-label clinical trial comparing tivozanib to an approved therapy, Nexavar® (sorafenib), in renal cell carcinoma, or RCC, patients whose disease had relapsed or become refractory to two or three prior systemic therapies, which we refer to as the TIVO-3 trial. The approval is also supported by three additional trials in RCC and includes safety data from over 1,000 clinical trial subjects.

We are actively preparing for the commercial launch of FOTIVDA in the United States. Our U.S. sales force, sales training, marketing, market access and medical affairs teams as well as distribution capabilities are in place and we expect to have full promotional capabilities and FOTIVDA available to patients by March 31, 2021.

FOTIVDA is also approved and commercialized through our development partner EUSA Pharma (UK) Limited, or EUSA, in the United Kingdom, Germany, Spain and certain other countries in their territory, for the treatment of adult patients with advanced RCC who are VEGFR pathway inhibitor-naïve and are either untreated or who have failed prior therapy with interferon-alpha (IFN-a) or interleukin-2 (IL-2).

Based on FOTIVDA's demonstrated anti-tumor activity, tolerability profile and reduction of regulatory T-cell production, we are studying FOTIVDA in combination with immune checkpoint inhibitors for the treatment of RCC and hepatocellular carcinoma, or HCC, in phase 2 clinical trials and we recently announced our entry into a collaboration with Bristol Myers Squibb, or BMS, to conduct a phase 3 study of FOTIVDA in combination with OPDIVO® (nivolumab), BMS's anti-PD-1 therapy, in patients with advanced relapsed or refractory RCC following prior immunotherapy exposure.

Our pipeline of product candidates includes ficlatuzumab, a potent humanized immunoglobulin G1, or IgG1, monoclonal antibody that targets hepatocyte growth factor, or HGF. We have previously reported promising early clinical data on ficlatuzumab in squamous cell carcinoma of the head and neck, or HNSCC, pancreatic cancer and acute myeloid leukemia, or AML. We are currently conducting a randomized phase 2 confirmatory study of ficlatuzumab for the potential treatment of HNSCC.

Our pipeline of product candidates also includes worldwide rights to AV-380, a potent humanized IgG1 monoclonal antibody that targets growth differentiation factor 15, or GDF15. In December 2020, the FDA accepted our investigational new drug application, or IND, for AV-380 for the potential treatment of cancer cachexia, and we have initiated a phase 1 clinical trial in healthy subjects.

Our earlier-stage pipeline under development includes AV-203 and AV-353, both as potential oncology treatments. AV-203 is a potent humanized IgG1 monoclonal antibody that targets ErbB3 (also known as HER3) to which we expect to regain worldwide rights in September 2021. AV-353 is a potent IgG1 monoclonal antibody that targets the Notch 3 pathway.

Commercial Launch

During 2020 and early 2021, in preparation for the commercial launch of FOTIVDA in the United States, we:

- expanded our organization with approximately 65 field-based employees, which includes approximately 50 oncology sales professionals;
- developed our commercial capabilities with implementation of systems and infrastructure to support our virtual and in person commercial sales organization, patient-focused programs and appropriate quality systems and compliance policies, systems and procedures; and
- established our distribution network in order to be prepared to have full promotional capabilities and product available for sale by March 31, 2021.

Business Update Regarding COVID-19

The pandemic caused by an outbreak of a new strain of coronavirus, or the COVID-19 pandemic, that is affecting the U.S. and global economy and financial markets is also impacting our employees, patients, communities and business operations to varying degrees. In the paragraphs that follow, we have described impacts of the COVID-19 pandemic on our commercialization plans and clinical development programs, as applicable. The extent to which the COVID-19 pandemic will directly or indirectly impact our business, results of operations and financial condition will depend on future developments that are highly uncertain and cannot be accurately predicted, including new information that may emerge concerning COVID-19, the actions taken to contain it or treat its impact and the economic impact on local, regional, national and international markets. Certain of our operations had been conducted remotely prior to the COVID-19 pandemic, and we have now transitioned essentially all of our business operations to be conducted remotely in response to COVID-19. If the COVID-19 pandemic continues or becomes more severe, it may further impact our ability to maintain that level of productivity, to grow the company as we have anticipated and to execute our commercialization and other long-term business strategies. Management is actively monitoring this situation and the possible effects on our financial condition, liquidity, operations, suppliers, industry and workforce. For additional information on risks posed by the COVID-19 pandemic, please see "Part I, Item 1A. Risk Factors – Risks Related to the COVID-19 Pandemic," included elsewhere in this Annual Report on Form 10-K.

Our Product Candidates

The following summarizes our product candidates as of the date of filing this Annual Report on Form 10-K, each of which is described in further detail below:

Tivozanib

Our pipeline includes our lead product tivozanib, an oral, next-generation VEGFR TKI. Tivozanib was approved by the FDA for marketing and sale in the United States in March 2021 and will be sold under the brand name FOTIVDA for the treatment of adult patients with relapsed or refractory advanced RCC following two or more prior systemic therapies.

Tivozanib is a potent, selective inhibitor of VEGFRs 1, 2, and 3 with a long half-life designed to improve efficacy and tolerability. FOTIVDA has been shown to significantly reduce regulatory T-cell production in preclinical models. Tivozanib has been investigated in several tumor types, including renal cell, hepatocellular, colorectal, breast and ovarian cancers. We are currently executing studies with tivozanib both as a single agent and in combination with immune checkpoint inhibitors for the treatment of RCC and HCC.

We have exclusive rights to develop and commercialize tivozanib in oncology in all countries outside of Asia and the Middle East under a license from Kyowa Kirin Co., Ltd. (formerly Kirin Brewery Co., Ltd.), or KKC. We have sublicensed to EUSA the right to develop and commercialize tivozanib in our licensed territories outside of North America, including Europe (excluding Russia, Ukraine and the Commonwealth of Independent States), Latin America (excluding Mexico), Africa and Australasia. The EUSA sublicense excludes non-oncologic diseases or conditions of the eye. On August 1, 2019, KKC repurchased the non-oncology rights to tivozanib in our territory, excluding the rights that we sublicensed to EUSA. In September 2020, KKC initiated a phase 1 study of KHK4951, the reformulated tivozanib, in healthy volunteers and patients with wet age-related macular degeneration, or Wet AMD.

U.S. Commercialization of Tivozanib in Relapsed or Refractory Advanced RCC

In March 2020, we submitted an NDA to the FDA based on our TIVO-3 trial and supported by data from three additional trials, including the TIVO-1 trial comparing tivozanib to sorafenib in first-line RCC, and two phase 2 trials, Study 902, the open-label, crossover clinical study of tivozanib for patients who progressed on sorafenib in the TIVO-1 trial, and Study 201, a placebo-controlled study in first-line RCC. On March 10, 2021, the FDA approved FOTIVDA in the United States for the treatment of adult patients with relapsed or refractory RCC following two or more prior systemic therapies.

Our TIVO-3 trial is the first positive phase 3 study in RCC patients whose disease had relapsed or become refractory to two or three prior systemic therapies to meet its primary endpoint, as well as the first phase 3 study in RCC to systematically investigate a predefined subpopulation of patients who received prior checkpoint inhibitor therapy, a predominant standard of care for earlier lines of therapy. Key data from our TIVO-3 trial include the following:

- Tivozanib demonstrated a 44% improvement in median progression-free survival, or PFS, the primary endpoint, with a median PFS in the tivozanib arm of 5.6 months compared with 3.9 months in the sorafenib arm, and 27% reduction in risk of progression or death compared to sorafenib (hazard ratio (HR)=0.73, p=0.0165).
- Overall response rate, or ORR, for patients receiving tivozanib was 18% compared to 8% for patients receiving sorafenib (p=0.017).

- Median duration of response in patients receiving tivozanib was not reached (95% confidence interval (CI): 9.8, not reached (NR)) and in patients receiving sorafenib was 5.7 months (95% CI: 5.6, NR).
- The final overall survival, or OS, hazard ratio was 0.97 (p=0.82), and the final median OS was 16.4 months for tivozanib and 19.2 months for sorafenib. The final OS hazard ratio of 0.97 was similar to those observed in other phase 3 studies in RCC comparing a prior FDA-approved VEGFR TKI to another VEGFR TKI.
- Tivozanib also demonstrated a statistically significant improvement in median PFS for the prespecified subgroup of patients (approximately 26% of patients) who received prior checkpoint inhibitor therapy, with a hazard ratio of 0.55 (p=0.028), a 45% reduction in risk of progression or death compared to sorafenib and a median PFS in the tivozanib arm of 7.3 months compared with 5.1 months in the sorafenib arm. The ORR for patients in this subgroup receiving tivozanib was 24.4% compared to 7% receiving sorafenib. The final OS hazard ratio for this subgroup was 0.84 (HR < 1 favors tivozanib). Tivozanib also demonstrated a statistically significant improvement in median PFS for the prespecified subgroup of patients (approximately 45% of patients) who received two TKIs in earlier lines of treatment, with a hazard ratio of 0.57 (p=0.003), a 43% reduction in risk of progression or death compared to sorafenib and a median PFS in the tivozanib arm of 5.5 months compared with 3.7 months in the sorafenib arm. The ORR for patients in this subgroup receiving tivozanib was 15% compared to 8% receiving sorafenib. The final OS hazard ratio for this subgroup was 0.99.
- Tivozanib was generally better tolerated than sorafenib with fewer dose reductions and interruptions due to adverse events. In the tivozanib arm, 46% of patients experienced Grade 3 or higher adverse events compared to 55% of patients in the sorafenib arm. Infrequent but severe adverse events reported in greater number in the tivozanib arm were thrombotic events similar to those observed in previous tivozanib studies. The most common adverse events in patients receiving tivozanib was fatigue and asthenia, adverse events known to reflect effective VEGF pathway inhibition, which has shown a correlation with better PFS outcomes.

We believe there is significant commercial opportunity for FOTIVDA in the United States. We estimate that the current U.S. market for relapsed or refractory RCC therapy is approximately $1.0 billion, including $700 million in the second line and $300 million in the third and fourth lines. As the TIVO-3 study is the first positive phase 3 study in RCC patients whose disease had relapsed or become refractory to two or three prior systemic therapies as well as the first phase 3 study in RCC to investigate a predefined subpopulation of patients who received prior immunotherapy, a predominant standard of care for earlier lines of therapy, we believe that FOTIVDA could become a standard of care in this relapsed or refractory setting.

During 2020 and early 2021, in preparation for the commercial launch of FOTIVDA in the United States, we built our commercial infrastructure including our sales, marketing, market access and medical affairs teams and distribution capabilities. In light of the restrictions necessitated by the COVID-19 pandemic, we designed our strategic commercial approach to be optimized for remote as well as in-person customer engagement capabilities and expanded our digital marketing strategies. Our U.S. sales force, sales training, marketing, market access and medical affairs teams as well as distribution capabilities are in place and we expect to have full promotional capabilities by March 31, 2021.

Commercialization of Tivozanib in RCC Outside the United States

First-Line Approval in Europe: In August 2017, the European Commission granted marketing authorization to EUSA for tivozanib in all 28 countries of the European Union, or the EU, (which included the United Kingdom at that time), Norway and Iceland based on the data from our active comparator-controlled supportive phase 3 trial, which we refer to as the TIVO-1 trial, comparing tivozanib to sorafenib (Nexavar®) in first-line RCC. Tivozanib is sold under the brand name FOTIVDA, and is approved for the first-line treatment of adult patients with RCC and for those who are VEGFR and mTOR pathway inhibitor-naïve following disease progression after one prior treatment with cytokine therapy for RCC.

In the updated Clinical Practice Guidelines for the diagnosis, treatment and follow-up of RCC by the European Society for Medical Oncology, or ESMO, published in February 2019, tivozanib has been added as a first-line treatment for patients with good or intermediate risk and as a second-line treatment for patients following first-line TKIs.

Commercial Launch of FOTIVDA: EUSA has received reimbursement approval for and commercially launched FOTIVDA in Germany, the United Kingdom and Spain as well as in some additional EU countries, exclusive of France, Germany, Italy, Spain and the United Kingdom, which we refer to collectively as the EU5. In February 2018, November 2018 and February 2019, EUSA obtained reimbursement approvals from the United Kingdom's National Institute for Health and Care Excellence, or the NICE, the German Federal Association of the Statutory Health Insurances, or GKV-SV, and Spain's Ministry of Health, Consumer Affairs and Social Welfare, or MSCBS, respectively, for the first-line treatment of RCC. EUSA is working to secure reimbursement approval in and commercially launch FOTIVDA in additional European countries.

First-Line Approval in New Zealand and South Africa: In July 2019, the New Zealand Medicines and Medical Devices Safety Authority approved FOTIVDA for the first-line treatment of adult patients with RCC and for adult patients who are VEGFR and mTOR pathway inhibitor-naïve following disease progression after one prior treatment with cytokine therapy for RCC. In September 2020, the South African Health Products Regulatory Authority approved FOTIVDA for the first-line treatment of adult patients with advanced RCC and for adult patients who are VEGFR and mTOR pathway inhibitor-naïve following disease progression after one prior treatment with cytokine therapy for advanced RCC.

Clinical Development of Tivozanib in RCC

First-Line Phase 3 Trial (TIVO-1): We conducted the TIVO-1 trial, a global phase 3 clinical trial comparing the efficacy and safety of tivozanib with sorafenib, an approved therapy, for the first-line treatment of RCC. The trial met its primary endpoint of improving 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 ORR of 33.1% for tivozanib versus 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 OS in the intent to treat population. The protocol-specified final OS analysis at 24 months since the last patient enrolled showed a median OS for the tivozanib arm of 28.8 months versus a median OS for the sorafenib arm of 29.3 months (HR=1.245, p=0.105). An OS hazard ratio assesses the relative risk of death for the entirety of the data set and the median OS is a point in time value of the OS when half of the patients within each arm are still alive. Subsequently, in connection with EUSA's application for the use of tivozanib as a first-line treatment for RCC to the European Medicines Agency, or EMA, in February 2016, which was approved in August 2017 and is further discussed below, the survival status of additional patients was taken into account and the updated median OS for the tivozanib arm was 28.2 months and the updated median OS for the sorafenib arm was 30.8 months (HR=1.147, p=0.276). We believe that an imbalance in subsequent therapy, which was more prevalent in patients treated in certain countries such as Russia and the Ukraine, 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 an NDA to the FDA seeking U.S. marketing approval for tivozanib. In June 2013, the FDA issued a complete response letter, which we refer to as the 2013 CRL, informing us that it would not approve tivozanib for the first-line treatment of RCC based solely on the data from this single pivotal trial (TIVO-1), and recommended that we perform an additional clinical trial with a PFS primary endpoint and adequately sized to assure the FDA that tivozanib does not adversely affect OS. A post hoc analysis was conducted to evaluate differences in the use of second-line therapy between geographic regions and the impact on the OS results. When analyzing results from treatment centers in North America and the EU only where the imbalance in subsequent therapy was substantially reduced, the benefit in PFS was preserved and the HR for PFS was 0.84 (HR<1 favors tivozanib).

Second-Line TIVO-1 Extension Study - One-sided crossover from sorafenib to tivozanib (Study 902): We completed a TIVO-1 extension study, which we refer to as the 902 trial, in which patients with RCC received tivozanib as second-line treatment subsequent to disease progression on the sorafenib treatment arm in the TIVO-1 first-line RCC trial. We presented the results at the 2015 American Society of Clinical Oncology, or ASCO, Annual Meeting. In March 2018, long-term follow-up results from the 902 trial were published in the European Journal of Cancer under the title "Efficacy of Tivozanib Treatment after Sorafenib in Patients with Advanced Renal Cell Carcinoma: Crossover of a Phase 3 Study," reporting a median PFS of 11.0 months, a median OS of 21.6 months and an 18% ORR, further supporting the rationale for our current phase 3 TIVO-3 trial discussed below.

Third-Line and Fourth-Line Phase 3 Trial (TIVO-3): In May 2016, we initiated enrollment in the TIVO-3 trial. The TIVO-3 trial is the first positive phase 3 study in the third- and fourth-line treatment of patients with RCC as well as the first phase 3 study in RCC to investigate a predefined subpopulation of patients who received prior immunotherapy, a predominant standard of care for earlier lines of therapy. The trial enrolled a total of 350 patients and was designed to address the FDA's concern about the negative OS trend in TIVO-1. TIVO-3, together with the previously completed TIVO-1 and 902 trials of tivozanib in the first-line and second-line treatment of RCC, is designed to support a regulatory submission of tivozanib in the United States as a treatment for RCC in relapsed or refractory patients. Our TIVO-3 trial design, which we reviewed with the FDA, provides for a randomized, controlled, multi-center, open-label phase 3 clinical trial, with subjects 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 exclusively in North America and Europe. The TIVO-3 trial does not include a crossover design; accordingly, the protocol does not provide for patients who progress on one therapy to cross over to the other therapy.

On November 5, 2018, we announced that the TIVO-3 trial met its primary endpoint of improving PFS, with a median PFS in the tivozanib arm of 5.6 months compared with 3.9 months in the sorafenib arm. Tivozanib demonstrated a 44% improvement in median PFS and 27% reduction in risk of progression or death compared to sorafenib (HR=0.73, p=0.02). Approximately 26% of patients received checkpoint inhibitor therapy in earlier lines of treatment. Patients who received prior checkpoint inhibitor therapy had a 45% reduction in risk of progression or death. The secondary endpoint of ORR for patients receiving tivozanib was 18% compared to 8% for patients receiving sorafenib (p=0.02). Median duration of response in patients receiving tivozanib was not reached and in patients receiving sorafenib was 5.7 months. Tivozanib was generally better tolerated than sorafenib, as indicated by fewer dose reductions and interruptions. Grade 3 or higher adverse events were consistent with those observed in previous tivozanib trials. Infrequent but severe adverse events reported in greater number in the tivozanib arm were thrombotic events similar to those observed in previous tivozanib studies. The most common adverse events in patients receiving tivozanib was fatigue and asthenia, adverse events known to reflect effective VEGF pathway inhibition, which has shown a correlation with better PFS outcomes. In December 2019, previously reported data from the TIVO-3 trial was published in The Lancet Oncology.

RCC PD-1 Phase 1b/2 Combination Trial with OPDIVO® (TiNivo): In March 2017, we initiated enrollment in a phase 1b/2 clinical trial of tivozanib in combination with OPDIVO (nivolumab), BMS's anti-PD-1 therapy, in the first-line and the second-line treatment of RCC, which we refer to as the TiNivo trial. The TiNivo trial enrolled a total of 28 patients. We sponsored the trial, for which BMS supplied nivolumab. The TiNivo trial was 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 TiNivo trial enrolled six patients and demonstrated that the combination of tivozanib and nivolumab was able to be dosed at the full dose and schedule of single agent tivozanib, with no dose limiting toxicities observed.

The phase 2 portion of the trial, which enrolled an additional 22 patients split evenly between treatment naïve and previously treated patients, was designed to assess the safety, tolerability and anti-tumor activity of the full dose and schedule of the combination of tivozanib (1.5 mg daily for 21 days, followed by seven days off treatment) and nivolumab (240 mg every two weeks) as established in the phase 1b portion of the study. On September 30, 2019, we presented final results at the ESMO 2019 Congress. The final results showed that the combination required few dose reductions and showed additive or synergistic activity for ORR and PFS in both treatment naïve and previously treated patients with RCC with no apparent difference in activity despite the different line of treatment. Out of 25 patients who were treated with the full dose and schedule of oral tivozanib in combination with intravenous nivolumab, thirteen (52%) had received at least one prior systemic therapy, including two (8%) that had received prior PD-1 therapy, and twelve (48%) that were treatment naïve. The overall median PFS for the 25 patients was 18.9 months. The median PFS for the twelve previously untreated patients was 18.5 months and the median PFS for the thirteen previously treated patients had not yet been achieved as of the final data cut-off date of August 27, 2019. An ORR was observed in 14 patients (56%) (complete response plus partial response), including one treatment naïve patient (4%) achieving a complete response, and a disease control rate (complete response plus partial response plus stable disease) was observed in 24 patients (96%). Of the two patients (8%) who received prior PD-1 therapy, one achieved a partial response and the other achieved stable disease. Treatment-related Grade 3/4 adverse events occurred in 80% of patients, the most common of which was hypertension, and only 17% of patients required a dose reduction.

In November 2020, we announced that previously reported results from the TiNivo trial were published in Annals of Oncology in an article titled "TiNivo: Safety and Efficacy of Tivozanib-Nivolumab Combination Therapy in Patients with Metastatic Renal Cell Carcinoma".

RCC PD-1 Phase 3 Combination Trial with OPDIVO® (TiNivo-2): On March 12, 2021, following the FDA's approval of FOTIVDA, we announced our plans to advance our trials of the combination of tivozanib and nivolumab in RCC pursuant to a clinical trial collaboration and supply agreement with BMS to evaluate FOTIVDA in combination with OPDIVO (nivolumab) in a randomized, open-label, controlled phase 3 TiNivo-2 trial in patients with advanced relapsed or refractory RCC following prior immunotherapy exposure, which we refer to as the TiNivo-2 trial. The TiNivo-2 trial is expected to enroll approximately 326 patients

with advanced RCC who have progressed following prior immunotherapy treatment. The trial plans to enroll across clinical sites in the United States, Europe and Latin America. Patients will be randomized 1:1 to receive either FOTIVDA (1.34 mg/QD for 21 days followed by 7 days off treatment) in combination with OPDIVO (480 mg every 4 weeks) or FOTIVDA alone. The TiNivo-2 trial's primary endpoint will assess PFS, with key secondary endpoints to include overall survival, overall response rate and duration of response, and safety. The study design was submitted to the FDA for review and we expect feedback from the FDA regarding the study design in the second quarter of 2021.

Clinical Development of Tivozanib in HCC

HCC PD-L1 Combination Trial with IMFINZI® (DEDUCTIVE): In September 2019, we opened enrollment in an open-label, multi-center, randomized phase 1b/2 clinical trial of tivozanib in combination with IMFINZI (durvalumab), a human monoclonal antibody directed against programmed death-ligand 1, or PD-L1, as a first-line treatment for patients with advanced, unresectable HCC who have not received prior systemic therapy, which we refer to as the DEDUCTIVE trial. Pursuant to the clinical supply agreement that we entered into with a wholly-owned subsidiary of AstraZeneca PLC, or AstraZeneca, in December 2018, we serve as the study sponsor, each party contributes the clinical supply of its study drug, key decisions are made by both parties by consensus and external study costs are otherwise shared equally.

The DEDUCTIVE trial is being led by the Roswell Park Comprehensive Cancer Center under the direction of Dr. Renuka Iyer. A total of seven patients with advanced or metastatic HCC were enrolled in the phase 1b portion of the study, which was designed to determine the recommended phase 2 dose and assess preliminary safety and efficacy of the tivozanib/durvalumab combination. The DEDUCTIVE trial progressed to phase 2 following the successful completion of the phase 1b portion of the trial, where 1.0 mg of tivozanib was administered for 21 days followed by seven days off treatment together with 1,500 mg of durvalumab every 28 days. The combination was well-tolerated, with no dose limiting toxicities. The combination demonstrated a 29% partial response (PR) rate and 71% disease control rate (PR + stable disease), which was similar to what was observed in the bevacizumab and atezolizumab combination trial in a similar disease setting. We anticipate completion of enrollment in the ongoing phase 2 portion of the study, which is expected to enroll up to an additional 30 subjects, in 2021. The primary outcome measure of the DEDUCTIVE trial is incidence of treatment emergent adverse events and the secondary outcome measures include ORR, PFS and OS. In January 2021, we presented preliminary results from the phase 1b portion of the DEDUCTIVE trial in a poster session at the 2021 American Society of Clinical Oncology Gastrointestinal, or ASCO GI, Cancers Symposium.

Twelve clinical trial sites have been initiated for the DEDUCTIVE trial. At certain sites enrollment has been suspended at times due to COVID-19 related restrictions. We cannot guarantee the future pace of enrollment. Further, certain trial functions, including trial monitoring, will continue to be conducted remotely where possible. We do not yet know whether remote management of these functions will prove to be sufficient.

We believe we have sufficient clinical supply of tivozanib manufactured to complete the DEDUCTIVE trial. The DEDUCTIVE trial also requires treatment with durvalumab, which is administered intravenously and supplied by AstraZeneca. Any interruptions in the supply or delivery of study drug for the trial would impact patient treatment. The extent and impact of any future disruptions on enrollment, patient treatment and trial management of our DEDUCTIVE trial due to the COVID-19 pandemic are uncertain and may change with the local and global fluctuations in the incidence of COVID-19.

NCCN-AVEO Phase 1b/2 Trial. In February 2020, final results from a multicenter, investigator-sponsored phase 1b/2 clinical trial of tivozanib in previously untreated patients with advanced, unresectable HCC were published in the British Journal of Cancer under the title, "A Multicentre Phase 1b/2 Study of Tivozanib in Patients with Advanced Inoperable Hepatocellular Carcinoma." The trial was led by the Roswell Park Comprehensive Cancer Center under the direction of Dr. Iyer and was approved and funded by the National Comprehensive Cancer Network Oncology Research Program from general research support provided by us. The trial was designed to evaluate the safety and efficacy of tivozanib in advanced HCC, and enrolled a total of 27 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 or 1.5 mg daily for 21 days followed by 7 days off treatment. No dose-limiting toxicities were seen in cycle one in patients treated with 1.0 mg, and tivozanib at 1.0 mg daily was selected for the phase 2 expansion portion of the trial. The phase 2 trial's primary endpoint of median PFS and 24-week PFS probability were 24 weeks and 58%, respectively. Of 19 evaluable patients in the trial, a partial response was seen in 4 of 19 patients (21%) and stable disease in 8 of 19 patients (42%), for a disease control rate of 63%. Median OS was 9.0 months. A significant decrease in soluble plasma VEGFR-2 was also observed, suggesting adequate target engagement. There were no significant changes in hepatitis B or hepatitis C viral load during study treatment and adverse events were consistent with those observed in previous tivozanib trials.

Clinical Development of Tivozanib in Ovarian Cancer

On June 1, 2019, Dr. Wendy Swetzig at Northwestern University Feinberg School of Medicine presented data at the 2019 ASCO Annual Meeting from an investigator-sponsored phase 2 clinical trial of tivozanib in patients with recurrent, platinum-resistant ovarian cancer, including fallopian tube or primary peritoneal cancer. The trial was one of several studies funded by a grant we provided to the National Comprehensive Cancer Network. The trial was designed to measure the safety and activity of tivozanib in ovarian cancer and enrolled a total of 31 patients, 30 of which were treated with tivozanib. With four patients showing a partial response and twelve patients with stable disease, the clinical benefit rate (partial response + stable disease) was reported to be 53.3%. The trial concluded that tivozanib is active in patients with recurrent ovarian cancer, without substantial toxicity.

Ficlatuzumab

Ficlatuzumab is a potent humanized IgG1 monoclonal antibody that blocks cMET receptor, or cMET, signaling by binding HGF, the natural ligand of cMET, which is believed to trigger many activities that are involved in cancer development and metastasis. We have seen promising results for ficlatuzumab as a potential treatment of HNSCC, pancreatic cancer and AML in early clinical trials. The estimated number of annual new cases of head and neck cancer, pancreatic cancer and AML in the United States is 57,600, 53,260 and 19,940, respectively (American Cancer Society, Cancer Facts & Figures 2020). In September 2020, we made the decision to fund additional clinical manufacturing of ficlatuzumab to enable a potential registrational phase 3 clinical trial in HNSCC after final results from the open-label, randomized phase 2 study are available, as well as to enable additional potential development in pancreatic cancer and AML. In September 2020, we regained full global rights to ficlatuzumab, as a result of our former development partner Biodesix, Inc., or Biodesix, exercising its Opt-Out rights under the Biodesix Agreement, each as defined below. For more information, see *"Part I, Item 1. Business – Strategic Partnerships – Ficlatuzumab"* below.

Development in HNSCC. We and our previous partner, Biodesix, funded an investigator-sponsored phase 1 clinical trial of ficlatuzumab in combination with ERBITUX® (cetuximab) in 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 twelve patients), a disease control rate of 67% and prolonged PFS and OS compared to historical controls of cetuximab alone. A randomized, phase 2, multicenter, investigator-initiated trial, or the Phase 2 HNSCC Trial, to confirm these findings was initiated in the fourth quarter of 2017. The Phase 2 HNSCC Trial is being conducted at seven academic centers under the direction of Julie E. Bauman, MD, MPH, Chief, Division of Hematology/Oncology at the University of Arizona Cancer Center. The trial was designed to enroll approximately 60 patients randomized to receive either ficlatuzumab alone or ficlatuzumab and cetuximab, and enrollment was completed in the fourth quarter of 2020. We expect to receive top line data from the Phase 2 HNSCC Trial in the middle of 2021, and we expect to announce a phase 3 clinical trial decision for ficlatuzumab in that timeframe. We have initiated manufacturing of the clinical supply for this potential phase 3 clinical trial.

Development in pancreatic cancer. We and our previous partner, Biodesix, funded an investigator-sponsored phase 1b/2 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, or PDAC. In January 2020, results from the phase 1b portion of the trial were presented at the 2020 ASCO GI Cancers Symposium. The trial, which was based on preclinical findings demonstrating a synergistic effect of the combination in a preclinical model of PDAC, was designed to determine maximum tolerated dose of ficlatuzumab when combined with gemcitabine and nab-paclitaxel. Secondary outcome measures include response rate and PFS. A total of 24 patients enrolled in the trial, which was conducted under the direction of Kimberly Perez, M.D. at the Dana-Farber Cancer Institute. The average number of 28-day treatment cycles received was 7.5 (range 1-15), with three patients remaining on active treatment at the end of the trial. The combination showed a 29% partial response rate and a 92% disease control rate (partial response and stable disease), which was promising relative to data observed for gemcitabine and nab-paclitaxel alone. Treatment with this regimen was associated with significant hypoalbuminemia and edema, and therefore a follow-up safety study is under consideration to evaluate ficlatuzumab in combination with an alternate cytotoxic regimen.

Development in AML. We and our previous partner, Biodesix, have also funded an investigator-sponsored phase 1b/2 clinical trial of ficlatuzumab in combination with cytarabine in AML, which we refer to as the CyFi-1 trial, which showed a favorable complete response rate in the 18 primary refractory AML patients enrolled in the trial and an acceptable tolerability profile. Based on the encouraging findings from the CyFi-1 trial, we designed a randomized phase 2 clinical trial evaluating ficlatuzumab in combination with high-dose cytarabine versus high-dose cytarabine alone in patients with AML, which we referred to as the CyFi-2 trial. However, in March 2020, we discontinued the CyFi-2 trial prior to the initiation of patient enrollment due to the urgent shift in priorities among clinical trial sites toward efforts to combat the COVID-19 pandemic, which had impacted the trial enrollment timeline and the feasibility of completing the study within the shelf-life of the current ficlatuzumab clinical trial drug supply.

We continue to evaluate additional opportunities for the further clinical development of ficlatuzumab. The expansion of the ficlatuzumab clinical program, beyond what we are currently committed to, will require additional manufacturing efforts and costs.

AV-380

AV-380 is a potent humanized IgG1 monoclonal antibody that targets GDF15, which is associated with cachexia and has been linked to immunosuppression in the tumor microenvironment. We are developing AV-380 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. It is estimated that cachexia affects approximately 9 million individuals in North America, Europe and Japan (J Cachexia Sarcopenia Muscle 2010). Cachexia is associated with various cancers, and it is estimated that approximately 50% of all cancer patients suffer from cachexia and 30% of all cancer patients die due to cachexia (World J Gastrointest Oncol 2015; J Cachexia Sarcopenia Muscle 2010). We believe AV-380 has the potential to address a significant unmet need. Cachexia also affects patients with chronic kidney disease, congestive heart failure, chronic obstructive pulmonary disease, anorexia nervosa, AIDS and other diseases.

We believe that AV-380 represents a unique approach to treating cachexia because it has been demonstrated in preclinical studies to address key underlying mechanisms of the syndrome. Our research suggests that greater than 70% of cancer patients have increased GDF15 expression, starting at the pre-cachectic stage. If GDF15 inhibitors such as AV-380 are proven clinically successful, we believe there is a significant market opportunity with potential application in multiple tumor types in combination with multiple anti-cancer treatment standards. In addition to our patents and patent applications covering our proprietary AV-380 antibody 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. We have milestone and royalty payment obligations under our license agreement with St. Vincent's.

In December 2020, the FDA accepted our IND filing for AV-380 for the potential treatment of cancer cachexia and, in the first quarter of 2021, we initiated a phase 1 clinical trial in healthy subjects.

AV-203

AV-203 is a potent humanized IgG1 monoclonal antibody that targets ErbB3 (also known as HER3). In March 2016, we entered into a collaboration and license agreement with CANbridge Life Sciences Ltd., or CANbridge, which we refer to as the CANbridge Agreement, under which we granted CANbridge the exclusive right to develop, manufacture and commercialize AV-203 in all countries outside of North America. In December 2017, CANbridge filed an IND application in China seeking regulatory authorization to initiate clinical trials of AV-203, which CANbridge refers to as CAN017, in esophageal squamous cell carcinoma, or ESCC. In August 2018, the National Medical Products Administration, or NMPA (formerly the China Food and Drug Administration), approved this IND application but a clinical trial was never initiated.

In March 2021, CANbridge exercised its right to terminate for convenience the CANbridge Agreement. Under the terms of the CANbridge Agreement, we expect the transfer of the AV-203 program to be complete in September 2021 and, at that time, we will regain worldwide rights to the AV-203 program.

AV-353

AV-353 is a potent IgG1 monoclonal antibody that targets the Notch 3 pathway. 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, such as pulmonary arterial hypertension, and neurodegenerative conditions. AV-353 is being studied by collaborators at the Mayo Clinic in pre-clinical models of triple negative breast cancer.

Competition

The biotechnology and pharmaceutical industries are highly competitive. Our future success depends on our ability to maintain a competitive advantage with respect to our product candidates.

Our core competitors include pharmaceutical and biotech organizations, as well as academic research institutions, clinical research laboratories and government agencies that are pursuing research activities in the same therapeutic areas as us. Many of our competitors have greater financial, technical and human resources than we do. Additionally, many competitors have greater experience in product discovery and development, obtaining FDA and other regulatory approvals and commercialization capabilities, which may provide them with a competitive advantage.

We believe that our ability to compete will depend on our ability to execute on the following objectives:

- design, develop and commercialize products that are superior to other products in the market in terms of, among other things, safety, efficacy and/or convenience;
- 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/or 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.

Tivozanib

The competitive landscape and treatment regimens for RCC and HCC continue to rapidly evolve, particularly given the entrance of immune checkpoint inhibitor combination therapies and the potential entrance of immune checkpoint inhibitor and VEGFR TKI combination therapies into the RCC treatment landscape. The utilization of such regimens may affect sequencing of certain drugs and combinations across different lines of therapy. Additionally, there are several therapies in clinical development for RCC and HCC that may alter the competitive landscape for the treatment of these cancers. As such, it is difficult to predict how these changes will inform our perspective on the key competitors of tivozanib in RCC and HCC in the future.

RCC. We believe the key competitors for FOTIVDA in relapsed or refractory RCC include the following FDA-approved treatments: Cabometyx (cabozantinib), marketed by Exelixis, Inc., or Exelixis; Afinitor (everolimus), marketed by Novartis International Pharmaceutical, Ltd., or Novartis; Inlyta (axitinib), marketed by Pfizer Inc., or Pfizer; Opdivo (nivolumab), marketed by BMS; Nexavar (sorafenib), marketed by Bayer Healthcare AG, or Bayer; Novartis' Votrient (pazopanib); Pfizer's Sutent (sunitinib); and Pfizer's Torisel (temsirolimus), all as single-agent therapies; along with the combination of Lenvima (lenvatinib), marketed by Eisai Co., Ltd., or Eisai, and Novartis' Afinitor (everolimus). Additionally, there are a number of therapies in development for relapsed or refractory RCC, including Merck & Co., Inc., or Merck's, belzutifan as a single agent, the combination of Eisai's Lenvima (lenvatinib) and Merck's belzutifan and the combination of Roche Holding Ltd., or Roche's, Tecentriq (atezolizumab) and Exelixis' Cabometyx (cabozantinib).

HCC. We believe the key competitors for tivozanib in advanced HCC include the following FDA-approved treatments: Roche's Tecentriq (atezolizumab) and Avastin (bevacizumab) in combination and BMS's Yervoy (ipilimumab) and Opdivo (nivolumab) in combination; as well as Bayer's Nexavar (sorafenib); Bayer's Stivarga (regorafenib); Eisai's Lenvima (lenatinib); Exelixis' Cabometyx (cabozantinib); Cyramza (ramucirumab), marketed by Eli Lilly and Company, or Eli Lilly; BMS's Opdivo (nivolumab); and Merck's Keytruda (pembrolizumab), all as single agents. Additionally, there are a number of therapies in clinical development for advanced HCC and it is difficult to predict which will be the key competitors to tivozanib in this indication.

Ficlatuzumab

We believe the products that currently compete with ficlatuzumab are primarily those that are approved and in development that target the HGF/cMET pathway.

FDA-approved treatments or therapies in clinical development which target the HGF/cMET pathway, though not exclusively, include Pfizer's PF-2341066 (Xalkori, crizotinib), Exelixis' XL-184 (Cometriq/Cabometyx, cabozantinib), Mirati Therapeutics, Inc.'s glesatinib, Incyte Corporation, or Incyte's, and Novartis' INCB-028060, Amgen Inc., or Amgen's, and BioPharma Global, or BioPharma's, AMG-337, Eli Lilly's merestinib (LY2801653), AstraZeneca's and Hutchison MediPharma Limited's savolitinib, Merck KGaA's Tepmetko (tepotinib), AbbVie Inc.'s ABBV-299 and Betta Pharmaceuticals Co., Ltd.'s BPI-9016.

AV-380

In the United States, a significant unmet need exists for patients afflicted with cachexia, as Megace is the only approved agent for the treatment of cachexia. A number of agents with unique mechanisms of action are in various stages of clinical development in cachexia or muscle wasting. We believe the key competitors for our AV-380 program are other companies pursuing the GDF15 pathway for cachexia or as an anti-cancer therapeutic, including NGM Biopharmaceuticals Inc., Pfizer and CatalYm GmbH's clinical GDF15 program focused on immunosuppression.

AV-203

We believe the most direct competitors to our AV-203 program are monoclonal antibodies that specifically target the ErbB3 receptor. The clinical stage agents that are known to target ErbB3 receptors include Daiichi Sankyo, Inc.'s and Amgen Inc.'s patritumab (AMG-888), Elevation Oncology's seribantumab, Merus N.V.'s MCLA-128, AstraZeneca's sapitinib, Celldex Therapeutics Inc.'s CDX-3379, Sihuan Pharmaceutical Holdings Group Ltd.'s pirotinib and Roche's duligotuzumab.

AV-353

Currently, there are no ongoing clinical trials of Notch 3-specific inhibitors, nor any approved Notch 3-specific inhibitors in oncology; however, a number of agents for applications in oncology are being explored which target the Notch 3 receptor and may inhibit other Notch receptors.

Strategic Partnerships and Collaboration Agreements

We have established various strategic partnerships and collaboration agreements with leading pharmaceutical companies for our product candidates and programs in our portfolio. Under each of our strategic partnerships, we are entitled to receive or required to pay upfront, milestone payments and/or royalties.

For information on our collaboration agreements focused solely on the clinical development of FOTIVDA in combination with immune checkpoint inhibitors, see "Part I, Item 1. Business – Our Product Candidates — Tivozanib — Clinical Development of Tivozanib in RCC — RCC PD-1 Phase 1b/2 Combination Trial with OPDIVO® (TiNivo)", "Part I, Item 1. Business – Our Product Candidates — Tivozanib — Clinical Development of Tivozanib in RCC — RCC PD-1 Phase 3 Combination Trial with OPDIVO® (TiNivo-2)", "Part II, Item 9B. Other Information – Bristol- Myers Squibb Company Clinical Trial Collaboration and Supply Agreement" and "Part I, Item 1. Business – Our Product Candidates — Tivozanib — Clinical Development of Tivozanib in HCC — HCC PD-L1 Combination Trial with IMFINZI (DEDUCTIVE)".

Tivozanib

Kyowa Kirin Co. (KKC)

In December 2006, we entered into a license agreement with KKC, or the KKC Agreement, under which we obtained an exclusive, sublicensable license to develop, manufacture and commercialize tivozanib in all territories in the world except for Asia and the Middle East, where KKC retained the rights to tivozanib. Under the KKC Agreement, we obtained exclusive rights to tivozanib in our territory under certain KKC patents, patent applications and know-how for the diagnosis, prevention and treatment of all human diseases and conditions. On August 1, 2019, we entered into an amendment to the KKC Agreement pursuant to which KKC repurchased the non-oncology rights to tivozanib in our territory, excluding the rights we have sublicensed to EUSA under the EUSA Agreement. We have upfront, milestone and royalty payment obligations to KKC under the KKC Agreement, and following the amendment, KKC also has upfront, milestone and royalty payment obligations to us related to non-oncology development by KKC in our territory. Pursuant to the amendment to the KKC Agreement, KKC was required to make a non-refundable upfront payment to us in the amount of $25.0 million that we received in September 2019 and KKC waived a one-time milestone payment of $18.0 million otherwise payable by us upon our obtaining marketing approval for tivozanib in the United States.

If we sublicense any of our rights to tivozanib to a third-party, as we have done with EUSA pursuant to the EUSA Agreement, the sublicense defines the payment obligations of the sublicensee, which may vary from the milestone and royalty payment obligations under our KKC Agreement relating to rights we retain. We are required to pay KKC 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 were not subject to sublicense revenue payments to KKC. For example, if EUSA elects to opt-in to the TIVO-3 trial, the additional research and development reimbursement payment from EUSA of 50% of the total trial costs, up to $20.0 million, would also not be subject to a sublicense revenue payment to KKC, subject to certain limitations. We would, however, owe KKC 30% of other, non-research and development payments we may receive from EUSA pursuant to the EUSA Agreement, including reimbursement approvals for RCC in up to five specified EU countries, marketing approvals for RCC in three specified non-EU licensed territories, EU marketing approval filings and corresponding marketing approvals by the EMA for up to three additional indications beyond RCC, and sales-based milestones and royalties. The $2.0 million milestone payments we earned in each of February 2018, November 2018 and February 2019 upon EUSA's reimbursement approval for FOTIVDA as a first-line treatment for RCC in the United Kingdom, Germany and Spain, respectively, were subject to the 30% KKC sublicense fee, or $0.6 million each.

We are also required to pay tiered royalty payments on net sales we make of FOTIVDA 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 FOTIVDA sales. Our royalty payment obligations in a particular country in our territory begin on the date of the first commercial sale of FOTIVDA in that country, and end on the later of 12 years after the date of the first commercial sale of FOTIVDA in that country or the date of the last to expire of the patents covering tivozanib that have been issued in that country.

Pursuant to the amendment to the KKC Agreement, KKC is also required to make milestone payments to us of up to an aggregate of $390.7 million upon the successful achievement of certain development and sales milestones of tivozanib in non-oncology indications. In August 2020, KKC paid us a $2.8 million development milestone upon acceptance by the Pharmaceuticals and Medical Devices Agency of Japan of KKC's IND for a non-oncology formulation of tivozanib. In September 2020, KKC initiated a phase 1 study of KHK4951, the reformulated tivozanib, in healthy volunteers and patients with Wet AMD. In addition, KKC is required to make tiered royalty payments to us on net sales of tivozanib in non-oncology indications in our territory, which range from high single digit to low double digits as a percentage of net sales. The royalty rate escalates within this range based on increasing tivozanib sales, subject to certain adjustments. KKC's 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 the expiration date of the last valid claim of a patent application or patent owned by KKC covering tivozanib or 10 years after the date of the first commercial sale of tivozanib in non-oncology indications in that country.

If KKC sublicenses any of its non-oncology rights to tivozanib to a third-party, KKC is required to pay us a percentage of amounts received from the respective sublicensees related to our territory, including upfront license fees, milestone payments and royalties, but excluding amounts received in respect of research and development reimbursement payments or equity investments, subject to certain limitations.

We and KKC 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 KKC Agreement, as related to oncology development. Under the KKC Agreement, we are obligated to use commercially reasonable efforts to develop and commercialize tivozanib in our territory.

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

EUSA

In December 2015, we entered into a license agreement with EUSA, or the EUSA Agreement, 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 and Australasia for all diseases and conditions in humans, excluding non-oncologic diseases or conditions of the eye. 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.

EUSA made research and development reimbursement payments to us of $2.5 million upon the execution of the EUSA Agreement in 2015, and $4.0 million in September 2017 upon its receipt of marketing authorization from the European Commission in August 2017 for FOTIVDA (tivozanib) 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 a research and development reimbursement payment from EUSA of $20 million of our total TIVO-3 trial costs if EUSA chooses to opt-in to use the TIVO-3 dataset to seek an expanded RCC indication in the EU, or for other regulatory or commercialization purposes. The leadership of EUSA has informed us that it is interested in exercising its opt-in right with respect to our TIVO-3 data and seeking an expanded label under the EUSA Agreement, but has requested to more closely align the payment stream under which it would satisfy its $20 million reimbursement obligation with the occurrence of the incremental value creation for EUSA. We are currently in negotiations with EUSA regarding the structuring of this payment stream. We cannot be certain that we will arrive at mutually acceptable terms, or that EUSA will ultimately exercise the opt-in.

We are entitled to receive milestone payments of $2.0 million per country upon reimbursement approval, if any, for RCC in each of countries in the EU5 and, to date, we have received payments upon reimbursement approval for RCC in the UK (February 2018), Germany (November 2018) and Spain (February 2019). We are also entitled to receive $2.0 million for the grant of marketing approval for RCC, if any, in three of the licensed countries outside of the EU, as mutually agreed by the parties, the first two of which were obtained in New Zealand in July 2019 and South Africa in September 2020.

We are also eligible to receive a payment of $2.0 million per indication 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 FOTIVDA (tivozanib) with the initiation of product sales in Germany. EUSA has received reimbursement approval for and commercially launched FOTIVDA in Germany, the United Kingdom, and Spain as well as in additional non-EU5 countries.

The research and development reimbursement payments under the EUSA Agreement are not subject to the 30% sublicensing payment payable to KKC, subject to certain limitations. We would, however, owe KKC 30% of other, non-research and development payments we may receive from EUSA pursuant to the EUSA Agreement, including any reimbursement approvals for RCC in the EU5, marketing approvals for RCC in three specified non-EU licensed territories, EU marketing approval filings and corresponding marketing approvals by the EMA for up to three additional indications beyond RCC, and sales-based milestones and royalties, as set forth above. The $2.0 million milestone payments we earned in each of February 2018, November 2018 and February 2019 upon EUSA's reimbursement approval for FOTIVDA in the United Kingdom, Germany and Spain, respectively, were subject to the 30% KKC sublicense fee, or $0.6 million, each.

The term of the EUSA Agreement continues on a product-by-product and country-by-country basis until the last 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 tenth anniversary of the effective date. Either party may terminate the EUSA 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 EUSA Agreement, and (b) ninety (90) days in the case of any other material breach. EUSA may terminate the EUSA Agreement at any time upon one hundred eighty (180) days' prior written notice. In addition, we may terminate the EUSA Agreement upon thirty (30) days' prior written notice if EUSA challenges any of the patent rights licensed under the EUSA Agreement.

EUSA has reported to us that to date, it has not experienced a decrease in sales trends or interruptions in supply or distribution of FOTIVDA during the COVID-19 pandemic; however, the future impact of the COVID-19 pandemic on FOTIVDA sales is difficult to predict.

Ficlatuzumab

Biodesix

In April 2014, we entered into a worldwide co-development and collaboration agreement, or the Biodesix Agreement, with Biodesix to develop and commercialize ficlatuzumab, our potent humanized IgG1 monoclonal antibody that targets HGF. In September 2020, we regained full global rights to ficlatuzumab, effective December 2, 2020, when Biodesix exercised its "Opt-Out" rights (as defined below) under the Biodesix Agreement.

The Biodesix Agreement generally provided for each party to contribute 50% of all clinical, regulatory, manufacturing and other costs to develop ficlatuzumab and to share equally in any future revenue from development or commercialization. Under the Biodesix Agreement, prior to the first commercial sale of ficlatuzumab, each party had the right to elect to discontinue its funding obligation for further development or commercialization efforts with respect to ficlatuzumab in exchange for reduced economics in the program, which is referred to as an "Opt-Out." Pursuant to the terms of the Biodesix Agreement, as a result of Biodesix's election to Opt-Out, Biodesix will (i) continue to be responsible for reimbursement of development costs with respect to the ongoing phase 2 investigator-sponsored clinical trial of ficlatuzumab in combination with ERBITUX® (cetuximab) in HNSCC, (ii) cease to be entitled to 50% sharing of profits resulting from commercialization of ficlatuzumab, (iii) be entitled to a low double digit royalty on future product sales and 25% of future licensing revenue (excluding contributions to research and development expenses), less approximately $2.5 million that Biodesix would be required to pay to us pursuant to the October 2016 amendment to the Biodesix Agreement and (iv) remain responsible for development obligations under the Biodesix Agreement with respect to VeriStrat®. We and Biodesix also remain obligated to negotiate a commercialization agreement to delineate our respective rights and obligations in the event of any commercialization of VeriStrat® with ficlatuzumab. As a result of Biodesix's decision to Opt-Out, we now have worldwide licensing

rights and sole decision-making authority with respect to further development and commercialization of ficlatuzumab. The payment obligations between the parties under the Biodesix Agreement are in effect until completion of the Phase 2 HNSCC Trial.

AV-380

St. Vincent's Hospital

In July 2012, we entered into a license agreement with St. Vincent's, or the St. Vincent's Agreement, under which we obtained an exclusive, worldwide sublicensable right 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 St. Vincent's Agreement, we have non-exclusive rights to certain related diagnostic products and research tools and also 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. We are obligated to use diligent efforts to conduct research and clinical development and commercially launch at least one licensed therapeutic product.

In 2012, we paid St. Vincent's an upfront license fee of $0.7 million. In August 2015, in connection with the execution of the license agreement with Novartis, or the Novartis Agreement, we amended and restated the St. Vincent's Agreement and paid St. Vincent's an additional upfront fee of $1.5 million. As of December 31, 2019, we are required to make future milestone payments, up to an aggregate total of $14.4 million, upon the earlier of the 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 milestone payments made after we grant any sublicense, depending on the sublicensed territory.

In February 2017, Novartis agreed to pay $1.8 million out of its then future payment obligations to us under the former Novartis Agreement. These funds were used to satisfy a $1.8 million time-based milestone obligation that we owed to St. Vincent's in March 2017. In December 2018, we entered into a new agreement with Novartis to further establish and clarify the terms on which the AV-380 program was to be returned to us, or the AV-380 Transfer Agreement. The $2.3 million payment we received from Novartis in January 2019 pursuant to the AV-380 Transfer Agreement was used to cover a $2.3 million time-based milestone obligation that became due to St. Vincent's in January 2019. See *"Part I, Item 1. Business – Our Product Candidates – AV-380"* and Note 4 *"Collaborations and License Agreements – Out-License Agreements – Novartis"*, to our consolidated financial statements included elsewhere in this Annual Report on Form 10-K regarding details of the AV-380 Transfer Agreement.

In addition, we will be required to pay St. Vincent's tiered royalty payments equal to a low-single-digit percentage of any net sales we or our sublicensees make from licensed therapeutic products. The royalty rate escalates within the low-single-digit range during each calendar year based on increasing licensed therapeutic product sales during such calendar year. 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 St. Vincent's 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 St. Vincent's Agreement earlier. We have the right to terminate the St. Vincent's 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 St. Vincent's Agreement.

AV-203

CANbridge

In March 2016, we entered into the CANbridge Agreement under which we granted CANbridge the exclusive right to develop, manufacture and commercialize AV-203, a potent humanized IgG1 monoclonal antibody that targets ErbB3 (also known as HER3), for the diagnosis, treatment and prevention of disease in all countries outside of North America.

Upon entry into the CANbridge Agreement, CANbridge paid us an upfront fee of $1.0 million in April 2016, net of foreign withholding taxes. CANbridge also reimbursed us for $1.0 million in certain AV-203 manufacturing costs that we previously incurred. CANbridge paid this manufacturing reimbursement in two installments of $0.5 million each, one in March 2017 and one in September 2017, net of foreign withholding taxes, following CANbridge's validation of the manufacturing process for real drug substance. In December 2017, CANbridge filed an IND application with the NMPA for a clinical study of AV-203 in ESCC. In August 2018, CANbridge obtained regulatory approval of its IND application from the NMPA for a clinical study of AV-203 in ESCC and, accordingly, we earned a $2.0 million development and regulatory milestone payment that was received from CANbridge in August 2018.

A percentage of any milestone and royalty payments received by us under the CANbridge Agreement, or under future partnership agreements related to the AV-203 program, excluding upfront and reimbursement payments, are due to Biogen Idec International GmbH, or Biogen, as a sublicensing fee under our option and license agreement with Biogen dated March 18, 2009, as amended. The $2.0 million development and regulatory milestone we earned in August 2018 for regulatory approval from the NMPA of an IND application for a clinical study of AV-203 in ESCC was subject to this sublicense fee, or $0.7 million, which was paid to Biogen in October 2018.

In March 2021, CANbridge exercised its right to terminate for convenience the CANbridge Agreement. Under the terms of the CANbridge Agreement, we expect the transfer of the AV-203 program to be complete in September 2021 and, at that time, we will regain worldwide rights to the AV-203 program.

Biogen Idec International GmbH

In March 2009, we entered into an exclusive option and license agreement with Biogen 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, 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 the CANbridge Agreement. We are obligated to pay Biogen a percentage of milestone payments we receive under a partnership agreement related to the AV-203 program and single-digit royalty payments on net sales related to the sale of AV-203, up to a cumulative maximum amount of $50.0 million.

The $2.0 million development and regulatory milestone we earned in August 2018 in connection with CANbridge's regulatory approval from the NMPA of an IND application for a clinical study of AV-203 in ESCC was subject to this sublicense fee, or $0.7 million, which was paid to Biogen in October 2018.

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.

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 a 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 term extensions 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. We expect to apply for patent term extensions on patents covering tivozanib and on any patents covering our product candidates that may obtain FDA approval in the future.

Tivozanib

With respect to tivozanib, we have exclusively licensed from KKC its patents that cover the molecule and its therapeutic use for the diagnosis, prevention and treatment of any and all oncologic diseases and conditions in humans and a crystal form of the molecule. As discussed in "—Strategic Partnerships—Tivozanib–Kyowa Kirin Co. (KKC)" above, pursuant to the amendment to the KKC Agreement in August 2019, KKC repurchased the non-oncology rights of tivozanib in our licensed territories, excluding the rights which are currently sublicensed to EUSA.

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

- U.S.: 2 granted patents with expirations ranging from 2022 to 2023
- Europe: 2 granted patents with expirations ranging from 2022 to 2023
- Canada: 1 granted patent expiring in 2022
- Australia: 1 granted patent expiring in 2022

With respect to the U.S. patents, the first patent covers the tivozanib molecule and its therapeutic use and is expected to expire in 2022. The second patent covers a crystalline form of tivozanib that is the active pharmaceutical ingredient in our tivozanib product candidate and is expected to expire in 2023. 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 Hatch-Waxman Act. Although we plan to apply for patent term extensions on each patent, only one patent may be extended, and, when appropriate, we will have to elect which patent is to be extended. If a five-year extension were to be granted, if applied to the first patent, the term could be extended to April 2027, and if applied to the second patent, the term could be extended to November 2028.

With respect to the European patents, Supplementary Protection Certificates, or SPCs, have been granted for the European patent covering the tivozanib molecule in Belgium, Finland, France, Germany, Italy, the Netherlands, Norway, Poland, Portugal, Spain and Sweden, extending the term of the patents in each of these countries up to April 2027. SPC applications are pending in Denmark and Great Britain for the corresponding patents 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. An SPC has been granted for the patent covering the crystalline form of tivozanib in Ireland extending the term of that patent to October 2028.

Additionally, we have filed an international (PCT) patent application directed to our clinical protocol for using tivozanib to treat refractory cancers, including, following therapy with checkpoint inhibitors. If nationalized, we expect that a patent granted on a patent application in this family would expire in 2039.

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-380 Platform

With respect to our anti-GDF15 platform, including AV-380, 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, which is expected to expire in 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: 2 granted patents expiring in 2025

- Japan: 2 granted patents expiring in 2025
- Canada: 1 granted patent expiring in 2025
- Australia: 1 granted patent expiring in 2025

Additionally, we own three 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-GDF15 antibody. These patent applications, if granted, would be expected to expire in 2035.

With respect to our anti-GDF15 platform, we have:

- U.S.: 3 granted patents, and 4 pending patent applications, if granted, with expirations ranging from 2033 to 2035
- Europe: 1 granted patent, and 4 pending patent applications, if granted, with expirations ranging from 2033 to 2035
- Japan: 2 granted patents, and 4 pending patent applications, if granted, with expirations ranging from 2033 to 2035
- Canada: 2 pending patent applications, if granted, with expirations ranging from 2033 to 2035
- Australia: 1 granted patent, and 1 pending patent application, if granted, with expirations ranging from 2033 to 2035

AV-203 Platform

With respect to our anti-ErbB3 platform, including AV-203, we have five issued U.S. patents and one pending U.S. patent application 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.: 5 granted patents, and 1 pending patent application, 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: 3 granted patents with expirations ranging from 2031 to 2032
- Canada: 1 granted patent expiring in 2031
- Australia: 2 granted patents, and 1 pending patent application, if granted, with expirations ranging from 2031 to 2032

AV-353 Platform

With respect to our AV-353 platform, we own two issued U.S. patents and two pending U.S. patent applications 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 two issued U.S. patents and the two non-provisional U.S. patent applications, if granted, would be expected to have expirations ranging from 2033 to 2037.

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

- U.S.: 2 granted patents expiring in 2033, and 2 pending patent applications, if granted, with expirations ranging from 2033 to 2037
- Europe: 1 granted patent expiring in 2033, and 1 pending patent application, if granted, expiring in 2037

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 ficlatuzumab, we are aware of one United States patent and its foreign counterparts that contain broad claims related to anti-HGF antibodies having certain binding properties and their use. In the event that the owner 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 United States and other jurisdictions where available and when appropriate. We have filed applications and obtained registrations for several trademarks intended for 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 EU registrations for a logo containing FOTIVDA in combination with a flame design. We own U.S. registrations for AVEO and AVEO (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 and rely on third parties for the manufacture of our product candidates and intend to do so in the future for both clinical and 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 third-party contract manufacturers, we have personnel with extensive manufacturing experience to oversee the relationships with our contract manufacturers. All manufacturing occurs at facilities that comply with FDA requirements and the requirements of regulatory agencies from the other jurisdictions where we have obtained approval.

One of our contract manufacturers has manufactured what we believe to be sufficient quantities of tivozanib drug product (capsules) to support our ongoing and planned clinical trials and commercial launch. A separate contract manufacturer, using our proprietary manufacturing process, has manufactured what we believe to be sufficient lots of drug substance. This drug substance may be used to manufacture tivozanib drug product (capsules) for any future clinical and commercial needs.

In preparation for the commercial launch of FOTIVDA in the United States, we engaged a separate contract manufacturer to bottle, package, label and serialize commercial supply of FOTIVDA on an as-needed basis. We rely on a separate third-party to distribute commercial supply of FOTIVDA in the United States.

We have engaged a separate third-party contract manufacturer to initiate clinical manufacture of ficlatuzumab to supply a potential phase 3 clinical trial in HNSCC, as well as to enable additional potential development in pancreatic cancer and AML. We currently have sufficient clinical trial supply for AV-380 to support our phase 1 clinical trial. The same contract manufacturer we engaged to initiate clinical manufacturing of ficlatuzumab will be manufacturing any future clinical supply needs for AV-380.

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 contract manufacturers 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 EU, extensively regulate, among other things, the research, development, testing, manufacture, quality control, approval, packaging, storage, recordkeeping, labeling, advertising, promotion, distribution, marketing, sales, pricing, reimbursement, 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 approves and regulates drugs under the Federal Food, Drug, and Cosmetic Act, or FDCA, and related regulations. Biological products are licensed for marketing under the Public Health Service Act, or PHSA, and subject to regulation under the FDCA and related regulations. An applicant seeking approval to market and distribute a new drug or biological product in the United States must typically secure the following:

- completion of preclinical laboratory tests 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 GCPs, to establish the safety and efficacy of the proposed drug product for each proposed indication;
- 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 of the request for approval by an FDA advisory committee, where appropriate or if applicable;
- 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,to assure the product's identity, strength, quality and purity;
- 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. 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 a request for FDA authorization to administer an investigational product candidate 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. Clinical holds are imposed by the FDA whenever there is concern for patient safety and may be a result of new data, findings, or developments in clinical, nonclinical, and/or chemistry, manufacturing, and controls (CMC). 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. 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. 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.

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.

Expanded Access to an Investigational Drug for Treatment Use

Expanded access, sometimes called "compassionate use," is the use of investigational new drug products outside of clinical trials to treat patients with serious or immediately life-threatening diseases or conditions when there are no comparable or satisfactory alternative treatment options. FDA regulations allow access to investigational drugs under an IND by the company or the treating physician for treatment purposes on a case-by-case basis for: individual patients (single-patient IND applications for treatment in emergency settings and non-emergency settings); intermediate-size patient populations; and larger populations for use of the drug under a treatment protocol or Treatment IND Application.

When considering an IND application for expanded access to an investigational product with the purpose of treating a patient or a group of patients, the sponsor and treating physicians or investigators will determine suitability when all of the following criteria apply: patient(s) have a serious or immediately life-threatening disease or condition, and there is no comparable or satisfactory alternative therapy to diagnose, monitor, or treat the disease or condition; the potential patient benefit justifies the potential risks of the treatment and the potential risks are not unreasonable in the context or condition to be treated; and the expanded use of the investigational drug for the requested treatment will not interfere initiation, conduct, or completion of clinical investigations that could support marketing approval of the product or otherwise compromise the potential development of the product.

On December 13, 2016, the 21st Century Cures Act, or the Cures Act, established (and the 2017 Food and Drug Administration Reauthorization Act later amended) a requirement that sponsors of one or more investigational drugs for the treatment of a serious disease(s) or condition(s) make publicly available their policy for evaluating and responding to requests for expanded access for individual patients.

In addition, on May 30, 2018, the Right to Try Act was signed into law. The law, among other things, provides a federal framework for certain patients to access certain investigational new drug products that have completed a phase 1 clinical trial and that are undergoing investigation for FDA approval. Under certain circumstances, eligible patients can seek treatment without enrolling in clinical trials and without obtaining FDA permission under the FDA expanded access program. There is no obligation for a drug manufacturer to make its drug products available to eligible patients as a result of the Right to Try Act, but the manufacturer must develop an internal policy and respond to patient requests according to that policy.

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.
- 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. The FDA will typically inspect one or more clinical sites to assure compliance with GCP and the integrity of the clinical data submitted.

Concurrent with clinical trials, companies often complete additional animal studies and must also develop additional information about the chemistry and physical characteristics of the candidate products well as finalize a process for manufacturing the product in commercial quantities in accordance with cGMP requirements. The manufacturing process must be capable of consistently producing quality batches of the drug candidate and, among other things, must develop methods for testing the identity, strength, quality, purity and potency of the final drug. Additionally, appropriate packaging must be selected and tested and stability studies must be conducted to demonstrate that the drug candidate does not undergo unacceptable deterioration over its shelf life.

Finally, under the Pediatric Research Equity Act of 2003, an application 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.

Submission and 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 application is the 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 product candidate must be the subject of an approved NDA or BLA before it may be commercialized in the United States. Under federal law, the submission of most applications is subject to an application user fee, which for federal fiscal year 2021 is $2,875,842 for an application requiring clinical data. The sponsor of an approved application is also subject to an annual program fee, which for fiscal year 2021 is $336,432. 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. If an application is withdrawn prior to the FDA acceptance for filing, 75% of these fees may be refunded to the sponsor. If an application is withdrawn after filing, a lower portion of these fees may be refunded in certain circumstances.

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. 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. 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 scheduling and execution of such pre-approval inspections may be impacted or delayed due to the COVID-19 pandemic. 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 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.

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.

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.

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, or ACA, which was signed into law on March 23, 2010, included a subtitle called the Biologics Price Competition and Innovation Act of 2009 or BPCIA. The BPCIA established a regulatory scheme authorizing the FDA to approve biosimilars and interchangeable biosimilars. As of January 1, 2021, the FDA has approved 29 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 BPCIA, a manufacturer may submit an application for licensure of a biologic product that is "biosimilar to" or "interchangeable with" a previously approved biological product or "reference product." In order for the FDA to approve a biosimilar product, it must find that there are no clinically meaningful differences between the reference product and proposed biosimilar product in terms of safety, purity and potency. For the FDA to approve a biosimilar product as interchangeable with a reference product, the agency must find that the biosimilar product can be expected to produce the same clinical results as the reference product, and (for products administered multiple times) that the biologic and the reference biologic may be switched after one has been previously administered without increasing safety risks or risks of diminished efficacy relative to exclusive use of the reference biologic.

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

Orphan Drug Designation and Exclusivity

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

If a product with orphan designation receives the first FDA approval for the disease or condition for which it has such designation or for a select indication or use within the rare disease or condition for which it was designated, the product generally will receive orphan drug exclusivity. Orphan drug exclusivity means that the FDA may not approve another sponsor's marketing application for the same drug for the same indication for seven years, except in certain limited circumstances. Orphan exclusivity does not block the approval of a different product for the same rare disease or condition, nor does it block the approval of the same product for different indications. If a drug or biologic designated as an orphan drug ultimately receives marketing approval for an indication broader than what was designated in its orphan drug application, it may not be entitled to exclusivity. Orphan exclusivity will not bar

approval of another product under certain circumstances, including if a subsequent product with the same drug or biologic for the same indication is shown to be clinically superior to the approved product on the basis of greater efficacy or safety, or providing a major contribution to patient care, or if the company with orphan drug exclusivity is not able to meet market demand.

Pediatric Exclusivity

Pediatric exclusivity is another type of non-patent marketing exclusivity in the United States and, if granted, provides for the attachment of an additional six months of marketing protection to the term of any existing regulatory exclusivity, including the non-patent and orphan exclusivity. This six-month exclusivity may be granted if an NDA or BLA sponsor submits pediatric data that fairly respond to a written request from the FDA for such data. The data do not need to show the product to be effective in the pediatric population studied; rather, if the clinical trial is deemed to fairly respond to the FDA's request, the additional protection is granted. If reports of requested pediatric studies are submitted to and accepted by the FDA within the statutory time limits, whatever statutory or regulatory periods of exclusivity or patent protection cover the product are extended by six months. This is not a patent term extension, but it effectively extends the regulatory period during which the FDA cannot approve another application.

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 the FDA determines that a companion diagnostic device is essential to the safe and effective use of a novel therapeutic product or indication, the 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.

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. For federal fiscal year 2021, the standard fee is $365,657 and the small business fee is $91,414.

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.

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 EU has been implemented through national legislation of the member states. Under this system, an applicant must obtain approval from the competent national authority of an EU 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, or 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. 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 Regulation was published on June 16, 2014 but has not yet become effective. In January 2020, the website of the European Commission reported that the implementation of the Clinical Trials Regulation was dependent on the development of a fully functional clinical trials portal and database, which would be confirmed by an independent audit, and that the new legislation would come into effect six months after the European Commission publishes a notice of this confirmation. The website indicated that the audit was expected to commence in December 2020. In late 2020, the EMA indicated that it plans to focus on the findings of a system audit; improving the usability, quality and stability of the clinical trial information system; and knowledge transfer to prepare users and their organizations for the new clinical trial system. The EMA has indicated that the system will go live in December 2021.

As in the United States, parties conducting certain clinical trials must post clinical trial information in the EU at the EudraCT website: https://eudract.ema.europa.eu.

PRIME Designation in the EU

In March 2016, the 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 CHMP or Committee for Advanced Therapies, or CAT, are appointed early in PRIME scheme facilitating increased understanding of the product at EMA's Committee level

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.

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 EU, 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 EU 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.

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.

Regulatory Requirements After Marketing Authorization

Following marketing authorization of a medicinal product in the EU, the holder of the authorization is required to comply with a range of requirements applicable to the manufacturing, marketing, promotion and sale of medicinal products. These include compliance with the EU's stringent pharmacovigilance or safety reporting, as well as rules potentially requiring post-authorization studies and additional monitoring obligations. In addition, the manufacturing of authorized medicinal products, for which a separate manufacturer's license is mandatory, must also be conducted in strict compliance with the applicable EU laws, regulations and guidance, including Directive 2001/83/EC, Directive 2003/94/EC, Regulation (EC) No 726/2004 and the European Commission Guidelines for Good Manufacturing Practice. These requirements include compliance with EU cGMP standards when manufacturing medicinal products and active pharmaceutical ingredients, including the manufacture of active pharmaceutical ingredients outside of the EU with the intention to import the active pharmaceutical ingredients into the EU. Finally, the marketing and promotion of authorized drugs, including industry-sponsored continuing medical education and advertising directed toward the prescribers of drugs and/or the general public, are strictly regulated in the EU notably under Directive 2001/83EC, as amended, and EU Member State laws. Direct-to-consumer advertising of prescription medicines is prohibited across the EU.

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 EU, commonly referred to as Brexit. Following protracted negotiations, the United Kingdom left the EU on January 31, 2020. Under the withdrawal agreement, there is a transitional period until December 31, 2020 (extendable by up to two years). On December 24, 2020, the United Kingdom and the EU entered into a Trade and Cooperation Agreement. The agreement sets out certain procedures for approval and recognition of medical products in each jurisdiction. 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 EU directives and regulations, Brexit could materially impact the future regulatory regime that applies to products and the approval of product candidates in the United Kingdom.

Furthermore, while the Data Protection Act of 2018 in the United Kingdom that "implements" and complements the European Union's General Data Protection Regulation, or GDPR, has achieved Royal Assent on May 23, 2018 and is now effective in the United Kingdom, it is still unclear whether transfer of data from the European Economic Area, or EEA, to the United Kingdom will remain lawful under GDPR. The Trade and Cooperation Agreement provides for a transitional period during which the United Kingdom will be treated like an EU member state in relation to processing and transfers of personal data for four months from January 1, 2021. This may be extended by two further months. After such period, the United Kingdom will be a "third country" under the GDPR unless the European Commission adopts an adequacy decision in respect of transfers of personal data to the United Kingdom. The United Kingdom has already determined that it considers all of the EU 27 and EEA member states to be adequate for the purposes of data protection, ensuring that data flows from the United Kingdom to the EU/EEA remain unaffected.

General Data Protection Regulation

The collection, use, disclosure, transfer, or other processing of personal data regarding individuals in the EU, including personal health data, is subject to the EU General Data Protection Regulation, or GDPR, which became effective on May 25, 2018. The GDPR is wide-ranging in scope and imposes numerous requirements on companies that process personal data, including requirements relating to processing health and other sensitive data, obtaining consent of the individuals to whom the personal data relates, providing information to individuals regarding data processing activities, implementing safeguards to protect the security and confidentiality of personal data, providing notification of data breaches, and taking certain measures when engaging third-party processors. The GDPR also imposes strict rules on the transfer of personal data to countries outside the EU, including the United States, and permits data protection authorities to impose large penalties for violations of the GDPR, including potential fines of up to €20 million or 4% of annual global revenues, whichever is greater. The GDPR also confers a private right of action on data subjects and consumer associations to lodge complaints with supervisory authorities, seek judicial remedies, and obtain compensation for damages resulting from violations of the GDPR. Compliance with the GDPR will be a rigorous and time-intensive process that may increase the cost of doing business or require companies to change their business practices to ensure full compliance.

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.

In the EU, 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 EU 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. EU 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 EU 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 EU. 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 EU 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 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, or the FCA, 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 be made or used a false record or statement to avoid, decrease or conceal an obligation to pay money to the federal government;

- Foreign Corrupt Practices Act, or FCPA, which prohibits companies and their intermediaries from making, or offering or promising to make improper payments to non-U.S. officials for the purpose of obtaining or retaining business or otherwise seeking favorable treatment;

- 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 ACA, as amended by the Health Care Education Reconciliation 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.

Further, 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.

Other legislative changes have been proposed and adopted in the United States since the ACA was enacted. 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.

Moreover, since enactment of the ACA, there have been, and continue to be, 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, or the TCJA, which was signed by President Trump 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, became effective in 2019. The Trump Administration also took executive actions to undermine or delay implementation of the ACA. Since January 2017, President Trump has signed two Executive Orders designed to delay the implementation of certain provisions of the ACA or otherwise circumvent some of the requirements for health insurance mandated by the ACA. One Executive Order directs 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. The second Executive Order terminates the cost-sharing subsidies that reimburse insurers under the ACA.

In addition, on December 14, 2018, a U.S. District Court judge in the Northern District of Texas ruled that the individual mandate portion of the ACA is an essential and inseverable feature of the ACA, and therefore because the mandate was repealed as part of the TCJA, the remaining provisions of the ACA are invalid as well. On November 10, 2020, the U.S. Supreme Court heard oral argument in this case and is expected to issue a ruling sometime this year. Litigation and legislation over the ACA are likely to continue, with unpredictable and uncertain results.

Finally, there have been both federal and state actions 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. For example, the Trump Administration finalized a rulemaking that allows states or certain other non-federal government entities to submit importation program proposals to FDA for review and approval. Applicants would be required to demonstrate their importation plans pose no additional risk to public health and safety and will result in significant cost savings for consumers. At the same time, the FDA issued draft guidance that would allow manufacturers to import their own FDA-approved drugs that are authorized for sale in other countries (multi-market approved products). It remains to be seen whether these Executive Orders and actions will be modified or rescinded by the Biden Administration.

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. We expect that additional state and federal healthcare reform measures will be adopted in the future, any of which could limit the amounts that federal and state governments will pay for healthcare products and services, which could result in reduced demand for our product candidates or additional pricing pressures.

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.

Employees and Human Capital Resources

As of December 31, 2020, we had 49 employees, which increased to 94 as of the date of filing this Annual Report on Form 10-K. Of these employees, approximately half are members of our sales team. Our next largest functions after sales are our technical operations, medical affairs and commercial operations functions. The recent increase in our employee base is primarily related to the building out of our sales, marketing, patient access, medical affairs and product reimbursement teams in preparation for the commercial launch of FOTIVDA in the United States. None of our employees are represented by a labor union or are covered by a collective bargaining agreement, and we consider our relationship with our employees to be good.

Our human capital is essential to fulfilling our commitment to deliver medicines that provide a better life for cancer patients. Our core corporate work values, which are integral to our culture and our recruitment and retention initiatives, include:

- Respect: Trusting, Honest Communication, Collaborative, Considerate, Humility
- Sense of Thoughtful Urgency: Realistic, Disciplined, Quality Driven, Diligent, Dynamic
- Integrity: Ethical, Objective, Data Driven, Patient Focused
- Goal Oriented: Strong Work Ethic, Individual Accountability, Courageous, Perseverance
- Engaging Working Environment: Fun, Diverse, Sense of Community, Flexibility, Developmental

We are committed to creating a culture where our employees are valued. Our board of directors approves corporate goals on an annual basis, which aids in the development of annual individual employee goals. We invest in our human capital through formal and informal development training. We engage an independent compensation consultant to advise on our compensation packages and we believe we provide a comprehensive and competitive total rewards program, which includes perks to enhance employee engagement and well-being. We follow a management by objective format in establishing measurable and relevant goals that tie to the variable compensation components of our total rewards program.

We are committed to creating an environment of diversity and inclusion. We believe that diverse backgrounds and perspectives provide us with better ideas and collaboration across our organization. It is our policy to maintain a work environment free from

discrimination based on race, color, religion, national origin, gender, gender identity, transgender status, sexual orientation, age, physical or mental disability, genetic information, veteran status or marital status.

Information about our Executive Officers

The following table lists the positions, names and ages of our executive officers as of March 15, 2021:

Executive Officers

Michael P. Bailey	55	Chief Executive Officer, President and Director
Michael J. Ferraresso	47	Chief Commercial Officer
Erick J. Lucera	53	Chief Financial Officer
Michael N. Needle	61	Chief Medical Officer

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. Since July 2020, Mr. Bailey has served as a member of the board of directors and member of the audit and compensation committees of IMV Inc. 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.

Michael J. Ferraresso was appointed Chief Commercial Officer in March 2021. Mr. Ferraresso joined our company in December 2017 as Senior Vice President, Business Analytics and Commercial Operations. Prior to joining our company, Mr. Ferraresso served as Vice President, Commercial Operations at Verastem, Inc., a biopharmaceutical company, from January 2017 to November 2017. From August 2013 to January 2017, Mr. Ferraresso served as Vice President, Commercial at Infinity Pharmaceuticals, Inc., a biopharmaceutical company. Prior to his role at Infinity Pharmaceuticals, Inc., Mr. Ferraresso served in sales and commercial operations roles of increasing responsibility at several biotechnology and pharmaceutical companies, including at AMAG Pharmaceuticals, Inc., Critical Therapeutics, Inc., Praecis Inc., Ascent Pediatrics Inc. and Muro Pharmaceutical Inc. Mr. Ferraresso has extensive experience in commercial strategy including partnerships, development, pricing and field deployment models and has launched Oprapred™, Plenaxis™, Zyflo™ and Feraheme™. Mr. Ferraresso holds a B.A. in economics from Assumption College.

Erick J. Lucera was appointed Chief Financial Officer in January 2020. From August 2016 to December 2019, Mr. Lucera served as Chief Financial Officer of Valeritas Holdings, Inc., a commercial-stage medical technology company. From May 2015 to August 2016, Mr. Lucera served as the Chief Financial Officer, Treasurer and Secretary of Viventia Bio Inc., a biotechnology company focused on developing targeted protein therapeutics for the treatment of cancer. From December 2012 to April 2015, Mr. Lucera served as Vice President, Corporate Development at Aratana Therapeutics, Inc., a veterinary biopharmaceutical company. Mr. Lucera also previously served as Vice President, Corporate Development at Sunshine Heart, Inc., a medical device manufacturer, from March 2012 to December 2012. Prior to his role at Sunshine Heart, Mr. Lucera also served as Vice President, Healthcare Analyst at Eaton Vance Management, a global asset management company from 2008 to 2011 and held various positions at Intrepid Capital Partners, Independence Investment Associates, LLC and Price Waterhouse & Co. from 1990 to 2008. Since August 2017, Mr. Lucera has served as a member of the board of directors and chairman of the audit committee of Beyond Air, Inc. Mr. Lucera holds a C.P.H. from Harvard University, an M.S. in finance from Boston College, an MBA from Indiana University, Bloomington, and a B.S. in accounting from the University of Delaware. Mr. Lucera currently holds a CFA designation.

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 B.A. in Physics and received his M.D. from SUNY Downstate Medical Center, in Brooklyn, New York.

Corporate Information

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 30 Winter Street, Boston, Massachusetts, 02108. Our telephone number is (857) 400-0101. Our Internet website is located at www.aveooncology.com.

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 review our electronically filed reports and other information that we file with the SEC on the SEC's web site at www.sec.gov.

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.

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" sub-section of the "Investors" section of our website, which you can access free of charge. 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 each of the sections entitled "Investors" and "Media," as a source of information about us.

References to our website and information found on our website should not be deemed incorporated by reference into this Annual Report on Form 10-K.

Item 1A. Risk Factors

You should carefully consider the risks described below in addition to the other information set forth in this Annual Report on Form 10-K, including the Management's Discussion and Analysis of Financial Condition and Results of Operations section and the consolidated financial statements and related notes. These risks, some of which have occurred and any of which may occur in the future, can have a material adverse effect on our business, financial condition, results of operations or the price of our publicly traded securities. The risks described below are not the only risks we face. Additional risks and uncertainties not currently known to us, or that we currently deem to be immaterial, may occur or become material in the future and adversely affect our business, reputation, financial condition, results of operations or the price of our publicly traded securities. Therefore, historical operating results, financial and business performance, events and trends are often not a reliable indicator of future operating results, financial and business performance, events or trends. If any of the following risks occurs, our business, financial condition, and results of operations and future growth prospects could be materially and adversely affected.

Risks Related to Our Financial Position and Need for Additional Capital

We have incurred significant operating losses since inception and anticipate that we will continue to incur significant operating expenses for the foreseeable future. It is uncertain if we will ever achieve or sustain profitability.

We have a history of incurring operating losses and as of December 31, 2020, we had an accumulated deficit of $621.2 million. To date, we have not commercialized any products nor generated any revenues from the sale of products. Our operating losses have resulted principally from costs incurred in our discovery and development activities. On March 10, 2021, the FDA approved FOTIVDA in the United States for the treatment of adult patients with relapsed or refractory advanced RCC following two or more

prior systemic therapies. We anticipate that we will continue to incur significant operating expenses for the foreseeable future as we commercialize FOTIVDA in the United States and continue our planned development activities for our clinical stage assets. Our future product revenues will depend upon the size of markets in which FOTIVDA, and any future products, have received approval, and our ability to achieve sufficient market acceptance, reimbursement from third-party payers and adequate market share for FOTIVDA and any future products in those markets. The likelihood of our long-term success must be considered in light of the expenses, difficulties and potential delays to be encountered in the development and commercialization of new pharmaceutical products, competitive factors in the marketplace and the complex regulatory environment in which we operate.

If we do not effectively manufacture, market and sell FOTIVDA in the United States and if we do not successfully develop, obtain and maintain regulatory approval for our existing and future pipeline of product candidates and any product candidate for which we may obtain marketing approval in the future, we may never generate sufficient revenues from product sales to support our cost structure in order to attain 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 may require substantial additional funding to advance our pipeline of clinical stage assets, 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 may require substantial additional funding to advance our pipeline of clinical stage assets, and the timing and nature of these activities will be conducted subject to the availability of sufficient financial resources.

We believe that our $61.8 million in cash and cash equivalents as of December 31, 2020, along with proceeds from the $20.0 million drawdown under the 2020 Loan Facility in March 2021 and from warrant exercises to date, together with anticipated partnership cost sharing reimbursements, royalties from EUSA's FOTIVDA sales, product revenues upon the commercial launch of FOTIVDA in the United States and the potential additional $10.0 million in credit under the 2021 Loan Amendment as described below in "Part II, Item 7. Management's Discussion and Analysis of Financial Condition and Results of Operations — Liquidity and Capital Resources — Hercules Loan Facility" would allow us to fund our planned operations into 2022.

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:

- the cost of commercialization activities of FOTIVDA in the United States and any of our product candidates that may be approved for sale, including marketing, sales and distribution costs;
- the cost of manufacturing FOTIVDA in the United States, our product candidates and any additional products we may successfully commercialize;
- 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, completing our clinical trials and 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, or under any other agreements with third parties;
- the cost and outcome of any legal actions against us;

- the timing, receipt and amount of sales of, or royalties on, tivozanib and our future products, if any;
- general economic, industry and market conditions; and
- the impact of COVID-19 on our operations, business and prospects.

We may require substantial additional funding to advance our pipeline of clinical stage assets. 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. For example, we may never achieve the milestones specified in the Loan Agreement that would allow us to access the remaining $10.0 million in available credit. 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 product 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 funding to advance our pipeline of clinical stage assets, whether on terms that are acceptable to us, or at all, or we were to default under the Loan Agreement and Hercules accelerates the then remaining principal payments and fees due under the Loan Agreement, 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.

Failure to comply with the covenants or payment obligations under the Loan Agreement could result in an event of default, which could materially and adversely affect our business and our financial condition.

The Loan Agreement includes certain financial and operational covenants and provide for certain occurrences that constitute events of default. Certain of those covenants may be out of our control, such as failure to achieve net product revenue at a certain percentage of projected net product revenue. Potential events of default also include circumstances occurring that have a material adverse effect on our business, our insolvency or bankruptcy, or default on our other obligations or agreements. If we fail to make payments when due, breach any operational covenant or have any event of default, Hercules could require us to immediately repay all outstanding principal and accrued interest on the loan, plus a prepayment charge, which could have a material adverse effect on our business and financial condition.

We have only recently transitioned from a development stage biopharmaceutical company to a commercial and clinical development stage biopharmaceutical 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 marketing approvals for FOTIVDA received by our partner EUSA and the FDA marketing approval for FOTIVDA received in the United States in March 2021, all of our product candidates are in the development stage. We have not yet demonstrated our ability to 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. Consequently, any predictions you make about our future success or viability may not be as accurate as they could be if we had more experience commercializing our product candidates. In addition, as a newly commercial stage business, we may encounter unforeseen expenses, difficulties, complications, delays and other known and unknown factors. To be profitable, we will need to successfully 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 Development and Commercialization of Our Product Candidates

In the near term, we are substantially dependent on the success of FOTIVDA (tivozanib). If we are unable to successfully commercialize FOTIVDA or maintain marketing approval for FOTIVDA in its approved indication, or if we are unable to complete the clinical development of tivozanib and obtain marketing approval for tivozanib in other indications, either alone or with our collaborators, or if we experience significant delays in doing so, our business could be substantially harmed.

Our prospects are substantially dependent on our ability to successfully commercialize FOTIVDA in the United States and maintain marketing approval for FOTIVDA in the United States, or, through EUSA, in those countries outside the United States where FOTIVDA is currently approved. We are also dependent on the success of tivozanib in clinical development and our ability to obtain marketing approval for tivozanib in one or more other indications.

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

- our ability to secure the substantial additional capital required to complete clinical trials of tivozanib, including the DEDUCTIVE trial and the TiNivo-2 trial;
- our ability to fund the activities necessary to successfully commercially launch FOTIVDA in the United States;
- commercial acceptance by patients, the medical community and third-party payors;
- successful design, 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 such as the FDA;
- the performance of the contract research organizations, or CROs, we have hired to manage our clinical studies, as well as that of our collaborators and other 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 KKC;
- protection of our rights in our intellectual property portfolio, including our ability to maintain our license agreement with KKC;
- a continued acceptable safety profile following any marketing approval; and
- our ability to compete with other therapies.

Many of these factors are beyond our control. If we are unable to successfully commercialize FOTIVDA in the United States or to develop or receive marketing approval for tivozanib in other indications, 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.

FOTIVDA, or any one of our product candidates that may receive marketing approval in the future, 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 and the market opportunity for FOTIVDA or any one of our product candidates may be smaller than our estimates.

We have never commercialized a product. Despite the recent FDA marketing approval of FOTIVDA in the United States, FOTIVDA, or any one of our product candidates that may be approved in the future by the appropriate regulatory authorities for marketing and sale, 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. There are already a number of therapies on the market competitive 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. In light of the COVID-19 pandemic, we designed our strategic commercial approach for FOTIVDA to be flexible by building remote as well as in-person customer engagement capabilities in preparation for commercialization. However, it is uncertain whether obstacles and changes to standard sales and marketing practices resulting from the COVID-19 pandemic, including the shift from in-person to telephonic and virtual interactions with healthcare professionals, could negatively impact our commercialization efforts.

If FOTIVDA, or any of our product candidates that may be approved for marketing and sale in the future, 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 FOTIVDA, or any of our product candidates that may be approved for marketing and sale in the future, 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 and success of us as compared with our competitors;
- the prevalence and severity of any side effects;
- how the product is positioned in physician treatment guidelines and pathways;
- 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 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.

In addition, the potential market opportunities for FOTIVDA and our product candidates are difficult to estimate precisely. Our estimates of the potential market opportunities are predicated on many assumptions, including industry knowledge and publications, third-party research reports and other surveys. While we believe that our internal assumptions are reasonable, these assumptions involve the exercise of significant judgment on the part of our management, are inherently uncertain and the reasonableness of these assumptions has not been assessed by an independent source. If any of the assumptions proves to be inaccurate, the actual markets for our product candidate could be smaller than our estimates of the potential market opportunities.

We depend heavily on the success of our product, FOTIVDA, and on our clinical stage assets, including tivozanib (in other indications), ficlatuzumab and AV-380. Preclinical studies and clinical trials of our product candidates may not be successful. If we are unable to complete the clinical development of, obtain marketing approval for or successfully commercialize our product candidates, either alone or with a collaborator, or if we experience significant delays in doing so, our business will be materially harmed.

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, can take many years to complete and is inherently uncertain as to outcome. We cannot guarantee that any clinical trials will be conducted as planned or completed on schedule, if at all, particularly given that many of our clinical trial sites are research hospitals that have imposed restrictions on entry and other activity as a result of the COVID-19 pandemic. The preclinical and clinical development of our product candidates is susceptible to the risk of failure inherent at any stage of product development. Moreover, we, or any collaborators, may experience any of a number of possible unforeseen adverse events in connection with clinical trials, many of which are beyond our control, including:

- we, or our collaborators, may fail to demonstrate efficacy in a clinical trial or across a broad population of patients;
- it is possible that even if one or more of our product candidates has a beneficial effect, that effect (x) will not be detected during preclinical or clinical evaluation or (y) may indicate an apparent positive effect of a product candidate that is greater than the actual positive effect as a result of one or more of a variety of factors, including the size, duration, design, measurements, conduct or analysis of our clinical trials;
- 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;

- adverse events or undesirable side effects caused by, or other unexpected properties of, any product candidates that we may develop could cause us, any collaborators, an institutional review board or regulatory authorities to interrupt, delay or halt clinical trials of one or more of our product candidates and could result in a more restrictive label or the delay or denial of marketing approval by the FDA or comparable foreign regulatory authorities;

- if any of our product candidates is associated with adverse events or undesirable side effects or has properties that are unexpected, we, or any collaborators, may need to abandon development or limit development of that product candidate to certain uses or subpopulations in which the undesirable side effects or other characteristics are less prevalent, less severe or more acceptable from a risk-benefit perspective;

- regulators or institutional review boards may not authorize us, any collaborators or our or their investigators to commence a clinical trial or conduct a clinical trial at a prospective trial site;

- we, or any collaborators, may have delays in reaching or fail to reach agreement on acceptable clinical trial contracts or clinical trial protocols with prospective trial sites;

- clinical trials of our product candidates may produce unfavorable or inconclusive results, including with respect to the safety, tolerability, efficacy or pharmacodynamic and pharmacokinetic profile of the product candidate;

- we, or any collaborators, may decide, or regulators may require us or them, to conduct additional clinical trials or abandon product development programs;

- the number of patients required for clinical trials of our product candidates may be larger than we, or any collaborators, anticipate, patient enrollment in these clinical trials may be slower than we, or any collaborators, anticipate or participants may drop out of these clinical trials at a higher rate than we, or any collaborators, anticipate;

- our estimates of the patient populations available for study may be higher than actual patient numbers and result in our inability to sufficiently enroll our trials;

- the cost of planned clinical trials of our product candidates may be greater than we anticipate;

- our third-party contractors or those of any collaborators, including those manufacturing our product candidates or components or ingredients thereof or conducting clinical trials on our behalf or on behalf of any collaborators, may fail to comply with regulatory requirements or meet their contractual obligations to us or any collaborators in a timely manner or at all;

- patients that enroll in a clinical trial may misrepresent their eligibility to do so or may otherwise not comply with the clinical trial protocol, resulting in the need to increase the needed enrollment size for the clinical trial, extend the clinical trial's duration, or drop the patients from the final efficacy analysis for the clinical trial, which can negatively affect the statistical power of the results;

- our decision, or a decision by regulators or institutional review boards, that may require us to suspend or terminate clinical research for various reasons, including noncompliance with regulatory requirements or their standards of conduct, a finding that the participants are being exposed to unacceptable health risks, undesirable side effects or other unexpected characteristics of the product candidate or findings of undesirable effects caused by a chemically or mechanistically similar product or product candidate;

- the FDA or comparable foreign regulatory authorities may disagree with our, or any collaborators', clinical trial designs or our or their interpretation of data from preclinical studies and clinical trials;

- the FDA or comparable foreign regulatory authorities may fail to approve or subsequently find fault with the manufacturing processes or facilities of third-party manufacturers with which we, or any collaborators, enter into agreements for clinical and commercial supplies;

- the supply or quality of raw materials or manufactured product candidates or other materials necessary to conduct clinical trials of our product candidates may be insufficient, inadequate or not available at an acceptable cost, or we may experience interruptions in supply;

- 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; and

- constraints on our, or any collaborators', ability to conduct or complete clinical trials for our product candidates due to the COVID-19 pandemic, including slowdowns in patient enrollment, restrictions on patient monitoring at hospital clinical trial sites, closures of third-party facilities, and other disruptions to clinical trial activities.

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, which 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 fail to develop and commercialize other product candidates, we may be unable to grow our business.

Although the continued development and commercialization of FOTIVDA (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 will be more effective than other commercially available alternatives.

We may not obtain marketing approval for tivozanib in other indications or our other 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.

If the FDA or other comparable foreign regulatory agency does not accept or approve any future 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 they 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 tivozanib in other indications or our product candidates and generating revenues related thereto. 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.

Results of early clinical trials may not be predictive of results of later clinical trials, and interim results of clinical trials may not be predictive of the final results or the success of clinical trials.

The outcome of early clinical trials, such as our DEDUCTIVE trial and our ficlatuzumab trials in HNSCC, pancreatic cancer and AML, may not be predictive of the success of later clinical trials. Many companies in the pharmaceutical and biotechnology industries have suffered significant setbacks in late-stage clinical trials after achieving positive results in earlier development, and we have, and could in the future, face similar setbacks. In addition, interim results and analyses of clinical trials do not necessarily predict the final results or the success of a trial once it is complete.

While the design of a clinical trial may help to establish whether its results will support approval of a product, 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, we suffered such a setback when the FDA issued a complete response letter, or the 2013 CRL, informing us that it would not approve tivozanib for the first-line treatment of RCC 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 did not adversely affect OS. We then designed and initiated our TIVO-3 trial to address the FDA's concerns about the negative OS trend expressed in the 2013 CRL, which took time and resources and delayed our efforts to obtain marketing approval for tivozanib in the United States.

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.

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 impact of the COVID-19 pandemic;
- 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; and
- competing clinical trials.

In addition, participation in our clinical trials will be affected by 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. For example, at the request of the FDA, we have updated the forms used to obtain consent from patients in ongoing and future trials with tivozanib to include information about the OS results from the TIVO-3 trial as well as the other tivozanib clinical trial OS results to date. These results may impact the interest of clinicians and patients in participating in future clinical trials with tivozanib.

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, the 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 rate fluctuations; and
- diminished protection of intellectual property in some countries.

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, and could cause regulatory authorities to take certain regulatory actions.

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. For example, despite the recent FDA marketing approval of FOTIVDA in the United States, we, or others, may discover that FOTIVDA is less effective or tolerable than previously believed. If, we, or others, discover that a 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.

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 their potential for marketing approval and commercialization, as well as those that are most aligned with our strategic goals. 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 the commercial launch of FOTIVDA for which we recruited a sales force and established marketing, market access and medical affairs teams and distribution capabilities is not successful for any reason, we could incur substantial costs and our investment would be lost if we cannot retain or reposition our sales, marketing, market access and medical affairs personnel.

To achieve commercial success for FOTIVDA, we have expended and anticipate that we will continue to expend significant resources to support our sales force, marketing, market access and medical affairs teams and distribution capabilities. There are risks involved with establishing our own sales, marketing, distribution, training and support capabilities. For example, recruiting and training sales and marketing personnel is expensive and time consuming and could delay our ability to focus on other priorities. If the commercial launch of FOTIVDA is not successful for any reason, this would be costly, and our investment would be lost if we cannot retain or reposition our sales, marketing, market access and medical affairs personnel or terminate on favorable terms any agreements entered into with third parties to support our commercialization efforts.

Factors that may inhibit our efforts to commercialize FOTIVDA on our own include:

- our inability to train and retain adequate numbers of effective sales, marketing, training and support personnel;
- the inability of sales personnel to obtain access to physicians, including key opinion leaders, or to persuade adequate numbers of physicians to use tivozanib;
- the lack of complementary products to be offered by sales personnel, which may put us at a competitive disadvantage relative to companies with more extensive or integrated product offerings; and
- unforeseen costs and expenses associated with establishing and maintaining an independent sales, marketing, training and support organization.

If our efforts to establish our own salesforce, marketing, market access and medical affairs teams and distribution capabilities are unsuccessful and instead we enter into arrangements with third parties to perform these services, our product revenues, gross margins and our profitability, if any, are likely to be lower than if we were to market, sell and distribute FOTIVDA ourselves. In addition, we may not be successful in entering into arrangements with third parties to market, sell and distribute FOTIVDA, or may be unable to do so on terms that are favorable to us. If we do not establish sales, marketing, distribution, training and support capabilities successfully, either on our own or in collaboration with third parties, we will not be successful in commercializing FOTIVDA and achieving profitability, and our business would be harmed.

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, and 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. There are many companies focused on the development of small molecules and antibodies for cancer treatment. Our core competitors include pharmaceutical and biotech organizations, as well as academic research institutions, clinical research laboratories and government agencies that are pursuing research activities in the same therapeutic area. See “Part I, Item 1. Business—Competition.” Many of our competitors have greater financial, technical and human resources than we do. Further, mergers and

acquisitions in the biotechnology and pharmaceutical industries may result in even more resources being concentrated in favor of our competitors. Additionally, many competitors have greater experience in product discovery and development, obtaining FDA and other regulatory approvals and commercialization capabilities, which may provide them with a competitive advantage.

We believe that our ability to compete will depend on our ability to execute on the following objectives:

- 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.

The competitive landscape and treatment regimens for RCC and HCC continue to rapidly evolve, particularly given the entrance of immune checkpoint inhibitor combination therapies and the entrance of immune checkpoint inhibitor and VEGFR TKI combination therapies into the RCC treatment landscape. The utilization of such regimens may affect sequencing of certain drugs and combinations across different lines of therapy. Additionally, there are several therapies in clinical development for RCC and HCC that may alter the competitive landscape for the treatment of these cancers. As such, it is difficult to predict how these changes will inform our perspective on the key competitors of tivozanib in RCC and HCC in the future.

For a description of the key competitors for tivozanib in relapsed or refractory RCC and in advanced HCC and the products that are considered competitive with ficlatuzumab and certain of our other product candidates, see “Part I, Item 1. Business – Competition”.

FOTIVDA, or any other product candidate that we or our collaborators are able to commercialize, 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 FOTIVDA, EUSA, is currently in the process of seeking reimbursement approval for FOTIVDA in many of the countries in which FOTIVDA 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 successfully commercialize 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, such as FOTIVDA, and coverage may be more limited for FOTIVDA than the indication 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. We cannot be sure that coverage will be available for any product candidate that we, or third-parties, commercialize and, if available, that the reimbursement rates will be adequate. 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 regulatory 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 a risk of product liability as a result of the commercialization of FOTIVDA and the clinical testing of our product candidates. 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 a 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 FOTIVDA or our product candidates;
- withdrawal of clinical trial participants;
- delay or termination of our clinical trials;
- significant costs to defend the related litigation;
- 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.

Although we maintain general liability insurance and clinical trial liability insurance, this insurance may not fully cover potential liabilities that we may incur. The cost of any product liability litigation or other proceeding, even if resolved in our favor, could be substantial. Insurance coverage is becoming increasingly expensive. We will need to increase our insurance coverage for the commercialization of FOTIVDA and if we commercialize any other product that receives marketing approval. 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.

Our internal computer systems or other company technology to collect and store information, or those of any third parties with which we contract, may fail or suffer security breaches, which could result in a material disruption of our product development programs.

Despite the implementation of security measures, our internal computer systems and those of third parties with which we contract are vulnerable to damage from computer viruses, worms and other destructive or disruptive software, unauthorized access, natural disasters, terrorism, war and telecommunication and electrical failures. Such systems are also vulnerable to service interruptions or to security breaches from inadvertent or intentional actions by our employees, third-party vendors and/or business partners, or from cyber incidents by malicious third parties. Sensitive commercial and personal information also may be subject to security breaches in other contexts, related to personal devices or other technology or systems where this information can be collected, stored and used. Cyber incidents are increasing in their frequency, sophistication and intensity, and have become increasingly difficult to detect. Cyber incidents could include the deployment of harmful malware, ransomware, denial-of-service attacks, unauthorized access to or deletion of files, social engineering and other means to affect service reliability and threaten the confidentiality, integrity and availability of information. Cyber incidents also could include phishing attempts or e-mail fraud to cause payments or information to be transmitted to an unintended recipient. We could be subject to risks caused by misappropriation, misuse, leakage, falsification or intentional or accidental release or loss of information maintained in the information systems and networks of our company, including personal information of our employees. In addition, we face other kinds of risks related to our commercial and personal information, including lost or stolen devices or other systems (including paper records) that collect and store our personal and commercial information.

System failures, accidents, cyber incidents 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, whether due to a loss of our trade secrets or other proprietary information or other similar disruptions, in addition to possibly requiring substantial expenditures of resources to remedy. For example, the loss of clinical trial data from completed or future trials 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 disclosure of confidential or proprietary information, we could incur liability, our competitive position could be harmed and our product research, development and commercialization efforts could be delayed. We may in certain instances be required to provide notification to individuals or others in connection with the loss of their personal or commercial information. In addition, we may not have adequate insurance coverage to provide compensation for any losses associated with such events.

If a material breach of our security or that of our vendors occurs, the market perception of the effectiveness of our security measures could be harmed, we could lose business and our reputation and credibility could be damaged. We could be required to expend significant amounts of money and other resources to repair or replace information systems or networks. Although we develop and maintain systems and controls designed to prevent these events from occurring, and we have a process to identify and mitigate threats, the development and maintenance of these systems, controls and processes is costly and requires ongoing monitoring and updating as technologies change and efforts to overcome security measures become more sophisticated. Moreover, despite our efforts, the possibility of these events occurring cannot be eliminated entirely.

Risks Related to Our Dependence on Third Parties

We rely on third parties, such as 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 CROs and other third parties to perform many of the functions in managing, monitoring and otherwise carrying out many of these trials. We compete with larger companies for the resources of these third parties. In addition, these third parties may be adversely affected by the COVID-19 pandemic.

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, including 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, process and analyze is compromised for any reason or if they otherwise fail to comply with clinical trial protocols or meet expected deadlines, our clinical trials may experience delays or may fail to 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 and third-party suppliers to produce and supply our preclinical and clinical product candidate supplies, and we intend to rely on third parties to produce commercial supplies of FOTIVDA, and any approved product candidates. Any failure by a third-party manufacturer or a third-party supplier to produce or provide supplies for us may delay or impair our ability to complete our clinical trials or commercialize our product candidates.

We have relied upon third-party manufacturers for the manufacture of our product candidates for preclinical and clinical testing purposes and intend to continue to do so in the future. 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, failure of the third-party to accept orders for supply of drug substance or drug product and the possibility of termination or nonrenewal of the agreement by the third-party, based on its own business priorities, at a time that is costly or damaging to us. In addition, the FDA and other regulatory authorities require that our product candidates be manufactured according to 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 commercial manufacturing. There are a small number of suppliers of 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 due to the COVID-19 pandemic, the need to replace a third-party supplier or other factors could considerably delay completion of our clinical studies, product testing and potential regulatory approval of our product candidates.

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

We rely on our licensee EUSA, over whom we have little control, for the sales, marketing and distribution efforts associated with the commercialization of FOTIVDA in certain European countries and any failure by EUSA to devote the necessary resources and attention to market and sell FOTIVDA effectively and successfully may materially impact our ability to generate revenue.

In December 2015, we entered into the EUSA Agreement, 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 and Australasia for all diseases and conditions in humans, excluding non-oncologic diseases or conditions of the eye. We have limited contractual rights to force EUSA to invest significantly in commercialization of tivozanib in jurisdictions covered by the EUSA Agreement. In the event that EUSA fails to adequately commercialize tivozanib because it lacks adequate financial or other resources, decides to focus on other initiatives or otherwise, our ability to successfully commercialize tivozanib in the applicable jurisdictions would be limited, which would adversely affect our business, financial condition, results of operations and prospects. In addition, the EUSA Agreement may be terminated by either party upon prior written notice. If EUSA terminated the EUSA Agreement, we may not be able to secure an alternative distributor in the

applicable territories on a timely basis or at all, in which case our ability to generate revenues from the sale of tivozanib, outside the United States would be materially harmed.

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 other 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.

If we are not able to establish and maintain strategic partnerships:

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

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 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. For example, in March 2020, CANbridge advised us that it was evaluating alternative development plans for AV-203, which would delay the initiation of clinical trials of AV-203. Since then, in March 2021, CANbridge exercised its right to terminate the CANbridge Agreement for convenience. Under the terms of the CANbridge Agreement, we expect the transfer of the AV-203 program to be complete in September 2021, which will delay the initiation of clinical trials of AV-203 even further.

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. For example, in September 2020 Biodesix exercised its Opt-Out right under the Biodesix Agreement. As a result, Biodesix is not required to contribute to the future development costs of ficlatuzumab in exchange for a reduced economic interest in any future ficlatuzumab revenues.

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 due to 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 reason, 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 patent 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. For example, we have filed a patent application directed to our clinical protocol for using tivozanib to treat refractory cancers, including, following therapy with checkpoint inhibitors. It is possible that we may not successfully obtain a granted patent based upon this patent application. The scope of patent protection that the USPTO will grant with respect to the antibodies in our antibody product pipeline is also 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 United States under the Hatch-Waxman Act, by 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 a 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. For example, we have exclusive license rights to a first U.S. patent covering the tivozanib molecule and its therapeutic use, which is scheduled to expire in 2022, and a second U.S. patent covering a crystalline form of tivozanib, which is scheduled to expire in 2023. In view of the length of time tivozanib has been under regulatory review at the FDA, a patent term extension of up to 5 years may be available. Although we plan to apply for patent term extensions on each U.S. patent, only one patent may be extended, and, when appropriate, we will have to elect which patent is to be extended. If a five-year extension were to be granted, if applied to the first patent, the term could be extended to April of 2027, and if applied to the second patent, the term could be extended to November of 2028. 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 granted for the patent covering the tivozanib molecule in Belgium, Finland, France, Germany, Italy, the Netherlands, Norway, Poland, Portugal, Spain and Sweden, extending the term of the patents in each of these countries up to April 2027. An SPC has been granted for the patent covering the crystalline form of tivozanib in Ireland extending the term of that patent to October 2028. The remaining pending applications for SPCs on the patent covering the tivozanib molecule in Denmark and Great Britain may not be similarly granted, or may be granted for a shorter period than requested. 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. In addition, if we have a product approved by the FDA (for example, if the FDA approves our tivozanib product candidate), generic manufacturers could challenge the patents covering the approved product as part of the process of obtaining regulatory approval via an ANDA. (The process by which generic manufacturers may seek regulatory approval via an ANDA and challenge our patents is discussed above in the section entitled “Part I, Item 1. Business – Government Regulation and Product Approval—Generic Drugs.”) 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 USPTO, 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 ficlatuzumab, we are aware of one United States patent and its foreign counterparts that contain broad claims related to anti-HGF antibodies having certain binding properties and their use. In the event that the owner 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 products. 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.

Tivozanib and AV-380 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 KKC for tivozanib and 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 use in our AV-380 program. 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, such as 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, consultants 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 and consultants are 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, consultant 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 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.

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 and result in a material disruption of our product development programs.

We could be subject to risks caused by misappropriation, misuse, leakage, falsification or intentional or accidental release or loss of information maintained in the information systems and networks of our company, including personal information of our employees. In addition, outside parties may attempt to penetrate our systems or those of our partners or fraudulently induce our employees or employees of our partners to disclose sensitive information to gain access to our data. Like other companies, we may experience threats to our data and systems, including malicious codes and computer viruses, cyber-attacks, or other system failures. Any system failure, accident or security breach that causes interruptions in our operations, for us or our partners, could result in a material disruption of our product development programs and business operations, in addition to possibly requiring substantial expenditures of resources to remedy. For example, the loss of clinical trial data from completed clinical trials could result in delays in our regulatory approval efforts and we could incur significant increases in costs to recover or reproduce the data. To the extent that any disruption or security breach results in a loss of, or damage to, our data or applications, or inappropriate public disclosure of confidential or proprietary information, we may incur liabilities and the further development of our product candidates may be delayed. In addition, we may not have adequate insurance coverage to provide compensation for any losses associated with such events.

The number and complexity of these threats continue to increase over time. If a material breach of our security or that of our partners occurs, the market perception of the effectiveness of our security measures could be harmed, we could lose business and our reputation and credibility could be damaged. We could be required to expend significant amounts of money and other resources to repair or replace information systems or networks. Although we develop and maintain systems and controls designed to prevent these events from occurring, and we have a process to identify and mitigate threats, the development and maintenance of these systems, controls and processes is costly and requires ongoing monitoring and updating as technologies change and efforts to overcome security measures become more sophisticated. Moreover, despite our efforts, the possibility of these events occurring cannot be eliminated entirely.

Additionally, the collection, use, disclosure, transfer or other processing of personal data regarding individuals in the EU, including personal health data, is subject to the EU General Data Protection Regulation, or GDPR, which became effective on May 25, 2018. The GDPR is wide-ranging in scope and imposes numerous requirements on companies that process personal data, including requirements relating to processing health and other sensitive data, obtaining consent of the individuals to whom the personal data relates, providing information to individuals regarding data processing activities, implementing safeguards to protect the security and

confidentiality of personal data, providing notification of data breaches, and taking certain measures when engaging third-party processors. The GDPR also imposes strict rules on the transfer of personal data to countries outside the EU, including the United States, and permits data protection authorities to impose large penalties for violations of the GDPR, including potential fines of up to €20 million or 4% of annual global revenues, whichever is greater. The GDPR also confers a private right of action on data subjects and consumer associations to lodge complaints with supervisory authorities, seek judicial remedies, and obtain compensation for damages resulting from violations of the GDPR. Compliance with the GDPR is a rigorous and time-intensive process that may increase our cost of doing business or require us to change our business practices, and despite those efforts, there is a risk that we may be subject to fines and penalties, litigation, and reputational harm in connection with any European activities.

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 or antibodies 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.
- The term of patents that we own or have exclusively licensed may be insufficient to prevent competitors from introducing products that are competitive with our product candidates.
- If the licenses we have that relate to our product candidates are terminated by the licensors, we may be prevented from commercializing our product candidates.
- 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 products competitive with one or more of our product candidates, 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 or our strategic partners' existing or potential 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 events in the last decade 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 United States. The patent law introduced changes including a first-to-file system for determining which inventors may be entitled to receive patents, and post-grant challenges, such as inter-partes review and post-grant review proceedings that allow third parties to challenge newly issued patents. The burden of proof required for challenging a patent in these proceedings is lower than in district court litigation, and patents in the biopharmaceutical industry have been successfully challenged using these new post-grant challenges. 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 further 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 the COVID-19 Pandemic

The COVID-19 pandemic has adversely disrupted, and is expected to continue to adversely disrupt our operations, including our ability to complete our ongoing clinical trials and may have other adverse effects on our business and operations. In addition, this

pandemic has caused substantial disruption in the financial markets and has adversely impacted economies worldwide, both of which could result in adverse effects on our business, operations and ability to raise capital.

The COVID-19 pandemic, which began in December 2019 and has spread worldwide, has caused many governments to implement measures to slow the spread of the outbreak through quarantines, strict travel restrictions, heightened border scrutiny and other measures. The outbreak and government measures taken in response have also had a significant impact, both direct and indirect, on businesses and commerce, as worker shortages have occurred, supply chains have been disrupted, facilities and production have been suspended, and demand for certain goods and services, such as medical services and supplies, has spiked, while demand for other goods and services, such as travel, has fallen. The future progression of the pandemic and its effects on our business and operations are uncertain.

We have enrolled and seek to enroll cancer patients in our ongoing clinical trials at sites located both in the United States and in Europe. The COVID-19 pandemic has delayed and may continue to delay or otherwise adversely affect these clinical development activities, including our ability to recruit and retain patients in our ongoing clinical trials, as a result of many factors, including:

- diversion of healthcare resources away from the conduct of our clinical trials in order to focus on pandemic concerns, including the availability of necessary materials, the attention of physicians serving as our clinical trial investigators, access to hospitals serving as our clinical trial sites, availability of hospital staff supporting the conduct of our clinical trials and the reluctance of patients enrolled in our clinical trials to visit clinical trial sites;
- potential interruptions in global shipping affecting the transport of clinical trial materials, such as investigational drug product, patient samples and other supplies used in our clinical trials;
- the impact of further limitations on travel that could interrupt key clinical trial activities, such as clinical trial site initiations and monitoring activities, travel by our employees, contractors or patients to clinical trial sites or the ability of employees at any of our CMOs or CROs to report to work, any of which could delay or adversely impact the conduct or progress of our clinical trials, and limit the amount of clinical data we will be able to report;
- any future interruption of, or delays in receiving, supplies of clinical trial material from our contract manufacturing organizations or, in the case of combination trials, our study collaborators, due to staffing shortages, production slowdowns or stoppages or disruptions in delivery systems; and
- availability of future capacity at CMOs to produce sufficient drug substance and drug product to meet forecasted clinical trial demand if any of these manufacturers elect or are required to divert attention or resources to the manufacture of other pharmaceutical products.

For example, some of the clinical trial sites for our DEDUCTIVE trial have suspended enrollment at times due to COVID-19 related hospital and governmental restrictions. Enrollment has occurred at a slower pace than initially forecasted prior to the onset of the pandemic, and we cannot guarantee the future pace of enrollment. In addition, in-person monitoring visits are currently on hold at certain of the clinical trial sites in our DEDUCTIVE trial and to the extent possible due to the COVID-19 pandemic, monitoring is being conducted remotely. We do not yet know whether remote management of this function will prove to be sufficient. The extent of any adverse impact on our clinical trials will depend on numerous evolving factors that cannot be predicted with any level of certainty. In addition, in March 2020 we decided to discontinue the CyFi-2 trial due to the urgent shift in priorities among clinical trial sites toward efforts to combat the COVID-19 pandemic, which had impacted the trial enrollment timeline and the feasibility of completing the study within the shelf-life of the ficlatuzumab clinical trial supply.

Any negative impact that the COVID-19 pandemic has on recruiting or retaining patients in our clinical trials, the ability of our suppliers to provide materials for our product candidates or the regulatory review process could cause additional delays with respect to product development activities, which could materially and adversely affect our ability to obtain regulatory approval for and to commercialize our product candidates, increase our operating expenses, affect our ability to raise additional capital and have a material adverse effect on our financial results. In addition, our clinical trial patients who contract COVID-19 may have adverse health outcomes unrelated to their cancer that could impact the results of our clinical trials.

The COVID-19 pandemic continues to evolve and its ultimate scope, duration and effects are unknown. The extent of the impact of the disruptions to our business, preclinical studies, clinical trials and commercialization efforts as a result of the outbreak will depend on future developments, which are highly uncertain and cannot be predicted with confidence, such as the ultimate geographic spread of the disease, the duration of the outbreak, travel restrictions and actions to contain the outbreak or treat its impact, such as social distancing and quarantines or lock-downs in the United States and other countries, business closures or business disruptions and the effectiveness of actions taken in the United States and other countries to contain and treat the disease.

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

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 CROs to assist us in this process.

The process of obtaining marketing approvals, both in the United States and abroad, is expensive and may take many years, especially if additional clinical trials are required. 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. It 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 delay or preclude our obtaining marketing approval or prevent or limit commercial use.

In addition, 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. 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. In addition, a regulatory agency's varying interpretations of the data obtained from preclinical and clinical testing could delay, limit or prevent marketing approval of a product candidate. For example, in June 2013, the FDA issued the 2013 CRL informing us that it would not approve tivozanib for the first-line treatment of RCC based solely on the data from the TIVO-1 trial.

In addition, disruptions at the FDA and other agencies due to COVID-19 may prolong the time necessary for new drugs to be reviewed and/or approved by necessary government agencies, which would adversely affect our business. For example, over the last several years, the U.S. government has shut down several times and certain regulatory agencies, such as the FDA, have had to furlough critical employees and stop critical activities. If a prolonged government shutdown occurs, it could significantly impact the ability of the FDA to timely review and process our regulatory submissions, which could have a material adverse effect on our business. The Trump Administration also took several executive actions that could impose significant burdens on, or otherwise materially delay, the FDA's ability to engage in routine regulatory and oversight activities.

Accordingly, if we or our collaborators experience delays in obtaining approval or if we fail to obtain approval of our product candidates, or executive actions impose constraints on FDA's ability to engage in oversight and implementation activities in the normal course, 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 abroad and may limit our ability to generate revenue from product sales.

In order to market and sell our medicines in the EU 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 particular market.

In many countries outside the United States, a product candidate must also be approved for reimbursement before it can be sold in that country. In some cases, the price that we intend to charge for our products, if approved, is also subject to approval. Obtaining non-U.S. regulatory approvals and compliance with non-U.S. regulatory requirements could result in significant delays, difficulties and costs for us and any future collaborators and could delay or prevent the introduction of our product candidates in certain countries.

In addition, if we or any future collaborators fail to obtain the non-U.S. approvals required to market our product candidates outside the United States or if we or any future collaborators fail to comply with applicable non-U.S. regulatory requirements, our target market will be reduced and our ability to realize the full market potential of our product candidates will be harmed and our business, financial condition, results of operations and prospects may be adversely affected.

Additionally, we could face heightened risks with respect to seeking marketing approval in the United Kingdom as a result of the recent withdrawal of the United Kingdom from the EU, commonly referred to as Brexit. Pursuant to the formal withdrawal arrangements agreed between the United Kingdom and the EU, the United Kingdom withdrew from the EU, effective December 31, 2020. On December 24, 2020, the United Kingdom and the EU entered into a Trade and Cooperation Agreement. The agreement sets out certain procedures for approval and recognition of medical products in each jurisdiction. Any delay in obtaining, or an inability to obtain, any marketing approvals, as a result of the Trade and Cooperation Agreement would prevent us from commercializing any product candidates in the United Kingdom and/or the EU 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 the EU for any 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. 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.

We or our collaborators may seek orphan drug designations for other product candidates and may be unable to obtain such designations. Moreover, even if we do secure such designations and 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. Further, 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. Finally, 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.

Our recently approved product, FOTIVDA, and any product candidate for which we or our collaborators obtain marketing approval are subject to ongoing regulation and 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.

Our recently approved product, FOTIVDA, and any product candidate for which we or our collaborators obtain marketing approval in the future 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. For example, FDA approval of FOTIVDA is subject to limitations on the indicated uses for which FOTIVDA may be marketed, specifically the treatment of adults with relapsed or refractory advanced RCC who have progressed following two or more systemic therapies. Accordingly, we expect to continue to expend time, money and effort in all areas of regulatory compliance, including manufacturing, production, product surveillance and quality control. If we fail to comply with these requirements, we could have the marketing approval for FOTIVDA 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.

We and our collaborators must also comply with requirements concerning advertising and promotion for FOTIVDA or any of our product candidates for which we may obtain regulatory 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. 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. Violations of the FDCA and other statutes, including the FCA, 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.

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 EU 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 EU's requirements regarding the protection of personal information can also lead to significant penalties and sanctions.

Our relationships with healthcare providers, physicians and third-party payors are 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 FOTIVDA and any product candidate for which we may obtain marketing approval in the future. Our 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 FOTIVDA and any products for which we may obtain marketing approval in the future. Restrictions under applicable federal and state healthcare laws and regulations include the federal Anti-Kickback Statute, FCA, Health Insurance Portability and Accountability Act of 1996, or HIPAA, and the Physician Payments Sunshine Act. There are also analogous state and foreign laws and regulations that may apply to sales or marketing arrangements and claims involving healthcare items or services reimbursed by third-party payors, including private insurers. Further, some state laws require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines 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.

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 implementing a corporate compliance program designed to ensure that we will market and sell FOTIVDA and 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 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 FOTIVDA or any product candidates for which we may 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 FOTIVDA or any product candidate for which we may obtain marketing approval in the future.

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. 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 2030 under the Coronavirus Aid, Relief, and Economic Security Act, or the CARES Act. 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 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.

Since enactment of the ACA, there have been, and continue to be, numerous legal challenges and Congressional actions to repeal and replace provisions of the law. For example, with the enactment of the TCJA, which was signed by President Trump 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, became effective in 2019. Further, on December 14, 2018, a U.S. District Court judge in the Northern District of Texas ruled that the individual mandate portion of the ACA is an essential and inseverable feature of the ACA, and therefore because the mandate was repealed as part of the TCJA, the remaining provisions of the ACA are invalid as well. On December 18, 2019, the Court of Appeals for the Fifth Circuit court affirmed the lower court's ruling that the individual mandate portion of the ACA is unconstitutional and it remanded the case to the district court for reconsideration of the severability question and additional analysis of the provisions of the ACA. Thereafter, the U.S. Supreme Court agreed to hear this case. Oral argument in the case took place on November 10, 2020, and a ruling by the Court is expected sometime this year. Litigation and legislation over the ACA are likely to continue, with unpredictable and uncertain results.

The Trump Administration also took executive actions to undermine or delay implementation of the ACA, including 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. On January 28, 2021, however, President Biden rescinded that Executive Order and issued a new Executive Order which directs federal agencies to reconsider rules and other policies that limit Americans' access to health care, and consider actions that will protect and strengthen that access. Under this Executive Order, federal agencies are directed to re-examine:

- policies that undermine protections for people with pre-existing conditions, including complications related to COVID-19;
- demonstrations and waivers under Medicaid and the ACA that may reduce coverage or undermine the programs, including work requirements;
- policies that undermine the Health Insurance Marketplace or other markets for health insurance;
- policies that make it more difficult to enroll in Medicaid and the ACA; and
- policies that reduce affordability of coverage or financial assistance, including for dependents.

The costs of prescription pharmaceuticals have also been the subject of considerable discussion in the United States. To date, there have been several recent U.S. congressional inquiries, as well as proposed and enacted 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. To those ends, President Trump issued five Executive Orders intended to lower the costs of prescription drug products but it is unclear whether, and to what extent, these Executive Orders will remain in force under the Biden Administration. Further, on September 24, 2020, the Trump Administration finalized a rulemaking allowing states or certain other non-federal government entities to submit importation program proposals to the FDA for review and approval. Applicants are required to demonstrate that their importation plans pose no additional risk to public health and safety and will result in significant cost savings for consumers. The FDA has issued draft guidance that would allow manufacturers to import their own FDA-approved drugs that are authorized for sale in other countries (multi-market approved products).

At the state level, legislatures are increasingly 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. We expect that additional state and federal healthcare reform measures will be adopted in the future, any of which could limit the amounts that federal and state governments will pay for healthcare products and services, which could result in reduced demand for FOTIVDA or our product candidates or additional pricing pressures.

Finally, outside the United States, in some nations, including those of the EU, 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 FOTIVDA is unavailable or limited in scope or amount, or if pricing is set at unsatisfactory levels, our business could be materially harmed.

Compliance with global privacy and data security requirements could result in additional costs and liabilities to us or inhibit our ability to collect and process data globally, and the failure to comply with such requirements could subject us to significant fines and penalties, which may have a material adverse effect on our business, financial condition or results of operations.

The regulatory framework for the collection, use, safeguarding, sharing, transfer and other processing of information worldwide is rapidly evolving and is likely to remain uncertain for the foreseeable future. Globally, virtually every jurisdiction in which we operate has established its own data security and privacy frameworks with which we must comply, with additional laws and amendments being passed on a regular basis. As one example, the collection, use, disclosure, transfer or other processing of personal data regarding individuals in the EU, including personal health data, is subject to the EU General Data Protection Regulation, or the GDPR, which applies to all member states of the European Economic Area, or EEA. The GDPR is wide-ranging in scope and imposes numerous requirements on companies that process personal data. The GDPR imposes significant obligations with respect to clinical trials conducted in the EEA. In addition, the GDPR also imposes strict rules on the transfer of personal data to countries outside the EU, including the United States and, as a result, increases the scrutiny that clinical trial sites located in the EEA should apply to transfers of personal data from such sites to countries that are considered to lack an adequate level of data protection, such as the United States. The GDPR also permits data protection authorities to require destruction of improperly gathered or used personal information and/or impose substantial fines for violations of the GDPR and it also confers a private right of action on data subjects and consumer associations to lodge complaints with supervisory authorities, seek judicial remedies and obtain compensation for damages resulting from violations of the GDPR. In addition, the GDPR provides that EU member states may make their own further laws and regulations limiting the processing of personal data, including genetic, biometric or health data.

Given the breadth and depth of changes in data protection obligations, preparing for and complying with these requirements is rigorous and time intensive and requires significant resources and a review of our technologies, systems and practices, as well as those of any third-party collaborators, service providers, contractors or consultants that process or transfer personal data collected in the EU and otherwise across the world. The GDPR and other changes in laws or regulations associated with the enhanced protection of certain types of sensitive data, such as healthcare data or other personal information from our clinical trials, could require us to change our business practices and put in place additional compliance mechanisms, may interrupt or delay our development, regulatory and commercialization activities and increase our cost of doing business, and could lead to government enforcement actions, private litigation and significant fines and penalties against us and could have a material adverse effect on our business, financial condition or results of operations.

Similar actions are either in place or under way in the United States. There are a broad variety of data protection laws that are applicable to our activities, and a wide range of enforcement agencies at both the state and federal levels that can review companies for privacy and data security concerns based on general consumer protection laws. The Federal Trade Commission and state Attorneys General all are aggressive in reviewing privacy and data security protections for consumers. New laws also are being considered at both the state and federal levels. For example, the California Consumer Privacy Act—which went into effect on January 1, 2020—is creating similar risks and obligations as those created by GDPR, though the Act does exempt certain information collected as part of a clinical trial subject to the Federal Policy for the Protection of Human Subjects (the Common Rule). Many other states are considering similar legislation. A broad range of legislative measures also have been introduced at the federal level. Accordingly, failure to comply with federal and state laws (both those currently in effect and future legislation) regarding privacy and security of personal information could expose us to fines and penalties under such laws. There also is the threat of consumer class actions related to these laws and the overall protection of personal data. Even if we are not determined to have violated these laws, government investigations into these issues typically require the expenditure of significant resources and generate negative publicity, which could harm our reputation and our business.

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 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, marketing 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 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.

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. The loss of services of employees and, in particular, of a member of management could delay or prevent our ability to successfully commercialize FOTIVDA in the United States, 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. In addition, the COVID-19 pandemic may negatively impact our ability to recruit and build out our organization as planned. 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 or consultants 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 or consultant fraud or other misconduct. Misconduct by employees or consultants 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, marketing, sales 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 or consultant 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 or consultant 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, employees and consultants 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, employee or consultant 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, employee or consultant 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 on the Nasdaq Capital Market. We are required to meet specified requirements to maintain our listing on the Nasdaq Capital Market, including a minimum market value of listed securities of $35.0 million, a minimum bid price of $1.00 per share for our common stock and other continued listing requirements.

In the past we have, from time to time, received deficiency letters from Nasdaq as a consequence of our failure to satisfy such requirements. Although we have been able to regain compliance with the listing requirements within the manner and time periods prescribed by Nasdaq in the past, there can be no assurance that we will be able to maintain compliance with the Nasdaq continued listing requirements in the future or regain compliance with respect to any future deficiencies. If we fail to satisfy the Nasdaq Capital Market’s continued listing requirements, we may transfer to the OTC Bulletin Board, which generally has lower financial requirements for initial listing, to avoid delisting. However, we may not be able to satisfy the initial listing requirements for 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 event 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:

- announcements relating to our product, FOTIVDA, including as it relates to commercial launch, sales and any future regulatory matters;
- 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;
- the effect of the COVID-19 outbreak on the healthcare system and the economy generally and on our preclinical studies, clinical trials, commercial activities and other operations specifically;
- the results of regulatory reviews and other regulatory correspondence relating to our product, product candidates or our clinical trials;
- 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 revenue, expense or earnings estimates, development timelines or recommendations by securities analysts;
- general economic and market conditions on our industry 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, following our failure to obtain FDA approval for tivozanib in 2013, we and certain of our former officers and directors were involved in several legal proceedings. Following our January 2019 announcement that the FDA did not recommend we file an NDA for tivozanib at that time, several lawsuits were filed against us, our directors, and certain of our current and former officers. See Part II, Item 1 of this Annual Report on Form 10-K under the heading "Legal Proceedings." While the 2019 Class Action was dismissed, any litigation instituted against us in the future 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 estimated time frames that we publicly announce, 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, preparations for a commercial launch and other developments and milestones under our research and development programs and those of our partners and collaborators for tivozanib, ficlatuzumab, AV-380, AV-203 and AV-353. The actual timing of these events can vary significantly due to a number of factors, including those discussed in "Part I, Item 1A. Risk Factors." 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, that we will be successful in our commercial launch or that we will be able to adhere to our currently anticipated schedule for the achievement of key milestones under any of our programs. If we fail to achieve one or more of the events 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 level of net product revenues from the sales of FOTIVDA;
- the level of expenses incurred to commercialize FOTIVDA;
- 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 lawsuits described elsewhere in this Annual Report on Form 10-K under "Part II, Item 1. – Legal Proceedings";
- changes in our Loan Agreement, including the existence of any event of default that may accelerate then remaining principal payments and fees due thereunder;
- non-cash changes in fair value related to re-valuations of our outstanding warrant liability as a result of fluctuations in our stock price; and
- compliance with regulatory requirements.

In addition, in March 2020, we decided to discontinue our CyFi-2 trial of ficlatuzumab due to the urgent shift in priorities among clinical trial sites towards efforts to combat the COVID-19 pandemic, which has impacted the trial enrollment timeline and the feasibility of completing the study within the shelf-life of the current ficlatuzumab clinical trial supply. While the COVID-19 pandemic has not had a material adverse impact on our operations to date, the future impact of COVID-19 is highly uncertain and cannot be predicted and there can be no assurance that the outbreak will not have a material adverse impact on our future operations. The extent of the impact, if any, will depend on future developments, including the extent of the pandemic and governmental actions taken to contain the COVID-19 pandemic.

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.

Global credit and financial markets have been experiencing extreme volatility and disruptions in 2020 due to the COVID-19 pandemic and the government measures taken in response to the pandemic. We expect that rapid or extended periods of deterioration in credit and financial markets and confidence in economic conditions will continue. 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.

As of December 31, 2020, we had approximately $61.8 million of cash, cash equivalents and marketable securities, consisting of cash on deposit with banks, a U.S. government money market fund and high-grade debt securities, including short-term commercial paper, corporate bonds and other 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 or marketable securities. 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 and marketable securities or our ability to meet our financing objectives. Dislocations in the credit market may adversely impact the value and/or liquidity of cash equivalents and marketable securities owned by us.

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 extent 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.

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 of directors 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.

Our stockholders 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. In addition, the terms of the Loan Agreement preclude, and any future debt agreements may preclude us from, paying dividends. 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.

Changes in tax laws or in their implementation or interpretation may adversely affect our business and financial condition.

The rules dealing with U.S. federal, state and local income taxation are constantly under review by persons involved in the legislative process and by the Internal Revenue Service and the U.S. Treasury Department. Changes to tax laws (which changes may have retroactive application) could adversely affect us or holders of our common stock. In recent years, many such changes have been made and changes are likely to continue to occur in the future. For example, the TCJA was enacted in 2017 and significantly reformed the Internal Revenue Code of 1986, as amended, or the Code. In addition, as part of Congress' response to the COVID-19 pandemic, the Families First Coronavirus Response Act, or FFCR Act, was enacted on March 18, 2020, and the CARES Act was enacted on March 27, 2020. Both contain numerous tax provisions.

Regulatory guidance under the TCJA, the FFCR Act and the CARES Act is and continues to be forthcoming, and such guidance could ultimately increase or lessen impact of these laws on our business and financial condition. It is also possible that Congress will enact additional legislation in connection with the COVID-19 pandemic, some of which could have an impact on our company. In addition, it is uncertain if and to what extent various states will conform to the TCJA, the FFCR Act or the CARES Act. We urge investors to consult with their legal and tax advisers regarding the implications of the TCJA, the FFCR Act and the CARES Act and other changes in tax laws on an investment in our common stock. Recent changes in tax law may adversely affect our business or financial condition.

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

As of December 31, 2020, we had federal net operating loss carryforwards of $565.8 million, of which $502.6 million will, if not used, expire at various dates through 2037, and federal research and development tax credit carryforwards of $11.8 million, which will, if not used, expire at various dates through 2040. To the extent that they expire unused, these net operating loss and tax credit carryforwards will not be available to offset our future income tax liabilities. Federal net operating losses incurred in 2018 and in future years may be carried forward indefinitely, but the deductibility of such carryforwards is limited to 80% of our taxable income in the year in which such carryforwards are used.

In addition, under Section 382 of the Code 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 carryforwards to reduce its tax liability for post-change periods may be limited. We have not determined if we have experienced Section 382 ownership changes in the past and if a portion of our net operating loss and tax credit carryforwards is subject to an annual limitation under Section 382. We also may experience ownership changes in the future 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 carryforward. A detailed study could result in adjustment to our research and development credit carryforwards. If we determine that an ownership change has occurred and our ability to use our historical net operating loss and tax credit carryforwards is materially limited, or if our research and development carryforwards are adjusted, our use of those attributes to offset future income tax liabilities would be limited.

ITEM 1B. Unresolved Staff Comments

None.

ITEM 2. Properties

We currently sublease our corporate headquarters, which consist of approximately 10,158 square feet of office space located at 30 Winter Street, Boston, Massachusetts. Our sublease agreement continues through November 29, 2022. We believe that our existing facilities are sufficient for our current needs.

ITEM 3. Legal Proceedings

As of the date of filing this Annual Report on Form 10-K, there are no outstanding legal proceedings against us or our current officers or directors.

On July 24, 2020, the District Court for the District of Massachusetts dismissed a purported class action filed against us in 2019. This purported class action lawsuit, which we refer to as the 2019 Class Action, was filed against us and certain of our present and former officers, Michael Bailey, Matthew Dallas, and Keith Ehrlich, on February 25, 2019, in the Southern District of New York for the District of New York, captioned *David Hackel v. AVEO Pharmaceuticals, Inc., et al*, No. 1:19-cv-01722-AT. On April 12, 2019, the court granted the defendants' motion to transfer the action to the District of Massachusetts (Case No. 1:19-cv-10783-JCB). On May 6, 2019, the court appointed Andrej Hornak as lead plaintiff and approved Pomerantz LLP as lead counsel and Andrews DeValerio LLP as liaison counsel. On July 24, 2019, the plaintiffs filed an amended complaint naming Michael Needle as an additional defendant. The amended complaint purported to be brought on behalf of shareholders who purchased our common stock between May 4, 2017 through January 31, 2019. It generally alleged that we and our officers violated Sections 10(b) and/or 20(a) of the Securities Exchange Act of 1934 and Rule 10b-5 promulgated thereunder by failing to disclose and/or making allegedly false and/or misleading statements about the estimated dates by which we would report the topline results from the TIVO-3 trial, the preliminary overall survival results from the TIVO-3 trial, the sufficiency of the overall survival data from the TIVO-3 trial, the timing of the NDA submission and the risk of FDA approval. The complaint sought unspecified damages, interest, attorneys' fees, and other costs. On September 27, 2019, we filed a motion to dismiss the amended complaint. On July 24, 2020, the District Court granted our motion to dismiss. The time for appeal expired in August 2020 without appeal.

In connection with the filing of the 2019 Class Action, two derivative lawsuits were filed on July 8, 2019 and July 10, 2019 against us, certain of our present and former officers and our directors in the Suffolk Superior Court, Commonwealth of Massachusetts, captioned *Stephen Favre v. Michael P. Bailey, et al*. 19-2169-BLS2 and *Jianbin Yu v. Michael P. Bailey, et al.* 19-2188-BLS2, respectively. The complaints generally alleged breach of fiduciary duty, unjust enrichment, and waste of corporate assets due to the 2019 Class Action and the actions alleged therein. On July 26, 2019, the court granted the parties' joint motion to consolidate the cases and stay the consolidated matter pending the dismissal of, or filing of an answer to, the complaint in the 2019 Class Action. After the 2019 Class Action was dismissed and the time for appeal had expired, the parties' filed a joint stipulation to voluntarily dismiss the derivative lawsuit without prejudice. On December 8, 2020, the court entered an order dismissing the derivative action.

For a discussion of certain prior legal proceedings against us that are no longer pending, including two class action lawsuits filed against us and certain of our former officers and directors in 2013 and a lawsuit filed against us and our former officers by the SEC in 2016, each alleging that we violated federal securities laws by misleading investors about our efforts to obtain FDA approval for tivozanib, see Note 13 – "Legal Proceedings", in our consolidated financial statements included elsewhere in this Annual Report on Form 10-K

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 Information

Our common stock is traded on the Nasdaq Capital Market under the symbol "AVEO".

Holders

As of March 5, 2021, there were approximately 24 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.

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, 2020 and 2019 and the Statement of Operations Data for each of the three years in the period ended December 31, 2020 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, 2018, 2017 and 2016, and the Statement of Operations Data for each of the two years in the period ended December 31, 2017 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:	**2020**	**2019**	**2018**	**2017**	**2016**
	(in thousands, except per share data)				
Revenue (1)	$ 6,019	$ 28,795	$ 5,409	$ 7,579	$ 2,515
Operating expenses:					
Research and development	22,679	17,958	20,652	25,179	23,703
Selling, general and administrative	22,217	11,211	10,781	9,138	8,205
Settlement costs	—	—	(667)	2,073	—
Total operating expenses	44,896	29,169	30,766	36,390	31,908
Loss from operations	(38,877)	(374)	(25,357)	(28,811)	(29,393)
Interest expense, net	(1,605)	(1,815)	(2,191)	(2,373)	(1,949)
Change in fair value of PIPE Warrant liability	4,898	11,577	19,919	(33,740)	4,751
Other income (expense)	—	—	2,300	—	(195)
Net income (loss) before income taxes	(35,584)	9,388	(5,329)	(64,924)	(26,786)
Provision for income taxes	—	—	—	(101)	(101)
Net income (loss)	$ (35,584)	$ 9,388	$ (5,329)	$ (65,025)	$ (26,887)
Net income (loss) per share - basic	$ (1.66)	$ 0.61	$ (0.44)	$ (6.14)	$ (3.88)
Weighted average number of common shares outstanding (2)	21,402	15,331	12,059	10,593	6,926
Net income (loss) per share - diluted	$ (1.66)	$ 0.61	$ (1.93)	$ (6.14)	$ (3.88)
Weighted average number of common shares and dilutive common share equivalents outstanding (2)	21,402	15,376	13,073	10,593	6,926

	As of December 31,				
Balance sheet data:	**2020**	**2019**	**2018**	**2017**	**2016**
	(in thousands)				
Cash, cash equivalent, and marketable securities	$ 61,761	$ 47,745	$ 24,427	$ 33,525	$ 23,348
Working capital	48,563	29,482	9,818	18,059	15,966
Total assets	66,912	50,600	27,935	50,198	27,285
Loans payable, including current portion, net of discount	13,772	15,766	19,033	18,477	14,003
Accumulated deficit	(621,205)	(585,621)	(595,009)	(586,969)	(521,916)
Total stockholders' equity (deficit)	35,294	14,846	(27,227)	(40,763)	(1,923)

(1) Partnership-related revenues in 2020, 2019 and 2018 were recognized in accordance with ASC 606, *Revenue from Contracts with Customers*, while prior periods were recognized in accordance with legacy GAAP.

(2) On February 19, 2020, we effected a reverse stock split of our outstanding shares of common stock at a ratio of one-for-ten pursuant to a Certificate of Amendment to our Certificate of Incorporation filed with the Secretary of State of the State of Delaware. The reverse stock split was reflected on Nasdaq beginning with the opening of trading on February 20, 2020. As a result of the reverse stock split, every ten shares of our common stock issued and outstanding was converted into one share of common stock. All share amounts and per share amounts disclosed in this Annual Report on Form 10-K have been restated to reflect the reverse stock split on a retroactive basis.

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 consolidated 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 an oncology-focused biopharmaceutical company committed to delivering medicines that provide a better life for cancer patients. Our strategy is to focus our resources toward the development and commercialization of our product candidates in North America, while leveraging partnerships to support development and commercialization in other geographies. With the approval of our first commercial product, FOTIVDA® (tivozanib), in the United States, we have transitioned from a clinical development stage biopharmaceutical company to a commercial and clinical development stage biopharmaceutical company.

On March 10, 2021, the U.S. Food and Drug Administration, or FDA, approved FOTIVDA in the United States for the treatment of adult patients with relapsed or refractory advanced renal cell carcinoma, or RCC, following two or more prior systemic therapies. FOTIVDA is an oral, next-generation vascular endothelial growth factor receptor, or VEGFR, tyrosine kinase inhibitor, or TKI. The approval of FOTIVDA is based on our pivotal phase 3 randomized, controlled, multi-center, open-label clinical trial comparing tivozanib to an approved therapy, Nexavar® (sorafenib), in RCC patients whose disease had relapsed or become refractory to two or three prior systemic therapies, which we refer to as the TIVO-3 trial. The approval is also supported by three additional trials in RCC and includes safety data from over 1,000 clinical trial subjects.

We are actively preparing for the commercial launch of FOTIVDA in the United States. Our U.S. sales force, sales training, marketing, market access and medical affairs teams as well as distribution capabilities are in place and we expect to have full promotional capabilities and FOTIVDA available to patients by March 31, 2021.

FOTIVDA is also approved and commercialized through our development partner EUSA Pharma (UK) Limited, or EUSA, in the United Kingdom, Germany, Spain and certain other countries in their territory, for the treatment of adult patients with advanced RCC who are VEGFR pathway inhibitor-naïve and are either untreated or who have failed prior therapy with interferon-alpha (IFN-a) or interleukin-2 (IL-2).

Based on FOTIVDA's demonstrated anti-tumor activity, tolerability profile and reduction of regulatory T-cell production, we are studying FOTIVDA in combination with immune checkpoint inhibitors for the treatment of RCC and hepatocellular carcinoma, or HCC, in phase 2 clinical trials and we recently announced our entry into a collaboration with Bristol Myers Squibb, or BMS, to conduct a phase 3 study of FOTIVDA in combination with OPDIVO® (nivolumab), BMS's anti-PD-1 therapy, in patients with advanced relapsed or refractory RCC following prior immunotherapy exposure.

Our pipeline of product candidates includes ficlatuzumab, a potent humanized immunoglobulin G1, or IgG1, monoclonal antibody that targets hepatocyte growth factor, or HGF. We have previously reported promising early clinical data on ficlatuzumab in squamous cell carcinoma of the head and neck, or HNSCC, pancreatic cancer and acute myeloid leukemia, or AML. We are currently conducting a randomized phase 2 confirmatory study of ficlatuzumab for the potential treatment of HNSCC.

Our pipeline of product candidates also includes worldwide rights to AV-380, a potent humanized IgG1 monoclonal antibody that targets growth differentiation factor 15, or GDF15. In December 2020, the FDA accepted our investigational new drug application, or IND, for AV-380 for the potential treatment of cancer cachexia, and we have initiated a phase 1 clinical trial in healthy subjects.

Our earlier-stage pipeline under development includes AV-203 and AV-353, both as potential oncology treatments. AV-203 is a potent humanized IgG1 monoclonal antibody that targets ErbB3 (also known as HER3) to which we expect to regain worldwide rights in September 2021. AV-353 is a potent IgG1 monoclonal antibody that targets the Notch 3 pathway.

Commercial Launch

During 2020 and early 2021, in preparation for the commercial launch of FOTIVDA in the United States, we:

- expanded our organization with approximately 65 field-based employees, which includes approximately 50 oncology sales professionals;

- developed our commercial capabilities with implementation of systems and infrastructure to support our virtual and in person commercial sales organization, patient-focused programs and appropriate quality systems and compliance policies, systems and procedures; and
- established our distribution network in order to be prepared to have full promotional capabilities and product available for sale by March 31, 2021.

Other Recent Events

On December 28, 2017, we entered into the Amended and Restated Loan and Security Agreement, or the 2017 Loan Agreement, with Hercules Capital, Inc. and certain of its affiliates, or Hercules. On August 7, 2020, we entered into the first amendment to the 2017 Loan Agreement with Hercules, or the 2020 Loan Amendment, to provide us with additional term loans in an aggregate principal amount of up to $35.0 million, or the 2020 Loan Facility, in four tranches to be used to repay in full the outstanding loans under the 2017 Loan Agreement and for general working capital purposes through the commercial launch of FOTIVDA, subject to certain terms and conditions. On February 1, 2021, we entered into the second amendment to the 2017 Loan Agreement with Hercules, or the 2021 Loan Amendment, that increases the 2020 Loan Facility from up to $35.0 million to up to $45.0 million following FDA approval of FOTIVDA. On March 11, 2021, we completed a second drawdown, in the amount of $20.0 million, under the 2020 Loan Facility that was made available in connection with the FDA approval of FOTIVDA on March 10, 2021.

Financial Overview

We do not have a history of generating operating profits and, as of December 31, 2020, we had an accumulated deficit of $621.2 million. We anticipate that we will continue to incur significant operating expenses for the foreseeable future as we seek to commercialize FOTIVDA in the United States and continue our planned development activities for our clinical stage assets.

We may require substantial additional funding to advance our pipeline of clinical stage assets, and the timing and nature of these activities will be conducted subject to the availability of sufficient financial resources. Please see “Part II, Item 7. Management’s Discussion and Analysis of Financial Condition and Results of Operations — Liquidity and Capital Resources —Liquidity and Going Concern” for a further discussion of our funding requirements.

Revenue

Our revenues have historically been generated primarily through collaborative research, development and commercialization agreements. 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. In November 2017, we began earning sales royalties upon EUSA’s commencement of the first commercial launch of FOTIVDA (tivozanib).

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. On March 10, 2021, the FDA approved FOTIVDA in the United States for the treatment of adult patients with relapsed or refractory advanced RCC following two or more prior systemic therapies. We are actively preparing for the commercial launch of FOTIVDA in the United States and we expect to make FOTIVDA available to patients by March 31, 2021. We expect that any revenue we generate will fluctuate from quarter to quarter and year to year 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. If we or our strategic partners fail to complete the development of our product candidates in a timely manner or to obtain or maintain 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, including salaries, bonuses, benefits, stock-based compensation and research-related overhead;
- external development-related expenses, including clinical trials, preclinical studies, consultants and other outsourced services;
- costs of acquiring and manufacturing drug development related materials and related distribution;
- costs associated with our regulatory and quality assurance operations and medical affairs;
- upfront license payments, milestones, sublicense fees and royalties related to in-licensed products and technology; and
- allocated expenses for facilities and information technology.

Research and development expenses are net of amounts reimbursed under our agreements with Biodesix and AstraZeneca 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 will increase in 2021, principally related to increases for a full year of costs for the medical affairs function in support of the commercial launch of FOTIVDA, ficlatuzumab manufacturing of clinical supply for a potential phase 3 clinical trial in HNSCC and the conduct of the phase 1 clinical trial of AV-380 for the potential treatment of cancer cachexia. These increases will be partially offset by lower costs, principally related to the TIVO-3 trial as it nears completion and costs incurred in 2020 that will not be incurred in 2021 related to the submission of our tivozanib NDA in March 2020 and related FDA review support. The timing and nature of contemplated activities in 2021 will be conducted subject to the availability of sufficient financial resources.

Currently, we track direct external development expenses and direct salary on a program-by-program basis and allocate general-related expenses, such as indirect compensation, benefits and consulting fees, to each program based on the personnel resources allocated to such program. Facilities, IT costs and stock-based compensation are not allocated amongst programs and are considered overhead.

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 risk benefit profile of the product candidates' clinical activity, 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;
- the costs of preparing, filing and prosecuting patent applications and maintaining, enforcing and defending intellectual property-related claims; and
- additional manufacturing requirements.

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 for which we may obtain regulatory approval. 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.

Selling, General and Administrative Expenses

Selling, general and administrative expenses consist principally of compensation, benefits and travel for employees in executive, finance, legal, human resource and commercial functions. Other selling, general and administrative expenses include professional fees for audit, tax, general legal, patent legal, investor relations, commercial, consulting services and directors' fees, as well as facility and information technology-related costs not otherwise included in research and development expenses.

We anticipate that selling, general and administrative expenses will continue to increase significantly through the commercial launch of FOTIVDA and will remain consistent at that level in the second half of 2021, principally related to the addition of our salesforce, and continued expansion of our marketing, market access and commercial capabilities and general and administrative support. Accordingly, the timing and nature of contemplated activities in 2021 will be conducted subject to the availability of sufficient financial resources.

Interest Expense, Net

Interest expense consists of interest, amortization of debt discount, and amortization of deferred financing costs associated with our loans payable, and is shown net of interest income, which consists of interest earned on our cash, cash equivalents and marketable securities. The primary objective of our investment policy is capital preservation.

Income Taxes

We generated tax losses for the years ended December 31, 2020, 2019, and 2018, 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, 2020, 2019, and 2018.

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 and liabilities, the disclosure of contingent assets and liabilities at the date of the financial statements, the measurement of right-of-use assets and lease liabilities, the assessment of our ability to continue as a going concern, and the reported amounts of revenues and expenses during the reported periods. On an ongoing basis, we evaluate our estimates and judgments for changes in facts and circumstances, including those related to revenue recognition, contract research accruals, measurements of the PIPE Warrant liability, stock-based compensation, and estimates of our capital requirements over the next twelve months from the date of issuance of the annual consolidated financial statements. We base our estimates on historical experience and various other assumptions that we believe to be reasonable under the circumstances. Material changes in these estimates could occur in the future. Changes in estimates are recorded or reflected in our disclosures in the period in which they become known. Actual results may differ from our estimates if past experience or other assumptions do not turn out to be substantially accurate. Our significant accounting policies are described in the notes to our consolidated financial statements appearing elsewhere in this Annual Report on Form 10-K.

Revenue Recognition

As of December 31, 2020, our revenues have been generated primarily through collaborative research, development and commercialization agreements. The terms of these agreements generally contain multiple promised goods and services, 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 preclinical 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.

Collaboration Arrangements Within the Scope of ASC 808, Collaborative Arrangements

We analyze our collaboration arrangements to assess 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 and are therefore within the scope of ASC Topic 808, *Collaborative Arrangements*, or ASC 808. 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 606, *Revenue from Contracts with Customers*, or ASC 606. Our policy is generally to recognize amounts received from collaborators in connection with joint operating activities that are within the scope of ASC 808 as a reduction in research and development expense.

Arrangements Within the Scope of ASC 606, Revenue from Contracts with Customers

Under ASC 606, we recognize revenue when our customers obtain control of promised goods or services, in an amount that reflects the consideration which we determine we expect to receive in exchange for those goods or services. To determine revenue recognition for arrangements that we determine are within the scope of ASC 606, we perform the following five steps: (i) identify the contract(s) with a customer; (ii) identify the performance obligation(s) in the contract; (iii) determine the transaction price; (iv) allocate the transaction price to the performance obligation(s) in the contract; and (v) recognize revenue when (or as) we satisfy our performance obligation(s). As part of the accounting for these arrangements, we must make significant judgments, including identifying performance obligations in the contract, estimating the amount of variable consideration to include in the transaction price and allocating the transaction price to each performance obligation.

Once a contract is determined to be within the scope of ASC 606, we assess the goods or services promised within the contract and determine those that are performance obligations. Arrangements that include rights to additional goods or services that are exercisable at a customer's discretion are generally considered options. We assess if these options provide a material right to the customer and if so, they are considered performance obligations. The exercise of a material right is accounted for as a contract modification for accounting purposes.

We assess whether each promised good or service is distinct for the purpose of identifying the performance obligations in the contract. This assessment involves subjective determinations and requires management to make judgments about the individual promised goods or services and whether such are separable from the other aspects of the contractual relationship. Promised goods and services are considered distinct provided that: (i) the customer can benefit from the good or service either on its own or together with other resources that are readily available to the customer (that is, the good or service is capable of being distinct) and (ii) the entity's promise to transfer the good or service to the customer is separately identifiable from other promises in the contract (that is, the promise to transfer the good or service is distinct within the context of the contract). In assessing whether a promised good or service is distinct, we consider factors such as the research, manufacturing and commercialization capabilities of the collaboration partner and the availability of the associated expertise in the general marketplace. We also consider the intended benefit of the contract in assessing whether a promised good or service is separately identifiable from other promises in the contract. If a promised good or service is not distinct, an entity is required to combine that good or service with other promised goods or services until it identifies a bundle of goods or services that is distinct.

The transaction price is then determined and allocated to the identified performance obligations in proportion to their standalone selling prices, or SSP, on a relative SSP basis. SSP is determined at contract inception and is not updated to reflect changes between contract inception and when the performance obligations are satisfied. Determining the SSP for performance obligations requires significant judgment. In developing the SSP for a performance obligation, we consider applicable market conditions and relevant entity-specific factors, including factors that were contemplated in negotiating the agreement with the customer and estimated costs. We validate the SSP for performance obligations by evaluating whether changes in the key assumptions used to determine the SSP will have a significant effect on the allocation of arrangement consideration between multiple performance obligations.

If the consideration promised in a contract includes a variable amount, we estimate the amount of consideration to which we will be entitled in exchange for transferring the promised goods or services to a customer. We determine the amount of variable consideration by using the expected value method or the most likely amount method. We include the unconstrained amount of estimated variable consideration in the transaction price. The amount included in the transaction price is constrained to the amount for which it is probable that a significant reversal of cumulative revenue recognized will not occur. At the end of each subsequent reporting period, we re-evaluate the estimated variable consideration included in the transaction price and any related constraint, and if necessary, adjust our estimate of the overall transaction price. Any such adjustments are recorded on a cumulative catch-up basis in the period of adjustment.

In determining the transaction price, we adjust consideration for the effects of the time value of money if the timing of payments provides us with a significant benefit of financing. We do not assess whether a contract has a significant financing component if the expectation at contract inception is such that the period between payment by the licensees and the transfer of the promised goods or services to the licensees will be one year or less. We assess each of our revenue generating arrangements in order to determine whether a significant financing component exists and concluded that a significant financing component does not exist in any of our arrangements.

We then recognize as revenue the amount of the transaction price that is allocated to the respective performance obligation when (or as) each performance obligation is satisfied at a point in time or over time, and if over time based on the use of an output or input method.

Licenses of Intellectual Property: The terms of our license agreements include the license of functional intellectual property, given the functionality of the intellectual property is not expected to change substantially as a result of our ongoing activities. If the license to our intellectual property is determined to be distinct from the other performance obligations identified in the arrangement, we recognize revenues from the portion of the transaction price allocated to the license when the license is transferred to the licensee and the licensee is able to use and benefit from the license. For licenses that are bundled with other promises (that is, for licenses that are not distinct from other promised goods and services in an arrangement), we utilize judgment to assess the nature of the combined performance obligation to determine whether the combined performance obligation is satisfied over time or at a point in time and, if over time, the appropriate method of measuring progress for purposes of recognizing revenue. We evaluate the measure of progress each reporting period and, if necessary, adjusts the measure of performance and related revenue recognition.

Research and Development Funding: Arrangements that include payment for research and development services are generally considered to have variable consideration. If and when we assess the payment for these services is no longer subject to the constraint on variable consideration, the related revenue is included in the transaction price.

Milestone Payments: At the inception of each arrangement that includes non-refundable payments for contingent milestones, including preclinical research and development, clinical development and regulatory, we evaluate whether the milestones are considered probable of being achieved and estimate the amount to be included in the transaction price using the most likely amount method. If it is probable that a significant revenue reversal would not occur, the associated milestone value is included in the transaction price. Milestone payments that are not within the control of us or the licensee, such as regulatory approvals, are not considered probable of being achieved until those approvals are received. At the end of each reporting period, we re-evaluate the probability of the achievement of contingent milestones and the likelihood of a significant reversal of such milestone revenue, and if necessary, adjust our estimate of the overall transaction price. Any such adjustments are recorded on a cumulative catch-up basis, which would affect collaboration and licensing revenue in the period of adjustment. This quarterly assessment may result in the recognition of revenue related to a contingent milestone payment before the milestone event has been achieved.

Royalties: For arrangements that include sales-based royalties, including milestone payments based on the level of sales, and the license is deemed to be the predominant item to which the royalties relate, we recognize revenue at the later of (i) when the related sales occur, or (ii) when the performance obligation to which some or all of the royalty has been allocated has been satisfied (or partially satisfied).

The following table summarizes the total revenues earned in the years ended December 31, 2020, 2019 and 2018, respectively, by partner (in thousands). Refer to Note 4 *"Collaborations and License Agreements"* of the notes to our consolidated financial statements included elsewhere in this Annual Report on Form 10-K regarding specific details of these collaboration and license arrangements.

	Years Ended December 31,		
	2020	2019	2018
Strategic Partner:	($ in thousands)		
KKC	$ 2,800	$ 25,000	$ —
EUSA	3,219	3,795	3,409
CANbridge	—	—	2,000
Total revenues	$ 6,019	$ 28,795	$ 5,409

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, or CROs, 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 CROs, 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 CROs 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, 2020, 2019 and 2018, we had arrangements with multiple CROs 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.

Results of Operations

Comparison of Years Ended December 31, 2020, 2019 and 2018

Revenues

	Years Ended December 31,			2020 / 2019 Comparison		2019 / 2018 Comparison	
	2020	2019	2018	$	%	$	%
Strategic Partner:	($ in thousands)						
KKC	$ 2,800	$ 25,000	$ —	$ (22,200)	(89)%	$ 25,000	100%
EUSA	3,219	3,795	3,409	(576)	(15)%	386	11%
CANbridge	—	—	2,000	—	—%	(2,000)	(100)%
Total revenues	$ 6,019	$ 28,795	$ 5,409	$ (22,776)	(79)%	$ 23,386	432%

Our total revenues decreased by $22.8 million, or 79%, to $6.0 million in 2020 from $28.8 million in 2019, principally due to payments we earned pursuant to the amendment to the KKC Agreement for KKC's repurchase of the non-oncology rights to tivozanib in our territory, including the $25.0 million upfront payment we earned in 2019 offset by a $2.8 million development milestone we earned in 2020, as well as a $0.6 million decrease related to revenues from EUSA.

On August 1, 2019, we entered into an amendment to the KKC Agreement pursuant to which KKC repurchased the non-oncology rights to tivozanib in our territory, excluding the rights we have sublicensed to EUSA under the EUSA Agreement, and KKC made a $25.0 million non-refundable upfront payment to us that we received in September 2019. In the third quarter of 2019, we recognized this $25.0 million upfront payment as revenue in accordance with ASC 606. On August 2, 2020, we earned a $2.8 million development milestone payment from KKC for the acceptance of KKC's IND for a non-oncology formulation of tivozanib by the Pharmaceuticals and Medical Devices Agency of Japan. In the third quarter of 2020, we recognized this $2.8 million development milestone as revenue in accordance with ASC 606. Prior to the amendment to the KKC Agreement, KKC did not have any payment obligations to us for non-oncology rights to tivozanib in our territory. Refer to Note 4 "*Collaborations and License Agreements – In-License Agreements – Kyowa Kirin Co. (KKC)*", to our consolidated financial statements included elsewhere in this Annual Report on Form 10-K regarding the specific application of ASC 606 to our amendment to the KKC Agreement.

No milestone payments were earned under the CANbridge Agreement in 2020 or in 2019.

Revenues from EUSA decreased by $0.6 million, or 15%, in 2020 as compared to 2019. In February 2019, we earned a $2.0 million milestone payment under the EUSA Agreement for reimbursement approval for FOTIVDA (tivozanib) in the first-line treatment of RCC from the Ministry of Health, Consumer Affairs and Social Welfare in Spain. In accordance with ASC 606, we recognized $1.0 million in revenue in 2019 that was not recognized in 2020. No milestone payments were earned under the EUSA Agreement in 2020. The $1.0 million decrease in milestone revenue was partially offset by a $0.4 million increase in royalty revenue from sales of FOTIVDA to $1.2 million in 2020 from $0.8 million in 2019. Refer to Note 4 *"Collaborations and License Agreements – Out-License Agreements – EUSA*", to our consolidated financial statements included elsewhere in this Annual Report on Form 10-K regarding the specific application of ASC 606 to our EUSA Agreement.

Our total revenues increased by $23.4 million, or 432%, to $28.8 million in 2019 from $5.4 million in 2018, principally due to the $25.0 million upfront payment we earned from KKC under the August 1, 2019 amendment to the KKC Agreement, pursuant to which KKC repurchased the non-oncology rights to tivozanib in our territory, excluding the rights we have sublicensed to EUSA under the EUSA Agreement, partially offset by a $2.0 million development and regulatory milestone earned under the CANbridge Agreement in 2018 that was not earned in 2019.

Revenues from KKC were $25.0 million in 2019, as discussed above, and none in 2018. No revenues were earned from KKC in 2018 as KKC did not have any payment obligations to us for non-oncology rights to tivozanib in our territory prior to the August 1, 2019 amendment to the KKC Agreement.

Revenues from EUSA increased by $0.4 million, or 11%, in 2019 as compared to 2018. The $0.4 million increase in 2019 as compared to 2018 was principally due to the increase in royalty revenue from the sales of FOTIVDA to $0.9 million in 2019 from $0.5 million in 2018.

Revenues from CANbridge decreased by $2.0 million, or 100%, in 2019 as compared to 2018. In the third quarter of 2018, we earned a $2.0 million development and regulatory milestone under the CANbridge Agreement for regulatory approval from the NMPA of an IND application for a clinical study of AV-203 in ESCC and recognized $2.0 million as revenue in accordance with ASC 606.

Research and Development Expenses

	Years Ended December 31,			2020 / 2019 Comparison		2019 / 2018 Comparison	
	2020	2019	2018	$	%	$	%
	($ in thousands)						
Tivozanib	$ 17,435	$ 12,148	$ 18,249	$5,287	44%	$(6,101)	(33)%
AV-380	2,550	3,379	—	(829)	(25)%	3,379	100%
Ficlatuzumab	1,187	1,143	586	44	4%	557	95%
AV-203	—	—	670	—	—%	(670)	(100)%
Overhead	1,507	1,288	1,147	219	17%	141	12%
Total research and development expenses	$ 22,679	$ 17,958	$ 20,652	$4,721	26%	$(2,694)	(13)%

Our total research and development expenses increased by $4.7 million, or 26%, to $22.7 million in 2020 from $18.0 million in 2019, principally due to an increase of $5.3 million in tivozanib-related expenses, partially offset by a decrease of $0.8 million in AV-380 related expenses. Our total research and development expenses decreased by $2.7 million, or 13%, to $18.0 million in 2019 from $20.7 million in 2018, principally due to a decrease of $6.1 million in tivozanib-related expenses, partially offset by an increase of $3.4 million in AV-380 related expense.

Tivozanib expenses increased by $5.3 million, or 44%, in 2020 as compared to 2019. The $5.3 million increase was principally due to increases totaling $7.4 million, including: (i) $3.4 million related to the tivozanib NDA for RCC, including $0.5 million related to the completion of the NDA submission and ongoing support of the FDA's review of the NDA and the $2.9 million application user fee pursuant to the PDUFA that was due upon the filing of the tivozanib NDA on March 31, 2020, (ii) $0.6 million related to the DEDUCTIVE trial that was initiated in September 2019, net of cost sharing with AstraZeneca, and (iii) $3.4 million in commercial launch-readiness initiatives incurred in 2020 that were not incurred in 2019, including $1.7 million related to the conduct of certain post-commercial launch drug supply manufacturing, $1.3 million related to the buildout of our medical affairs function and $0.4 million related to other commercial-launch readiness initiatives.

These increases were partially offset by decreases totaling $2.3 million, principally including: (i) $1.8 million related to lower expenses in connection with the TIVO-3 and TiNivo trials that are nearing completion and (ii) $0.5 million related to fluctuations in the year-to-year sublicense fees due to KKC in connection with a milestone we earned under our EUSA Agreement in 2019 that was not earned in 2020.

Tivozanib expenses decreased by $6.1 million, or 33%, in 2019 as compared to 2018. The $6.1 million decrease in 2019 as compared to 2018 was principally due to decreases of $4.2 million related to lower expenses in connection with the TIVO-3 and TiNivo trials as a result of a lower number of patients on treatment, $1.1 million related to commercial drug manufacturing conducted in 2018 that was not incurred in 2019, $0.6 million related to fluctuations in the year-to-year sublicense fees due to KKC in connection with milestones we earned under our EUSA Agreement and $0.7 million related to fluctuations in the year-to-year conduct of NDA submission preparation. These decreases were partially offset by an increase of $0.4 million related to the commencement of the DEDUCTIVE trial in HCC in 2019, net of cost sharing with AstraZeneca.

AV-380 expenses were $2.6 million, $3.4 million and $0 in 2020, 2019 and 2018, respectively. The $0.8 million decrease in 2020 as compared to 2019 was principally due to the $2.3 million time-based milestone obligation due to St. Vincent's Hospital Sydney Limited, or St. Vincent's, under our license agreement with St. Vincent's, in the first quarter of 2019 that was not incurred in 2020, partially offset by an increase of $1.5 million related to pre-clinical development costs incurred in 2020 that were not incurred in 2019. In 2019, we incurred a total of $3.4 million in expenses, including the $2.3 million time-based milestone obligation due to St. Vincent's in January 2019 and $1.1 million of expenses related to the initiation of pre-clinical development following the return of the AV-380 program to us by Novartis International Pharmaceutical, Ltd., or Novartis. In 2018, we did not incur any AV-380 related expenses.

Ficlatuzumab expenses were flat in 2020 as compared to 2019. Ficlatuzumab expenses increased by $0.6 million, or 95%, in 2019 as compared to 2018 principally due to the commencement of the CyFi-2 trial in AML in November 2019, net of cost sharing with Biodesix. In March 2020, we decided to discontinue the CyFi-2 trial due to the urgent shift in priorities among clinical trial sites towards efforts to combat the COVID-19 pandemic, which had impacted the trial enrollment timeline and the feasibility of completing the study within the shelf-life of the current ficlatuzumab clinical trial drug supply.

We did not incur any expenses related to AV-203 in 2020 or 2019. AV-203 expenses were $0.7 million in 2018 and comprised the $0.7 million sublicense fee due to Biogen in connection with the $2.0 million development and regulatory milestone we earned in the third quarter of 2018 under the CANbridge Agreement for regulatory approval from the NMPA of an IND application for a clinical study of AV-203 in ESCC. No milestones were earned nor sublicense fees incurred under the CANbridge Agreement in 2020 or 2019.

We anticipate that research and development expenses will increase in 2021, principally related to increases for a full year of costs for the medical affairs function in support of the commercial launch of FOTIVDA, ficlatuzumab manufacturing of the clinical supply for a potential phase 3 clinical trial in HNSCC and the conduct of the phase 1 clinical trial of AV-380 for the potential treatment of cancer cachexia. These increases will be partially offset by lower costs, principally related to the TIVO-3 trial as it nears completion and costs incurred in 2020 that will not be incurred in 2021 related to the submission of our tivozanib NDA on March 31, 2020 and related FDA review support. The timing and nature of contemplated activities in 2021 will be conducted subject to the availability of sufficient financial resources.

Selling, General and Administrative Expenses

	Years Ended December 31,			2020 / 2019 Comparison		2019 / 2018 Comparison	
	2020	2019	2018	$	%	$	%
	($ in thousands)						
Selling, general and administrative	$ 22,217	$ 11,211	$ 10,781	$ 11,006	98%	$ 430	4%

Selling, general and administrative expenses increased by $11.0 million, or 98%, to $22.2 million in 2020 from $11.2 million in 2019. The $11.0 million increase was principally due to $11.2 million in total increases, including: (i) $8.5 million in commercial launch-readiness initiatives incurred in 2020 that were not incurred in 2019, including $3.1 million in compensation costs related to the growth in our commercial infrastructure and $5.4 million related to external commercial-launch readiness activities in marketing, market access and commercial operations, (ii) $2.3 million in other professional fees, and (iii) $0.4 million in other compensation-related costs. These increases were partially offset by $0.2 million in lower facility costs resulting from our corporate headquarters move in 2020 to 30 Winter Street in Boston, Massachusetts.

Selling, general and administrative expenses increased by $0.4 million, or 4%, to $11.2 million in 2019 from $10.8 million in 2018. The $0.4 million increase in 2019 as compared to 2018 was principally due to increases in compensation-related costs.

We anticipate that selling, general and administrative expenses will continue to increase significantly through the commercial launch of FOTIVDA and will remain consistent at that level in the second half of 2021, principally related to the addition of our salesforce, and continued expansion of our marketing, market access and commercial capabilities and general and administrative support. Accordingly, the timing and nature of contemplated activities in 2021 will be conducted subject to the availability of sufficient financial resources.

Settlement Costs

	Years Ended December 31,			2020 / 2019 Comparison		2019 / 2018 Comparison	
	2020	2019	2018	$	%	$	%
	($ in thousands)						
Settlement costs	$ —	$ —	$ (667)	$ —	—%	$ 667	(100)%

We did not incur any settlement costs in 2020 or 2019. Settlement costs were $(0.7) million in 2018. In December 2017, we entered into a binding memorandum of understanding related to a class action settlement that included the issuance of 200,000 warrants to purchase shares of our common stock, or the Settlement Warrants. The Settlement Warrants were revalued at each balance sheet date prior to their issuance on July 16, 2018. Refer to Note 3, "*Significant Accounting Policies - Prior Class Action Settlement and Settlement Warrants*" to our consolidated financial statements included elsewhere in this Annual Report on Form 10-K.

Change in Fair Value of PIPE Warrant Liability

	Years Ended December 31,			2020 / 2019 Comparison		2019 / 2018 Comparison	
	2020	2019	2018	$	%	$	%
	($ in thousands)						
Change in fair value of PIPE Warrant liability	$ 4,898	$ 11,577	$ 19,919	$ (6,679)	(58)%	$ (8,342)	(42)%

In May 2016, we issued PIPE Warrants, or 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 and any changes in fair value are recorded as a non-cash gain or (loss) in our Statement of Operations as a component of other income (expense).

In 2020, we recorded an approximate non-cash gain of $4.9 million in our Statement of Operations attributable to the decrease in the fair value of the PIPE Warrant liability that resulted from a lower stock price of $5.77 on December 31, 2020 compared to the stock price of $6.20 on December 31, 2019, a decrease in our stock volatility rate and a shorter remaining term as the PIPE Warrants approach expiration in May 2021.

In 2019, we recorded an approximate non-cash gain of $11.6 million in our Statement of Operations attributable to the decrease in the fair value of the PIPE Warrant liability that principally resulted from a lower stock price of $6.20 on December 31, 2019 compared to the stock price of $16.00 on December 31, 2018.

In 2018, we recorded an approximate non-cash gain of $19.9 million in our Statement of Operations attributable to the decrease in the fair value of the PIPE Warrant liability that principally resulted from a lower stock price of $16.00 on December 31, 2018 compared to the stock price of $27.90 on December 31, 2017.

Other Income (Expense)

	Years Ended December 31,			2020 / 2019 Comparison		2019 / 2018 Comparison	
	2020	2019	2018	$	%	$	%
	($ in thousands)						
Other income (expense)	$ —	$ —	2,300	$ —	—%	$ (2,300)	(100)%

In 2020 and 2019, we did not recognize any other income or other expense. Other income (expense) was $2.3 million in 2018. In 2018, we recognized other income for the one-time payment by Novartis to us of $2.3 million in connection with the return of the AV-380 program to us. In August 2015, in connection with our AV-380 program, we entered into a license agreement with Novartis that was subsequently terminated by Novartis effective August 28, 2018. In December 2018, we entered into an agreement with

Novartis to further establish and clarify the terms on which the AV-380 program was to be returned to us, or the AV-380 Transfer Agreement. Pursuant to the AV-380 Transfer Agreement, Novartis was obligated to make a one-time payment to us of $2.3 million. The $2.3 million payment due from Novartis was not considered a revenue transaction due to the effective termination of the Novartis Agreement on August 28, 2018 and was instead considered other income. Refer to Note 4 *"Collaborations and License Agreements – Novartis"*, to our consolidated financial statements included elsewhere in this Annual Report on Form 10-K.

Interest Expense, net

	Years Ended December 31,			2020 / 2019 Comparison		2019 / 2018 Comparison	
	2020	2019	2018	$	%	$	%
	($ in thousands)						
Interest expense, net	$ (1,605)	$ (1,815)	$ (2,191)	$ 210	(12)%	$ 376	(17)%

Interest expense, net decreased by $0.2 million, or 12%, in 2020 as compared to 2019. This decrease was principally due to the decrease in interest expense resulting from the paydown of principal under our 2017 Loan Agreement with Hercules and a lower interest rate that ranged from 9.45% to 9.65% in 2020 as compared to the interest rate that ranged from 9.70% to 10.2% in 2019. Principal payments to Hercules resumed during the period from August 1, 2019 through August 1, 2020.

In August 2020, we entered into the 2020 Loan Amendment with Hercules to provide us with the 2020 Loan Facility, an additional term loan in an aggregate principal amount of up to $35.0 million in four tranches to be used to refinance outstanding loans under the 2017 Loan Agreement and for general working capital purposes through the commercial launch of FOTIVDA, subject to certain terms and conditions. We received the initial $15.0 million of the 2020 Loan Facility upon the closing of the 2020 Loan Amendment, including approximately $9.7 million of which was used to retire the outstanding balance under the 2017 Loan Agreement and approximately $5.3 million of which is new loan funding. The 2020 Loan Amendment provides for an initial interest-only period effective for the period from September 1, 2020 through September 1, 2021. See "Part II, Item 7. Management's Discussion and Analysis of Financial Condition and Results of Operations — Liquidity and Capital Resources — Hercules Loan Facility" below for a description of the 2017 Loan Agreement, 2020 Loan Amendment and 2020 Loan Facility.

Interest expense, net decreased by $0.4 million, or 17%, in 2019 as compared to 2018 principally due to an increase in interest income from the investment of the higher balances of our cash equivalents and marketable securities.

We anticipate that interest expense, net will increase in 2021 due to the higher loan balance and interest-only period through September 1, 2021 pursuant to the 2020 Loan Amendment with Hercules, and lower investment income due to current market conditions.

Contractual Obligations and Commitments

Hercules Loan Facility

On August 7, 2020, we entered into the 2020 Loan Amendment with Hercules. The 2020 Loan Amendment provides us with the 2020 Loan Facility, an additional term loan of up to $35.0 million in four tranches to be used to refinance outstanding loans under the 2017 Loan Agreement and for general working capital purposes through the commercial launch of FOTIVDA, subject to certain terms and conditions. The 2020 Loan Facility includes (i) $15.0 million in initial funding upon execution of the 2020 Loan Amendment to retire the outstanding balance of approximately $9.7 million under the 2017 Loan Agreement and to provide approximately $5.3 million in new loan funding, and (ii) up to $20.0 million in additional loan funding following FDA approval of FOTIVDA and our net product revenues from sales of FOTIVDA, within certain time frames and subject to certain terms and conditions.

On February 1, 2021, we entered into the 2021 Loan Amendment with Hercules. The 2021 Loan Amendment increases the 2020 Loan Facility from up to $35.0 million to up to $45.0 million upon FDA approval of FOTIVDA. The 2021 Loan Amendment makes certain changes to the 2020 Loan Amendment, including, among other things, increasing the amount of Tranche Two funding for Performance Milestone I for FDA approval of FOTIVDA from $10.0 million to $20.0 million, thereby increasing the total amount of unfunded term loan commitments under the 2020 Loan Facility from $20.0 million to $30.0 million following FDA approval of FOTIVDA and our net product revenues from sales of FOTIVDA, within certain time frames and subject to certain terms and conditions. For more information, see "Part II, Item 7. Management's Discussion and Analysis of Financial Condition and Results of Operations — Liquidity and Capital Resources —Hercules Loan Facility" below, as well as Note 6, "—Hercules Loan Facility" of the Notes to our consolidated financial statements, each included elsewhere in this Annual Report on Form 10-K.

Collaborations and License Agreements

Under our license agreement with KKC, we are required to pay tiered royalty payments on net sales we make of FOTIVDA in our North American territory, which range from the low to mid-teens as a percentage of net sales. We are also required to pay KKC 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. Also, under our license agreement with St. Vincent's, we are required to make certain milestone payments upon the earlier of the 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. We are also obligated to pay Biogen a percentage of milestone payments received by us from future partnerships after March 28, 2016 and single digit royalty payments on net sales related to the sale of ErbB3 products, if any, up to a cumulative maximum amount of $50.0 million. In addition, we are obligated to pay Biodesix a low double digit royalty on future product sales and 25% of future licensing revenue (excluding contributions to research and development expenses), less approximately $2.5 million that Biodesix would be required to pay to us pursuant to the October 2016 amendment to the Biodesix Agreement. At this time, we cannot reasonably estimate when or if we may be required to make other additional payments to KKC, St. Vincent's, Biogen or Biodesix. For example, we are required to make future milestone payments to St. Vincent's, up to an aggregate total of $14.4 million, upon the earlier of the achievement of specified development and regulatory milestones or a specified date for the first indication and second indication, and upon the achievement of specified development and regulatory milestones for the third indication, for licensed therapeutic products, some of which payments may be increased by a mid to high double digit percentage rate for milestone payments made after we grant any sublicense under the license agreement, depending on the sublicensed territory. For more information, see Note 6, "—Collaborations and License Agreements" of the Notes to our consolidated financial statements, included elsewhere in this Annual Report on Form 10-K.

Winter Street Lease

On March 5, 2020, we entered into a sublease agreement for office space located at 30 Winter Street in Boston, Massachusetts (the "Winter Street Sublease") to relocate our corporate headquarters located at One Broadway in Cambridge, Massachusetts. Under the terms of the Winter Street Sublease, we lease 10,158 square feet of office space for $47.00 per square foot, or approximately $0.5 million per year in base rent subject to certain operating expenses, taxes and annual base rent increases of approximately 3%. The sublease term will continue through November 29, 2022.

Other Funding Commitments

We enter into contracts in the normal course of business with CROs for preclinical research studies and clinical trials. We have contracts with CROs for our TIVO-3, DEDUCTIVE and TiNivo trials, as well as our Phase 1 trial in AV-380. These contracts generally provide for termination on notice with no early termination fees. We have also entered into a contract with a third-party contract manufacturer for the manufacture of clinical drug supply for tivozanib and commercial drug supply for FOTIVDA in the United States, which includes minimum annual purchase requirements, in the approximate amount of $1.4 million for the next few years. In addition, we have entered into contracts with another contract manufacturer for the manufacture of clinical drug supply for ficlatuzumab and AV-380, for which we have manufacturing commitments in 2021, in the aggregate amount of approximately $10.3 million.

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, 2020, we had cash and cash equivalents of approximately $61.8 million. See "Part II, Item 7. Management's Discussion and Analysis of Financial Condition and Results of Operations — Liquidity and Capital Resources —Liquidity 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. Currently, our funds are invested in a United States government money market fund. The following table sets forth the primary sources and uses of cash for each of the periods set forth below (in thousands):

	Years Ended December 31,		
	2020	2019	2018
	(in thousands)		
Net cash used in operating activities	$ (37,983)	$ (2,919)	$ (25,026)
Net cash provided by (used in) investing activities	17,704	(17,917)	18,579
Net cash provided by financing activities	52,255	26,194	15,925
Net increase in cash and cash equivalents	$ 31,976	$ 5,358	$ 9,478

Our operating activities used cash of $38.0 million, $2.9 million and $25.0 million in 2020, 2019 and 2018, respectively. Cash used in operations was principally due to our net income (loss) adjusted for non-cash items and changes in working capital.

Our investing activities provided cash of $17.7 million and $18.6 million in 2020 and 2018, respectively, and used cash of $17.9 million in 2019, principally due to net changes in the maturities and purchases of marketable securities.

Our financing activities provided cash of $52.3 million, $26.2 million and $15.9 million in 2020, 2019 and 2018, respectively.

In 2020, we raised approximately $52.2 million in funding, including approximately $47.7 million in net proceeds from the sale of approximately 9.7 million shares of our common stock in an underwritten public offering in June 2020, approximately $5.1 million in new loan funding pursuant to the 2020 Loan Amendment with Hercules, net of transaction costs, and approximately $5.9 million in net proceeds from the sale of approximately 1.1 million shares of our common stock in November 2020 pursuant to our "at-the-market" sales agreement with SVB Leerink LLC, or SVB Leerink, which we refer to as the SVB Leerink Sales Agreement, partially offset by approximately $6.5 million in total principal payments pursuant to a prior loan facility with Hercules from May 2010, or the 2010 Loan Agreement, during the period from January 2020 through August 2020.

In 2019, we raised approximately $30.3 million in net proceeds from the issuance of our common stock, including $7.5 million in net proceeds from the sale of approximately 1.3 million shares of our common stock pursuant to the SVB Leerink Sales Agreement in February 2019 and approximately $22.8 million in net proceeds from the sale of approximately 2.2 million shares of our common stock and warrants to purchase an aggregate of 2.5 million shares of our common stock in an underwritten public offering in April 2019, offset in part by approximately $4.1 million in debt-related payments pursuant to our 2010 Loan Agreement, including approximately $3.8 million in total principal payments during the period from August 2019 through December 2019 and a $0.3 million end-of-term fee in December 2019.

In 2018, we raised approximately $16.4 million in net proceeds from the issuance of our common stock, including approximately $5.1 million in net proceeds from an underwritten public offering of approximately 0.3 million shares of our common stock in August 2018, $10.3 million in net proceeds from the sale of approximately 0.5 million shares of our common stock pursuant to the SVB Leerink Sales Agreement in the fourth quarter of 2018 and approximately $1.0 million from the exercise of PIPE Warrants and stock options, offset in part by a $0.5 million end-of-term debt payment in January 2018 pursuant to our 2010 Loan Agreement.

Public Offering – June 2020

On June 19, 2020, we completed an underwritten public offering of 9,725,000 shares of our common stock, including the partial exercise by the underwriters of their option to purchase an additional 1,225,000 shares, at the public offering price of $5.25 per share for gross proceeds of approximately $51.1 million. Three stockholders each beneficially holding more than 5% of our voting securities, including an entity affiliated with New Enterprise Associates and two other stockholders purchased an aggregate of 4,503,571 shares in this offering at the same public offering price per share as the other investors. At such time, entities affiliated with New Enterprise Associates (collectively) beneficially held more than 5% of our voting securities. The net offering proceeds to us were approximately $47.7 million after deducting underwriting discounts and commissions and estimated offering expenses payable by us.

Hercules Loan Facility

On December 28, 2017, we entered into the 2017 Loan Agreement to refinance in full the 2010 Loan Agreement. The 2017 Loan Agreement provided for a term loan, or the 2017 Loan, subject to certain terms and conditions, in the aggregate principal amount of $20.0 million. The 2017 Loan: (i) was scheduled to mature on July 1, 2021, (ii) accrued interest at the greater of 9.45% and an amount equal to 9.45% plus the prime rate minus 4.75% (subject to a 15.0% cap), and (iii) had an interest-only period that began on the closing date of the 2017 Loan Agreement and ended on August 1, 2019, with equal installments of principal due thereafter until the maturity date.

On August 7, 2020, we entered into the 2020 Loan Amendment, to provide us, subject to certain terms and conditions, with additional term loans in an aggregate principal amount of up to $35.0 million, or the 2020 Loan Facility, to be used to repay in full the 2017 Loan and for general working capital purposes. The 2020 Loan Facility was made available to us in four tranches, the first of which, in the amount of $15.0 million, was made available to us immediately upon the closing of the 2020 Loan Amendment. We used the $15.0 million in proceeds of the first tranche as follows: approximately $9.7 million was used to repay the outstanding balance of the 2017 Loan in full, and approximately $5.3 million was used for general working capital purposes. In connection with the 2020 Loan Amendment, we incurred approximately $0.3 million in loan issuance costs paid directly to Hercules, which are accounted for as a loan discount. The 2020 Loan Amendment was accounted for as a loan modification in accordance with ASC 470-50.

The remaining $20.0 million of term loans available to us under the 2020 Loan Facility subject to, among other terms and conditions, the achievement of the following milestones: (i) Tranche Two in the amount of $10.0 million, would be available through June 30, 2021 upon achieving Performance Milestone I for FDA approval of FOTIVDA, (ii) the third tranche, or Tranche Three, in the amount of $5.0 million, would be available from July 1, 2021 through January 31, 2022 if we achieve $20.0 million in net product revenues from sales of FOTIVDA, following FDA approval, by no later than December 31, 2021, or Performance Milestone II, and (iii) the fourth tranche, or Tranche Four, in the amount of $5.0 million, would be available through June 30, 2022 if we achieve both Performance Milestone I and Performance Milestone II, and if Hercules consents to the advancement of Tranche Four.

The 2020 Loan Amendment also amended the 2017 Loan Agreement by: (i) extending maturity of the loans from July 1, 2021 until September 1, 2023, which is extendable to September 1, 2024 upon our option if the Tranche Three funding has occurred, (ii) providing for an interest-only period beginning on the closing date of 2020 Loan Amendment and ending September 30, 2021, which period may be extended through September 30, 2022 provided we achieved Performance Milestone I, and further extendable through March 31, 2023 if the Tranche Three funding has occurred, and (iii) revising the interest rate to the greater of 9.65% and an amount equal to 9.65% plus the prime rate minus 3.25% (subject to a 15% cap). Principal payments are scheduled to commence on October 1, 2021, at the earliest, as described above. The interest rate as of December 31, 2020 was 9.65%.

Pursuant to the terms of the Loan Agreement, principal will be repaid in equal monthly installments following the conclusion of the interest-only period. We may prepay all of the outstanding principal and accrued interest under the Loan Agreement, subject to a prepayment charge up to 3.0% in the first year following the closing of the 2020 Loan Amendment, decreasing to 2.0% in year two and 1.0% in year three. We are obligated to make an end-of-term payment of (i) 6.95% of the aggregate amount of loan funding received under the Loan Agreement on the earlier of the maturity of the loans or the date on which we prepay the outstanding loan balance in full, and (ii) an approximate $0.8 million payment due on the earlier of July 1, 2021 or the date on which we prepay the outstanding loan balance in full.

The Loan Agreement includes (i) a financial covenant that we maintain minimum unrestricted cash positions of $10.0 million through the date the Second Tranche funding is received, $15.0 million through the date the Third Tranche funding is received and $10.0 million thereafter through the maturity of the Loan Agreement, and (ii) an operating covenant that we achieve greater than or equal to 75% of our forecasted net product revenues from our sales of tivozanib over a 6-month trailing period, as defined and measured on a monthly basis, commencing upon the earlier to occur of (x) the Third Tranche funding and (y) the month of April 2022. The Loan Agreement also includes various other affirmative and negative covenants, including covenants to deliver certain financial reports; to maintain insurance coverage; and to refrain from transferring assets, incurring additional indebtedness, engaging in mergers or acquisitions, paying dividends or making other distributions, making investments, creating liens, and suffering a change in control, in each case subject to certain exceptions.

On February 1, 2021, we entered into the 2021 Loan Amendment. The 2021 Loan Amendment increased the aggregate principal amount of loans available under the 2020 Loan Facility from up to $35.0 million to up to $45.0 million following FDA approval of FOTIVDA. The 2021 Loan Amendment also (i) increased Tranche Two funding upon achieving Performance Milestone I from $10.0 million to $20.0 million, (ii) increased the amount of net product revenues from sales of FOTIVDA required for us to achieve Performance Milestone II from $20.0 million to $35.0 million, and changed the deadline for achieving Performance Milestone II from December 31, 2021 to April 1, 2022, and (iii) increased the amount of unrestricted cash required for us to satisfy the minimum financial covenant during the period between receiving Tranche Two funding and Tranche Three funding from $10.0 million to $15.0 million.

On March 11, 2021, we completed the $20.0 million drawdown of Tranche Two funding under the 2021 Loan Amendment that was made available in connection with the achievement of Performance Milestone I upon FDA approval of FOTIVDA on March 10, 2021. The achievement of Performance Milestone I extended the interest-only period by twelve months from September 30, 2021 to September 30, 2022 and increased the amount of unrestricted cash required for us to satisfy the minimum financial covenant during the period between receiving Tranche Two funding and Tranche Three funding from $10.0 million to $15.0 million.

Obligations under the Loan Agreement are secured by substantially all of our assets, excluding intellectual property. The Loan Agreement provides that certain events shall constitute a default by us, including failure by us to pay amounts under the Loan Agreement when due; breach or default in the performance of any covenant under the Loan Agreement by us, subject to certain cure periods; our insolvency and certain other bankruptcy proceedings involving us; our default of obligations involving indebtedness in excess of $500,000; and the occurrence of an event or circumstance that would have a material adverse effect upon our business.

We have determined that the risk of subjective acceleration under the material adverse events clause included in the 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, 2020, 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 Agreement. We do not believe that there has been a material adverse change as defined in the Loan Agreement.

Universal Shelf Registration Statement

On November 9, 2020, we filed a shelf registration statement on Form S-3 with the SEC, which covers the offering, issuance and sale of up to $300.0 million of our common stock, preferred stock, debt securities, warrants and/or units, or the 2020 Shelf. The 2020 Shelf (File No. 333-249982) was declared effective by the SEC on November 18, 2020 and was filed to replace our then existing shelf registration statement, which was terminated. As of December 31, 2020, there was approximately $268.2 million available for future issuance of our common stock, preferred stock, debt securities, warrants and/or units.

Public Offering – April 2019

In April 2019, we completed an underwritten public offering of 2,173,913 shares of our common stock and warrants to purchase an aggregate of 2,500,000 shares of our common stock, which we refer to herein as the Offering Warrants, including warrants to purchase an aggregate of 326,086 shares of our common stock sold pursuant to the underwriter's partial exercise of its overallotment option, at the public offering price of $11.40 per share and $0.10 per warrant for gross proceeds of approximately $25.0 million. The Offering Warrants were immediately exercisable upon issuance at an exercise price of $12.50 per share, subject to adjustment in certain circumstances, and will expire two years from the date of issuance. Any Offering Warrants that have not been exercised for cash prior to their expiration shall be automatically exercised via cashless exercise on the expiration date. The shares and warrants were issued separately and are separately transferable. An entity affiliated with New Enterprise Associates purchased 434,782 shares and warrants to purchase an aggregate of 434,782 shares in this offering at the same public offering price per share as the other investors. At such time, entities affiliated with New Enterprise Associates (collectively) beneficially held more than 5% of our voting securities. The net offering proceeds to us were approximately $22.8 million after deducting underwriting discounts and commissions and estimated offering expenses payable by us. As of December 31, 2020, Offering Warrants to purchase 2,500,000 shares of our common stock were outstanding, at an exercise price of $12.50 per share, with an expiration date of April 8, 2021.

In March 2021, Offering Warrants exercisable for 247,391 shares of common stock had been exercised, for approximately $3.1 million in cash proceeds, and Offering Warrants exercisable for 2,252,609 shares of common stock were outstanding.

Sales Agreement with SVB Leerink

In February 2018, we entered into the SVB Leerink Sales Agreement with SVB 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 SVB Leerink as our sales agent, with any sales of common stock through SVB 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, or in other transactions. Any such shares of common stock will be sold pursuant to a prospectus supplement filed under the 2017 Shelf, as defined below. We agreed to pay SVB Leerink a commission of up to 3% of the gross proceeds of any sales of common stock pursuant to the SVB Leerink Sales Agreement. In the fourth quarter of 2018, we sold approximately 0.5 million shares pursuant to the SVB Leerink Sales Agreement, resulting in approximately $10.3 million in proceeds, net of commissions. In February 2019, we sold approximately 1.3 million shares pursuant to the SVB Leerink Sales Agreement, resulting in proceeds of approximately $7.5 million, net of commissions. In the fourth quarter of 2020, we sold approximately 1.1 million shares as a block pursuant to the SVB Leerink Sales Agreement, resulting in proceeds of approximately $5.9 million, net of commissions. As of December 31, 2020, approximately $25.7 million was available for future issuance pursuant to the SVB Leerink Sales Agreement.

Public Offering – August 2018

On August 21, 2018, we closed an underwritten public offering of approximately 0.3 million shares of our common stock at the public offering price of $22.60 per share for gross proceeds of approximately $5.7 million. Two greater than 5% stockholders, including an entity affiliated with New Enterprise Associates and another stockholder purchased approximately 0.2 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 $5.1 million after deducting underwriting discounts and estimated offering expenses payable by us.

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 1,764,242 units, at a price of $9.65 per unit, for gross proceeds of approximately $17.0 million. Each unit consisted of one share of our common stock and a PIPE Warrant to purchase one share of our common stock. The PIPE Warrants have an exercise price of $10.00 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 54,402 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. As of December 31, 2020, PIPE Warrants exercisable for 1,683,933 shares of common stock were outstanding, at an exercise price of $10.00 per share, with an expiration date of May 16, 2021.

Liquidity 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 commercialize FOTIVDA in the United States and develop our clinical stage assets and, ultimately, upon our ability to create shareholder value.

On March 10, 2021, the FDA approved FOTIVDA in the United States for the treatment of adult patients with relapsed or refractory advanced RCC following two or more prior systemic therapies. We anticipate that we will continue to incur significant operating expenses for the foreseeable future as we commercialize FOTIVDA in the United States and continue our planned development activities for our clinical stage assets. Our future product revenues will depend upon the size of markets in which FOTIVDA, and any future products, have received approval, and our ability to achieve sufficient market acceptance, reimbursement from third-party payers and adequate market share for FOTIVDA and any future products in those markets. The likelihood of our long-term success must be considered in light of the expenses, difficulties and potential delays that may be encountered in the development and commercialization of new pharmaceutical products, competitive factors in the marketplace and the complex regulatory environment in which we operate. Absent the realization of sufficient revenues from product sales to support our cost structure, we may never attain or sustain profitability. We may require substantial additional funding to advance our pipeline of clinical stage assets, and the timing and nature of these activities will be conducted subject to the availability of sufficient financial resources.

During the year ended December 31, 2020, we received approximately $65.3 million in funding, including approximately $53.6 million in equity funding, approximately $5.1 million in new loan funding pursuant to the August 2020 Loan Amendment with Hercules, net of transaction costs, and approximately $6.6 million in partnership funding for cost sharing obligations, royalties from the sales of FOTIVDA by EUSA and a development milestone payment by KKC. The $53.6 million in equity finding included approximately $47.7 million in net proceeds from the sale of approximately 9.7 million shares of our common stock in an underwritten public offering in June 2020 and approximately $5.9 million in net proceeds from the sale of approximately 1.1 million shares of our common stock pursuant to the SVB Leerink Sales Agreement.

We believe that our $61.8 million in cash and cash equivalents as of December 31, 2020, along with proceeds from the $20.0 million drawdown under the 2020 Loan Facility in March 2021 and from warrant exercises to date, together with anticipated partnership cost sharing reimbursements, royalties from EUSA's FOTIVDA sales, product revenues upon the commercial launch of FOTIVDA in the United States and the potential additional $10.0 million in credit under the Loan Agreement, as described above in "Liquidity and Capital Resources—Hercules Loan Facility", would allow us to fund our planned operations into 2022.

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:

- the cost of commercialization activities of FOTIVDA in the United States and any of our product candidates that may be approved for sale, including marketing, sales and distribution costs;
- the cost of manufacturing FOTIVDA in the United States, our product candidates and any additional products we may successfully commercialize;
- 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, completing our clinical trials and 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, or under any other agreements with third parties;
- the cost and outcome of any legal actions against us;
- the timing, receipt and amount of sales of, or royalties on, tivozanib and our future products, if any;
- general economic, industry and market conditions; and

- the impact of COVID-19 on our operations, business and prospects.

We may require substantial additional funding to advance our pipeline of clinical stage assets. 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 product 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 funding to advance our pipeline of clinical stage assets, whether on terms that are acceptable to us, or at all or if we were to default under the Loan Agreement, and Hercules accelerated the then remaining principal payments and fees due under the loan, 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, 2020, we had cash and cash equivalents of approximately $61.8 million, consisting of cash on deposit with banks and a U.S. government money market fund. 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, 2020, our aggregate principal balance outstanding on our 2017 Loan Agreement as amended by the 2020 Loan Amendment was approximately $15 million. Per annum interest is payable on the principal balance of the loan each month it remains outstanding at the greater of 9.65% or an amount equal to 9.65% plus the prime rate minus 3.25% as determined daily, provided however, that the per annum interest rate shall not exceed 15.0%. As of December 31, 2020, the interest rate was 9.65%. For every 1% increase in the prime rate over 3.25%, given the amount of debt outstanding under the 2017 Loan Agreement as amended by the 2020 Loan Amendment as of December 31, 2020, 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 CROs and investigational sites that are located around the world. We are subject to fluctuations in foreign currency rates in connection with these agreements. We do not currently hedge our foreign currency exchange rate risk.

ITEM 8. Financial Statements and Supplementary Data

AVEO PHARMACEUTICALS, INC.

INDEX TO CONSOLIDATED FINANCIAL STATEMENTS

REPORT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

To the 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, 2020 and 2019, the related consolidated statements of operations, comprehensive income (loss), stockholder's equity (deficit) and cash flows for each of the three years in the period ended December 31, 2020, 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, 2020 and 2019, and the results of its operations and its cash flows for each of the three years in the period ended December 31, 2020, 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, 2020, 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 16, 2021 expressed an unqualified opinion thereon.

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 risk of material misstatement of the financial statements, whether due to error or fraud, and performing procedures that respond to those risks. Such procedures included 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.

Critical Audit Matter

The critical audit matter communicated below is a matter arising from the current period audit of the financial statements that was communicated or required to be communicated to the audit committee and that: (1) relates to accounts or disclosures that are material to the financial statements and (2) involved our especially challenging, subjective or complex judgements. The communication of the critical audit matter does not alter in any way our opinion on the consolidated financial statements, taken as a whole, and we are not, by communicating the critical audit matter below, providing a separate opinion on the critical audit matter or on the accounts or disclosures to which it relates.

Accrued Clinical Trial Costs and Contract Research

Description of the Matter

As discussed in Note 3 to the consolidated financial statements, the Company records costs for clinical trial activities based upon estimates of costs incurred through the balance sheet date that have yet to be invoiced by contract research organizations, clinical study sites and other vendors. The Company's accruals for clinical trial costs and contract research totaled $4.6 million at December 31, 2020.

Auditing the Company's accrued clinical trial costs and contract research was especially challenging due to the significant judgment required to determine the nature and level of services that have been received, including determining the progress to completion of specific tasks and activities conducted under the Company's clinical trials and contract research arrangements and the costs of those tasks that will be invoiced in the future by the contract research organizations, clinical study sites and other vendors.

How We Addressed the Matter in Our Audit	We obtained an understanding, evaluated the design and tested the operating effectiveness of internal controls that addressed the identified risks related to the Company's process for recording accrued clinical trial costs and contract research. For example, we tested controls over management's review of the clinical trial and contract research expense calculations, the significant assumptions about the status of research and development services incurred, and the completeness and accuracy of the data used to calculate the estimates. To test the accrued clinical trial costs and contract research, our procedures included, among others, testing the completeness and accuracy of the underlying data used in the estimates and evaluating significant assumptions, including, but not limited to, estimated costs per patient and project duration, that are used by management to estimate the recorded accruals. To assess the reasonableness of the significant assumptions, we corroborated the progress of the clinical trials and contract research with the Company's operations personnel and to information obtained by the Company directly from third parties (e.g., number of patients on treatment, imaging received) and to information in contracts related to patient treatment activities, including costs for those activities, and project duration. We examined subsequent invoicing received from such third parties, inspected the Company's contracts with these third parties and any pending change orders and subsequent reporting received from the third-parties for evidence of the accuracy and completeness of the accruals at the balance sheet date.

/s/ Ernst & Young LLP

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

Boston, Massachusetts
March 16, 2021

AVEO PHARMACEUTICALS, INC.

Consolidated Balance Sheets
(In thousands, except par value amounts)

	December 31, 2020	December 31, 2019
Assets		
Current assets:		
Cash and cash equivalents	$ 61,761	$ 29,785
Marketable securities	—	17,960
Accounts receivable	1,197	1,631
Clinical trial retainers	355	589
Other prepaid expenses and other current assets	2,195	635
Total current assets	65,508	50,600
Property and equipment, net	343	—
Operating lease right-of-use asset	903	—
Other assets	158	—
Total assets	$ 66,912	$ 50,600
Liabilities and stockholders' equity		
Current liabilities:		
Accounts payable	$ 3,380	$ 1,466
Accrued clinical trial costs and contract research	4,550	5,680
Other accrued liabilities	4,463	2,336
Operating lease liability	369	—
Loans payable, net of discount	1,056	9,569
Deferred revenue	1,974	1,974
Deferred research and development reimbursements	164	93
PIPE Warrant liability (Note 7)	199	—
Other liabilities (Note 6)	790	—
Total current liabilities	16,945	21,118
Loans payable, net of current portion and discount	12,716	6,197
Deferred revenue	578	2,552
PIPE Warrant liability (Note 7)	—	5,097
Operating lease liability, non-current	336	—
Other liabilities (Note 6)	1,043	790
Total liabilities	31,618	35,754
Stockholders' equity:		
Preferred stock, $.001 par value: 5,000 shares authorized at December 31, 2020 and December 31, 2019; no shares issued and outstanding at each of December 31, 2020 and December 31, 2019	—	—
Common stock, $.001 par value: 50,000 shares authorized at December 31, 2020 and December 31, 2019; 26,883 shares issued and outstanding at December 31, 2020 and 16,081 issued and outstanding at December 31, 2019	27	16
Additional paid-in capital	656,472	600,451
Accumulated deficit	(621,205)	(585,621)
Total stockholders' equity	35,294	14,846
Total liabilities and stockholders' equity	$ 66,912	$ 50,600

See accompanying notes.

AVEO PHARMACEUTICALS, INC.

Consolidated Statements of Operations
(In thousands, except per share amounts)

	Year Ended December 31,		
	2020	2019	2018
Revenues:			
Collaboration and licensing revenue	$ 4,774	$ 27,934	$ 4,947
Partnership royalties	1,245	861	462
	6,019	28,795	5,409
Operating expenses:			
Research and development	22,679	17,958	20,652
Selling, general and administrative	22,217	11,211	10,781
Settlement costs	—	—	(667)
	44,896	29,169	30,766
Loss from operations	(38,877)	(374)	(25,357)
Other income (expense), net:			
Interest expense, net	(1,605)	(1,815)	(2,191)
Change in fair value of PIPE Warrant liability	4,898	11,577	19,919
Other income	—	—	2,300
Other income (expense), net	3,293	9,762	20,028
Net income (loss) before provision for income taxes	(35,584)	9,388	(5,329)
Provision for income taxes	—	—	—
Net income (loss)	$ (35,584)	$ 9,388	$ (5,329)
Basic net income (loss) per share:			
Net income (loss) per share	$ (1.66)	$ 0.61	$ (0.44)
Weighted average number of common shares outstanding	21,402	15,331	12,059
Diluted net income (loss) per share:			
Net income (loss) per share	$ (1.66)	$ 0.61	$ (1.93)
Weighted average number of common shares outstanding and dilutive share equivalents outstanding	21,402	15,376	13,073

See accompanying notes.

AVEO PHARMACEUTICALS, INC.

Consolidated Statements of Comprehensive Income (Loss)
(In thousands)

	Year Ended December 31,		
	2020	2019	2018
Net income (loss)	$ (35,584)	$ 9,388	$ (5,329)
Other comprehensive income (loss):			
Unrealized gain (loss) on available-for-sale securities	—	(1)	5
Comprehensive income (loss)	$ (35,584)	$ 9,387	$ (5,324)

See accompanying notes.

AVEO PHARMACEUTICALS, INC.

Consolidated Statements of Stockholders' Equity (Deficit)
(In thousands)

	Common Shares					
	Shares	Par Value	Additional Paid-in Capital	Accumulated Other Comprehensive Income (Loss)	Accumulated Deficit	Total Stockholders' Equity (Deficit)
Balance at December 31, 2017	11,833	$ 12	$ 546,198	$ (4)	$ (586,969)	$ (40,763)
Adjustment related to adoption of new revenue recognition standard ASC 606	—	—	—	—	(2,711)	$ (2,711)
Issuance of common stock in a public offering, excluding to related parties (net of issuance costs of $0.6 million)	51	—	597	—	—	597
Issuance of common stock in a public offering, to related parties	199	—	4,500	—	—	4,500
Issuance of common stock from the SVB Leerink sales agreement (net of issuance costs of $0.2 million)	470	1	10,329	—	—	10,330
Issuance of Settlement Warrants in connection with a class action settlement (Note 13)	—	—	1,406	—	—	1,406
Stock-based compensation expense related to equity-classified awards	—	—	2,546	—	—	2,546
Issuance of common stock in connection with warrant exercises	54	—	544	—	—	544
Reduction in PIPE Warrant liability in connection with warrant exercises	—	—	1,153	—	—	1,153
Exercise of stock options	40	—	478	—	—	478
Issuance of common stock under employee stock purchase plan	1	—	17	—	—	17
Change in unrealized gain (loss) on investments	—	—	—	5	—	5
Net loss	—	—	—	—	(5,329)	(5,329)
Balance at December 31, 2018	12,648	$ 13	$ 567,768	$ 1	$ (595,009)	$ (27,227)
Issuance of common stock and warrants in a public offering, excluding to related parties (net of issuance costs of $2.2 million)	1,739	2	17,765	—	—	17,767
Issuance of common stock and warrants in a public offering, to related parties	435	—	5,000	—	—	5,000
Issuance of common stock from the SVB Leerink sales agreement (net of issuance costs of $0.2 million)	1,251	1	7,511	—	—	7,512
Stock-based compensation expense related to equity-classified awards	—	—	2,358	—	—	2,358
Exercise of stock options	8	—	49	—	—	49
Change in unrealized gain (loss) on investments	—	—	—	(1)	—	(1)
Net income	—	—	—	—	9,388	9,388
Balance at December 31, 2019	16,081	$ 16	$ 600,451	$ —	$ (585,621)	$ 14,846
Issuance of common stock in a public offering, excluding to related parties (net of issuance costs of $3.4 million)	5,221	5	24,074	—	—	24,079
Issuance of common stock in a public offering, to related parties	4,504	5	23,639	—	—	23,644
Issuance of common stock from the SVB Leerink sales agreement (net of issuance costs of $0.2 million)	1,070	1	5,916	—	—	5,917
Stock-based compensation expense related to equity-classified awards	—	—	2,355	—	—	2,355
Exercise of stock options	1	—	5	—	—	5
Issuance of common stock under employee stock purchase plan	6	—	32	—	—	32
Net loss	—	—	—	—	(35,584)	(35,584)
Balance at December 31, 2020	**26,883**	**$ 27**	**$ 656,472**	**$ —**	**$ (621,205)**	**$ 35,294**

See accompanying notes.

AVEO PHARMACEUTICALS, INC.
Consolidated Statements of Cash Flows
(In thousands)

	Year Ended December 31,		
	2020	2019	2018
Operating activities			
Net income (loss)	$ (35,584)	$ 9,388	$ (5,329)
Adjustments to reconcile net income (loss) to net cash used in operating activities:			
Depreciation and amortization	21	—	—
Stock-based compensation	2,355	2,358	2,546
Non-cash interest expense	469	567	556
Non-cash change in fair value of PIPE Warrant liability	(4,898)	(11,577)	(19,919)
Non-cash charge for settlement costs (Note 13)	—	—	(667)
Amortization of premium and discount on investments	(106)	(44)	3
Changes in operating assets and liabilities:			
Accounts receivable	433	1,395	(2,624)
Insurance recovery (Note 13)	—	—	15,000
Prepaid expenses and other current assets	(1,326)	(742)	774
Operating lease right-of-use asset	(1,060)	—	—
Other noncurrent assets	—	—	15
Accounts payable	1,914	(2,033)	1,063
Accrued contract research	(1,130)	(574)	(2,067)
Other accrued liabilities	2,127	(362)	240
Operating lease liability	369	—	—
Settlement liability (Note 13)	—	—	(15,000)
Deferred revenue	(1,974)	(934)	1,052
Deferred research and development reimbursements	71	(361)	(669)
Operating lease liability, non-current	336	—	—
Net cash used in operating activities	(37,983)	(2,919)	(25,026)
Investing activities			
Purchases of marketable securities	(36,133)	(17,917)	(6,733)
Proceeds from maturities and sales of marketable securities	54,200	—	25,312
Purchases of property and equipment	(363)		
Net cash provided by (used in) investing activities	17,704	(17,917)	18,579
Financing activities			
Proceeds from issuance of common stock and warrants, net of issuance costs	29,996	25,279	11,471
Proceeds from issuance of common stock and warrants to related parties	23,644	5,000	4,500
Proceeds from issuance of loan payable	5,329	—	—
Proceeds from issuance of stock for stock-based compensation arrangements	38	49	494
Payment on principal of loan payable	(6,497)	(3,834)	—
Payment of loan maturity fees	—	(300)	(540)
Payments of debt issuance costs	(255)	—	0
Net cash provided by financing activities	52,255	26,194	15,925
Net increase in cash and cash equivalents	31,976	5,358	9,478
Cash and cash equivalents at beginning of period	29,785	24,427	14,949
Cash and cash equivalents at end of period	$ 61,761	$ 29,785	$ 24,427
Supplemental cash flow information			
Cash paid for interest	$ 1,337	$ 1,971	$ 1,986
Right-of-use asset obtained in exchange for operating lease liability	$ 1,225		
Non-cash adjustment			
Increase to deferred revenue due to adoption of ASC 606 - transition adjustment on January 1, 2018	$ —	$ —	2,711
Non-cash financing activity			
Fair value of warrants issued in connection with a class action settlement (Note 13)	$ —	$ —	1,406

See accompanying notes.

(1) Organization

AVEO Pharmaceuticals, Inc. (the "Company") is an oncology-focused biopharmaceutical company committed to delivering medicines that provide a better life for cancer patients. The Company's strategy is to focus its resources toward the development and commercialization of its product candidates in North America, while leveraging partnerships to support development and commercialization in other geographies. With the approval of its first commercial product, FOTIVDA® (tivozanib), in the United States, the Company has transitioned from a clinical development stage company to a commercial and clinical development stage biopharmaceutical company.

On March 10, 2021, the U.S. Food and Drug Administration (the "FDA"), approved FOTIVDA in the United States for the treatment of adult patients with relapsed or refractory advanced renal cell carcinoma ("RCC") following two or more prior systemic therapies. FOTIVDA is an oral, next-generation vascular endothelial growth factor receptor ("VEGFR") tyrosine kinase inhibitor ("TKI"). The approval of FOTIVDA is based on the Company's pivotal phase 3 randomized, controlled, multi-center, open-label clinical trial comparing tivozanib to an approved therapy, Nexavar® (sorafenib), in RCC patients whose disease had relapsed or become refractory to two or three prior systemic therapies (the "TIVO-3 trial"). The approval is also supported by three additional trials in RCC and includes safety data from over 1,000 clinical trial subjects.

The Company is actively preparing for the commercial launch of FOTIVDA in the United States. The Company's U.S. sales force, sales training, marketing, market access and medical affairs teams as well as distribution capabilities are in place and the Company expects to have full promotional capabilities and FOTIVDA available to patients by March 31, 2021.

FOTIVDA is also approved and commercialized through the Company's development partner EUSA Pharma (UK) Limited ("EUSA") in the United Kingdom, Germany, Spain and certain other countries in their territory, for the treatment of adult patients with advanced RCC who are VEGFR pathway inhibitor-naïve and are either untreated or who have failed prior therapy with interferon-alpha (IFN-a) or interleukin-2 (IL-2).

Based on FOTIVDA's demonstrated anti-tumor activity, tolerability profile and reduction of regulatory T-cell production, the Company is studying FOTIVDA in combination with immune checkpoint inhibitors for the treatment of RCC and hepatocellular carcinoma ("HCC") in phase 2 clinical trials. The Company recently announced its entry into a collaboration with Bristol Myers Squibb ("BMS") to conduct a phase 3 study of FOTIVDA in combination with OPDIVO® (nivolumab), BMS's anti-PD-1 therapy, in patients with advanced relapsed or refractory RCC following prior immunotherapy exposure.

The Company's pipeline of product candidates includes ficlatuzumab, a potent humanized immunoglobulin G1, or IgG1, monoclonal antibody that targets hepatocyte growth factor ("HGF"). The Company has previously reported promising early clinical data on ficlatuzumab in squamous cell carcinoma of the head and neck ("HNSCC"), pancreatic cancer and acute myeloid leukemia ("AML"). The Company is currently conducting a randomized phase 2 confirmatory study of ficlatuzumab for the potential treatment of HNSCC.

The Company's pipeline of product candidates also includes worldwide rights to AV-380, a potent humanized IgG1 monoclonal antibody that targets growth differentiation factor 15 ("GDF15"). In December 2020, the FDA accepted the Company's investigational new drug application ("IND") for AV-380 for the potential treatment of cancer cachexia, and the Company has initiated a phase 1 clinical trial in healthy subjects.

The Company's earlier-stage pipeline includes AV-203 and AV-353, both as potential oncology treatments. AV-203 is a potent humanized IgG1 monoclonal antibody that targets ErbB3 (also known as HER3) to which the Company expects to regain worldwide rights in September 2021. AV-353 is the Company's a potent IgG1 monoclonal antibody that targets the Notch 3 pathway.

The Company is subject to a number of risks, including the need for substantial additional capital to continue its development programs and to fulfill its planned operating goals. In particular, the Company's currently planned operating and capital requirements include the need for substantial working capital to support the development and commercialization activities for its lead product, FOTIVDA.

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

Liquidity and Going Concern

In accordance with Accounting Standards Update ("ASU") No. 2014-15, *Disclosure of Uncertainties about an Entity's Ability to Continue as a Going Concern* (Subtopic 205-40), the Company has evaluated whether there are conditions and 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 consolidated financial statements are issued. The Company's financial statements have been prepared on the basis of continuity of operations, realization of assets and the satisfaction of liabilities in the ordinary course of business. Through December 31, 2020, the Company has financed its operations 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 commercialize FOTIVDA in the United States and to develop its clinical stage assets and, ultimately, upon the Company's ability to create shareholder value. On March 10, 2021, the FDA approved FOTIVDA in the United States for the treatment of adult patients with relapsed or refractory advanced RCC following two or more prior systemic therapies. The Company's future product revenues will depend upon the size of markets in which FOTIVDA, and any future products, have received approval, and its ability to achieve sufficient market acceptance, reimbursement from third-party payers and adequate market share for FOTIVDA and any future products in those markets. The likelihood of the Company's long-term success must be considered in light of the expenses, difficulties and potential delays that may be encountered in the development and commercialization of new pharmaceutical products, competitive factors in the marketplace and the complex regulatory environment in which the Company operates. Absent the realization of sufficient revenues from product sales to support the Company's cost structure, the Company may never attain or sustain profitability.

The Company has incurred recurring losses and cash outflows from operations since its inception, including an accumulated deficit of $621.2 million as of December 31, 2020. The Company anticipates that it will continue to incur significant operating expenses for the foreseeable future as it commercializes FOTIVDA in the United States and continues its planned development activities for its clinical stage assets. The Company may require substantial additional funding to advance its pipeline of clinical stage assets, and the timing and nature of these activities will be conducted subject to the availability of sufficient financial resources.

As of March 16, 2021, the date of issuance of these consolidated financial statements, the Company expects that its cash and cash equivalents of $61.8 million as of December 31, 2020, along with proceeds from the $20.0 million drawdown under the 2020 Loan Facility with Hercules Capital, Inc. and certain of its affiliates (collectively "Hercules") in March 2021 and from warrant exercises to date, and product revenues upon the commercial launch of FOTIVDA in the United States, will be sufficient to fund its current operations for more than twelve months from the date of filing this Annual Report on Form 10-K.

Management's expectations with respect to its ability to fund current planned operations is based on estimates that are subject to risks and uncertainties. If actual results are different from management's estimates, the Company may need to seek additional strategic or financing opportunities sooner than would otherwise be expected. However, there is no guarantee that any of these strategic or financing opportunities would be executed or executed on favorable terms, and some could be dilutive to existing stockholders. If the Company is unable to obtain additional funding on a timely basis, it may be forced to significantly curtail, delay or discontinue one or more of its planned research or development programs or be unable to expand its operations or otherwise capitalize on its commercialization of its product and product candidates.

(2) Basis of Presentation

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

Effective as of 5:00 p.m. Eastern Time on February 19, 2020, the Company effected a 1-for-10 reverse stock split of its common stock. All references to shares of common stock outstanding and per share amounts in these consolidated financial statements and the notes to the consolidated financial statements have been restated to reflect the reverse stock split on a retroactive basis. Refer to Note 7, "*Common Stock—Reverse Stock Split – February 2020*" for further details.

(3) Significant Accounting Policies

Revenue Recognition

As of December 31, 2020, the Company's revenues have been generated primarily through collaborative research, development and commercialization agreements. The terms of these agreements generally contain multiple promised goods and services, 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 preclinical 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.

Collaboration Arrangements Within the Scope of ASC 808, Collaborative Arrangements

The Company analyzes its collaboration arrangements to assess 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 and are therefore within the scope of ASC Topic 808, *Collaborative Arrangements* ("ASC 808"). 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 606, *Revenue from Contracts with Customers* ("ASC 606"). The Company's policy is generally to recognize amounts received from collaborators in connection with joint operating activities that are within the scope of ASC 808 as a reduction in research and development expense.

Arrangements Within the Scope of ASC 606, Revenue from Contracts with Customers

Under ASC 606, the Company recognizes revenue when its customers obtain control of promised goods or services, in an amount that reflects the consideration which the Company determines it expects to receive in exchange for those goods or services. To determine revenue recognition for arrangements that the Company determines are within the scope of ASC 606, the Company performs the following five steps: (i) identify the contract(s) with a customer; (ii) identify the performance obligation(s) in the contract; (iii) determine the transaction price; (iv) allocate the transaction price to the performance obligation(s) in the contract; and (v) recognize revenue when (or as) the Company satisfies its performance obligation(s). As part of the accounting for these arrangements, the Company must make significant judgments, including identifying performance obligations in the contract, estimating the amount of variable consideration to include in the transaction price and allocating the transaction price to each performance obligation.

Once a contract is determined to be within the scope of ASC 606, the Company assesses the goods or services promised within the contract and determines those that are performance obligations. Arrangements that include rights to additional goods or services that are exercisable at a customer's discretion are generally considered options. The Company assesses if these options provide a material right to the customer and if so, they are considered performance obligations. The exercise of a material right is accounted for as a contract modification for accounting purposes.

The Company assesses whether each promised good or service is distinct for the purpose of identifying the performance obligations in the contract. This assessment involves subjective determinations and requires management to make judgments about the individual promised goods or services and whether such are separable from the other aspects of the contractual relationship. Promised goods and services are considered distinct provided that: (i) the customer can benefit from the good or service either on its own or together with other resources that are readily available to the customer (that is, the good or service is capable of being distinct) and (ii) the entity's promise to transfer the good or service to the customer is separately identifiable from other promises in the contract (that is, the promise to transfer the good or service is distinct within the context of the contract). In assessing whether a promised good or service is distinct, the Company considers factors such as the research, manufacturing and commercialization capabilities of the collaboration partner and the availability of the associated expertise in the general marketplace. The Company also considers the intended benefit of the contract in assessing whether a promised good or service is separately identifiable from other promises in the contract. If a promised good or service is not distinct, an entity is required to combine that good or service with other promised goods or services until it identifies a bundle of goods or services that is distinct.

The transaction price is then determined and allocated to the identified performance obligations in proportion to their standalone selling prices ("SSP") on a relative SSP basis. SSP is determined at contract inception and is not updated to reflect changes between contract inception and when the performance obligations are satisfied. Determining the SSP for performance obligations requires significant judgment. In developing the SSP for a performance obligation, the Company considers applicable market conditions and relevant entity-specific factors, including factors that were contemplated in negotiating the agreement with the customer and estimated costs. The Company validates the SSP for performance obligations by evaluating whether changes in the key assumptions used to determine the SSP will have a significant effect on the allocation of arrangement consideration between multiple performance obligations.

If the consideration promised in a contract includes a variable amount, the Company estimates the amount of consideration to which it will be entitled in exchange for transferring the promised goods or services to a customer. The Company determines the amount of variable consideration by using the expected value method or the most likely amount method. The Company includes the unconstrained amount of estimated variable consideration in the transaction price. The amount included in the transaction price is constrained to the amount for which it is probable that a significant reversal of cumulative revenue recognized will not occur. At the end of each subsequent reporting period, the Company re-evaluates the estimated variable consideration included in the transaction price and any related constraint, and if necessary, adjusts its estimate of the overall transaction price. Any such adjustments are recorded on a cumulative catch-up basis in the period of adjustment.

In determining the transaction price, the Company adjusts consideration for the effects of the time value of money if the timing of payments provides the Company with a significant benefit of financing. The Company does not assess whether a contract has a significant financing component if the expectation at contract inception is such that the period between payment by the licensees and the transfer of the promised goods or services to the licensees will be one year or less. The Company assessed each of its revenue generating arrangements in order to determine whether a significant financing component exists and concluded that a significant financing component does not exist in any of its arrangements.

The Company then recognizes as revenue the amount of the transaction price that is allocated to the respective performance obligation when (or as) each performance obligation is satisfied at a point in time or over time, and if over time based on the use of an output or input method.

Licenses of Intellectual Property: The terms of the Company's license agreements include the license of functional intellectual property, given the functionality of the intellectual property is not expected to change substantially as a result of the Company's ongoing activities. If the license to the Company's intellectual property is determined to be distinct from the other performance obligations identified in the arrangement, the Company recognizes revenues from the portion of the transaction price allocated to the license when the license is transferred to the licensee and the licensee is able to use and benefit from the license. For licenses that are bundled with other promises (that is, for licenses that are not distinct from other promised goods and services in an arrangement), the Company utilizes judgment to assess the nature of the combined performance obligation to determine whether the combined performance obligation is satisfied over time or at a point in time and, if over time, the appropriate method of measuring progress for purposes of recognizing revenue. The Company evaluates the measure of progress each reporting period and, if necessary, adjusts the measure of performance and related revenue recognition.

Research and Development Funding: Arrangements that include payment for research and development services are generally considered to have variable consideration. If and when the Company assesses the payment for these services is no longer subject to the constraint on variable consideration, the related revenue is included in the transaction price.

Milestone payments: At the inception of each arrangement that includes non-refundable payments for contingent milestones, including preclinical research and development, clinical development and regulatory, the Company evaluates whether the milestones are considered probable of being achieved and estimates the amount to be included in the transaction price using the most likely amount method. If it is probable that a significant revenue reversal would not occur, the associated milestone value is included in the transaction price. Milestone payments that are not within the control of the Company or the licensee, such as regulatory approvals, are not considered probable of being achieved until those approvals are received. At the end of each reporting period, the Company re-evaluates the probability of the achievement of contingent milestones and the likelihood of a significant reversal of such milestone revenue, and if necessary, adjusts its estimate of the overall transaction price. Any such adjustments are recorded on a cumulative catch-up basis, which would affect collaboration and licensing revenue in the period of adjustment. This quarterly assessment may result in the recognition of revenue related to a contingent milestone payment before the milestone event has been achieved.

Royalties: For arrangements that include sales-based royalties, including milestone payments based on the level of sales, and the license is deemed to be the predominant item to which the royalties relate, the Company recognizes revenue at the later of (i) when the related sales occur, or (ii) when the performance obligation to which some or all of the royalty has been allocated has been satisfied (or partially satisfied).

The following table summarizes the total revenues earned in the years ended December 31, 2020, 2019 and 2018, respectively, by partner (in thousands). Refer to Note 4, “Collaborations and License Agreements” regarding specific details.

	Years Ended December 31,		
	2020	2019	2018
Strategic Partner:	($ in thousands)		
KKC	$ 2,800	$ 25,000	$ —
EUSA	3,219	3,795	3,409
CANbridge	—	—	2,000
Total revenues	$ 6,019	$ 28,795	$ 5,409

Leases

The Company adopted ASU 2016-02, *Leases (Topic 842)* (“ASU 2016-02”), effective January 1, 2019 using the required modified retrospective approach and utilizing the effective date as its date of initial application. As a result, prior periods are presented in accordance with the previous guidance in ASC 840, *Leases*. In connection with the adoption of ASU 2016-02, the Company elected the package of practical expedients permitted under the transition guidance within the new standard, which does not require the reassessment of the following: (i) whether existing or expired arrangements are or contain a lease, (ii) the lease classification of existing or expired leases, and (iii) whether previous initial direct costs would qualify for capitalization under the new lease standard. The Company made an accounting policy election not to recognize right-of-use assets or related lease liabilities with a lease term of twelve months or less in its Consolidated Balance Sheet. Such short-term lease payments are recorded in its Consolidated Statements of Operations in the period in which the obligation for those payments was incurred.

As of the date of initial application of ASU 2016-02, the Company’s lease arrangement for its former corporate headquarters at One Broadway, Cambridge, Massachusetts was cancellable within 30 days’ notice to its landlord and excluded any extension incentives or disincentives to renew for an extended period of time. In addition, the Company has drug storage arrangements with multiple storage providers that are cancellable at any time without penalty to the Company. The Company recognized short-term operating lease expense in its Consolidated Statements of Operations of approximately $0.5 million, $1.0 million and $0.7 million in the years ended December 31, 2020, 2019 and 2018, respectively.

Application of ASC 842 policy elections to leases post adoption

The Company has made certain accounting policy elections to apply to its leases executed post adoption of ASU 2016-02 , or subsequent to January 1, 2019, as further described below.

In accordance with ASC 842, components of a lease should be split into three categories: lease components, non-lease components, and non-components. The fixed and in-substance fixed contract consideration (including any consideration related to non-components) must be allocated based on the respective relative fair values to the lease components and non-lease components. The Company made an accounting policy election to combine lease and non-lease components as a single lease component for all underlying assets and allocate all of the contract consideration to the lease component only.

At the inception of an arrangement, the Company determines whether the arrangement is or contains a lease based on the unique facts and circumstances present in the arrangement. Leases with a term greater than one year are recognized on the balance sheet as right-of-use assets and short-term and long-term lease liabilities, as applicable.

Operating lease liabilities and their corresponding right-of-use assets are initially recorded based on the present value of lease payments over the expected remaining lease term. Certain adjustments to the right-of-use asset may be required for items such as incentives received. The interest rate implicit in lease contracts is typically not readily determinable. As a result, the Company utilizes its incremental borrowing rate to discount lease payments, which reflects the fixed rate at which the Company could borrow on a collateralized basis the amount of the lease payments in the same currency, for a similar term, in a similar economic environment. To estimate its incremental borrowing rate, a credit rating applicable to the Company is estimated using a synthetic credit rating analysis since the Company does not currently have a rating agency-based credit rating.

ASC 842 allows for the use of judgment in determining whether the assumed lease term is for a major part of the remaining economic life of the underlying asset and whether the present value of lease payments represents substantially all of the fair value of the underlying asset. The Company applies the bright line thresholds referenced in ASC 842-10-55-2 to assist in evaluating leases for appropriate classification.

30 Winter Street Lease

On March 5, 2020, the Company entered into a sublease agreement for office space located at 30 Winter Street in Boston, Massachusetts (the "Winter Street Sublease") to relocate the Company's corporate headquarters previously located at One Broadway in Cambridge, Massachusetts. Under the terms of the Winter Street Sublease, the Company leases 10,158 square feet of office space for $47.00 per square foot, or approximately $0.5 million per year in base rent subject to certain operating expenses, taxes and annual base rent increases of approximately 3%. The Winter Street Sublease commenced when the space became available for use by the Company on March 24, 2020 and will continue until its expiration on November 30, 2022. Upon commencement of the Winter Street Sublease, the Company paid a security deposit, in the amount of $0.3 million, which is subject to certain reductions to be applied to future base rent payments provided that no event of default has occurred in the preceding twelve months.

The Company is accounting for the Winter Street Sublease under ASC 842 using its initial 2.7-year term through November 30, 2022. In applying ASC 842, the Company classified the Winter Street Sublease as an operating lease and recorded a right-of-use asset of approximately $1.2 million and a lease liability of approximately $1.0 million upon the effective lease commencement date. In calculating the lease liability, the Company used the present value of all future lease payments using an incremental borrowing rate of 7.58%. The Company is recognizing rent expense on a straight-line basis throughout the remaining term of the lease. In the year ended December 31, 2020, the Company recognized $0.4 million in rent expense.

In connection with the execution of the Winter Street Sublease, the Company also entered into a Purchase Agreement for furniture (the "Furniture Purchase Agreement") located on the premises upon the lease commencement. Upon execution of the Furniture Purchase Agreement, the Company paid the $0.1 million purchase price and recorded the furniture acquisition as property and equipment, net. The Company is recognizing depreciation using the straight-line method over the estimated useful life of 7 years.

As of December 31, 2020, future minimum lease payments under the Company's Winter Street Sublease are as follows (amounts in thousands):

Year Ending December 31:	
2021	385
2022	328
Total lease payments	713
Less imputed interest	(8)
Total operating lease liabilities	$ 705

Short-term arrangements

As of the date of initial application of ASU 2016-02, the Company's lease arrangement for its former corporate headquarters at One Broadway, Cambridge, Massachusetts was cancellable within 30 days' notice to its landlord and excluded any extension incentives or disincentives to renew for an extended period of time. In addition, the Company has drug storage arrangements with multiple storage providers that are cancellable at any time without penalty to the Company. The Company recognized short-term operating lease expense in its Consolidated Statements of Operations of approximately $0.5 million, $1.0 million and $0.7 million in the years ended December 31, 2020, 2019 and 2018, respectively.

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 (i) internal costs for salaries, bonuses, benefits, stock-based compensation, research-related overhead, and allocated expenses for facilities and information technology, and (ii) external costs for

clinical trials, drug manufacturing and distribution, preclinical studies, upfront license payments, milestones and sublicense fees related to in-licensed products and technology, consultants and other contracted services.

Warrants Issued in Connection with Private Placement

In May 2016, the Company issued warrants to purchase an aggregate of 1,764,242 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, 2020, PIPE Warrants exercisable for 80,309 shares of common stock had been exercised, for approximately $0.8 million in cash proceeds, and PIPE Warrants exercisable for 1,683,933 shares of common stock were outstanding. Refer to Note 7, "*Common Stock—Private Placement – May 2016"* 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 PIPE 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 gain of approximately $4.9 million in the year ended December 31, 2020 in its Statement of Operations principally attributable to the decreases in the fair value of the warrant liability that resulted from lower stock prices as of December 31, 2020 relative to prior periods, a decrease in the Company's stock volatility rate and a shorter remaining term as the PIPE Warrants approach their expiration in May 2021. The Company recorded non-cash gains of approximately $11.6 million and $19.9 million in the years ended December 31, 2019 and 2018, respectively, in its Statement of Operations principally attributable to the decreases in the fair value of the warrant liability that resulted from lower stock prices as of December 31, 2019 and 2018, relative to prior periods. The Company recorded a reduction in the warrant liability attributable to warrant exercises, with a corresponding increase to additional paid-in capital, of $0 in each of the years ended December 31, 2020 and 2019, respectively, and approximately $1.2 million in the year ended December 31, 2018.

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 years ended December 31, 2020, 2019 and 2018, respectively (in thousands):

Fair value at December 31, 2017	$	37,746
Decrease in fair value		(19,919)
Reduction in warrant liability for PIPE Warrant exercises		(1,153)
Fair value at December 31, 2018	$	16,674
Decrease in fair value		(11,577)
Fair value at December 31, 2019	$	5,097
Decrease in fair value		(4,898)
Fair value at December 31, 2020	$	199

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

	Original Issuance	December 31, 2017	December 31, 2018	December 31, 2019	December 31, 2020
Expected price volatility	76.25%	84.86%	82.64%	133.07%	56.79%
Expected term (in years)	5.00	3.50	2.50	1.50	0.50
Risk-free interest rates	1.22%	2.09%	2.47%	1.59%	0.09%
Stock price	$ 8.90	$ 27.90	$ 16.00	$ 6.20	$ 5.77
Dividend yield	—	—	—	—	—

Prior Class Action Settlement and Settlement Warrants

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 "2013 Class Action") that had been filed in 2013 and was pending in the United States District Court for the District of Massachusetts (the "District Court") against the Company and certain of the Company's 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 2013 Class Action was purportedly brought on behalf of stockholders who purchased the Company's common stock between May 16, 2012 and May 1, 2013 (the "Class").

In December 2017, upon entering into the MOU, the Company's liability related to 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 200,000 warrants to purchase shares of its common stock that the Company agreed to issue the Class (the "Settlement Warrants"), with a corresponding non-cash charge to the Statement of Operations as a component of operating expense. The Settlement Warrants were exercisable for a one-year period from their 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 $30.00 per share.

In February 2018, the District Court preliminarily approved a definitive stipulation of settlement agreement (the "Stipulation"), following which the insurance carriers funded the settlement escrow account related to the $15.0 million cash portion of the settlement. On May 30, 2018, the District Court approved the Stipulation in its order of final approval and final judgment (the "Final Judgment"), which became effective on June 29, 2018 (the "Effective Date"). Pursuant to the Final Judgment, all claims against the Company were released upon the Effective Date. In addition, pursuant to the Stipulation, the Company had no interest in the settlement escrow account subsequent to the Effective Date. Accordingly, the $15 million contingent liability associated with the cash portion of the settlement and the corresponding insurance recovery was eliminated on the Effective Date. On July 16, 2018, the Company issued and delivered the Settlement Warrants in accordance with the Stipulation and filed a corresponding shelf registration statement, File No. (333-226190) to register the shares of common stock underlying the Settlement Warrants which was declared effective by the SEC on July 25, 2018. All 200,000 Settlement Warrants expired on July 15, 2019 as none of the warrants had been exercised during the one-year exercise period.

Refer to Note 13, "*Legal Proceedings*" for further discussion of the 2013 Class Action settlement.

The estimated fair value of the Settlement Warrants was determined using the Black-Scholes pricing model. The estimated fair value of the Settlement Warrants was subject to revaluation at each balance sheet date and any changes in fair value were recorded as a non-cash gain or (loss) in the Statement of Operations as a component of operating expenses until the Settlement Warrants were issued. The fair value of the Settlement Warrants on June 30, 2018 was determined based on the estimated fair value of the Settlement Warrants at the time of issuance. The Company recorded a non-cash gain of approximately $0.7 million in the year ended December 31, 2018 in its Statement of Operations attributable to the decrease in the fair value of the Settlement Warrants that principally resulted from a lower volatility rate relative to prior periods.

In July 2018, upon the issuance of the Settlement Warrants, the Company reclassified the approximate $1.4 million value of the Settlement Warrants from a liability to stockholders equity as a component of additional paid-in-capital based upon the terms of the warrant agreement and, accordingly, the approximate $1.4 million contingent liability on the Company's balance sheet associated with the warrant portion of the settlement was eliminated.

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

	December 31, 2017	June 30, 2018
Expected price volatility	101.52%	62.74%
Expected term (in years)	1.00	1.00
Risk-free interest rates	1.76%	2.37%
Stock price	$ 27.90	$ 29.00
Dividend yield	—	—

Cash, Cash Equivalents and Marketable Securities

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 United States government money market funds, high-grade, short-term commercial paper, corporate bonds and other United States 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.

The Company does not have any restricted cash balances.

Marketable Securities

Marketable securities consist primarily of investments which have expected average maturity dates in excess of three 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, 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, 2020 and December 31, 2019:

	Amortized Cost	Unrealized Gains	Unrealized Losses	Fair Value
December 31, 2020				
Cash and cash equivalents:				
Cash and money market funds	$ 61,761	$ —	$ —	$ 61,761
Total cash, cash equivalents and marketable securities	**$ 61,761**	**$ —**	**$ —**	**$ 61,761**
December 31, 2019				
Cash and cash equivalents:				
Cash and money market funds	$ 25,278	$ —	$ —	$ 25,278
Corporate debt securities	4,507	—	—	4,507
Total cash and cash equivalents	**29,785**	**—**	**—**	**29,785**
Marketable securities:				
Corporate debt securities due within 1 year	$ 17,960	$ —	$ —	$ 17,960
Total marketable securities	17,960	—	—	17,960
Total cash, cash equivalents and marketable securities	**$ 47,745**	**$ —**	**$ —**	**$ 47,745**

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, 2020, the Company had financial assets valued based on Level 1 inputs consisting of cash and cash equivalents in a United States government money market fund. During the year ended December 31, 2020, the Company did not have any transfers of financial assets between Levels 1 and 2.

As of December 31, 2020, the Company's financial liability that was recorded at fair value consisted of the PIPE Warrant liability.

The fair value of the Company's loans payable at December 31, 2020 and December 31, 2019 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 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, 2020 and December 31, 2019:

	Fair Value Measurements as of December 31, 2020			
	Level 1	Level 2	Level 3	Total
	(in thousands)			
Financial assets carried at fair value:				
Cash and money market funds	$ 61,761	$ —	$ —	$ 61,761
Total cash, cash equivalents and marketable securities	**$ 61,761**	**$ —**	**$ —**	**$ 61,761**
Financial liabilities carried at fair value:				
Total PIPE Warrant liability	**$ —**	**$ —**	**$ 199**	**$ 199**

	Fair Value Measurements as of December 31, 2019			
	Level 1	Level 2	Level 3	Total
	(in thousands)			
Financial assets carried at fair value:				
Cash and money market funds	$ 25,278	$ —	$ —	$ 25,278
Corporate debt securities	—	4,507	—	4,507
Total cash and cash equivalents	$ 25,278	$ 4,507	$ —	$ 29,785
Marketable securities:				
Corporate debt securities due within 1 year	$ —	$ 17,960	$ —	$ 17,960
Total marketable securities	$ —	$ 17,960	$ —	$ 17,960
Total cash, cash equivalents and marketable securities	**$ 25,278**	**$ 22,467**	**$ —**	**$ 47,745**
Financial liabilities carried at fair value:				
Total PIPE Warrant liability	**$ —**	**$ —**	**$ 5,097**	**$ 5,097**

Basic and Diluted Net Loss per Common Share

Basic net income (loss) per share attributable to the Company's common stockholders is based on the weighted-average number of common shares outstanding during the period. Diluted net income (loss) per share attributable to the Company's common stockholders is based on the weighted-average number of common shares outstanding during the period plus additional weighted-average common equivalent shares outstanding during the period when the effect is dilutive.

For the year ended December 31, 2020, diluted net loss per share is the same as basic net loss per share as the inclusion of common stock issuable upon the exercise of warrants and stock options would be anti-dilutive under the treasury stock method. In the year ended December 31, 2020, the average market prices of the Company's common stock were below the exercise prices of $10.00 and $12.50 per share for the PIPE Warrants and Offering Warrants. Refer to Note 7, "*Common Stock—Private Placement – May 2016, - Public Offering – April 2019 and - Settlement Warrants"* for further discussion of these warrants.

For the year ended December 31, 2019, diluted net income per share (i) includes common equivalent shares issuable upon the exercise of in-the-money stock options, as determined using the treasury stock method, as the average market prices of the Company's common stock during the respective period exceeded the exercise prices of certain stock options, and (ii) excludes the incremental common shares issuable upon the exercise of the PIPE Warrants, Offering Warrants and out-of-the money stock options as their effect would be anti-dilutive. In the year ended December 31, 2019, the average market prices of the Company's common stock were below the exercise prices of $10.00 and $12.50 per share for the PIPE Warrants and Offering Warrants, respectively.

For the year ended December 31, 2018, diluted net income per share (i) includes common equivalent shares issuable upon the exercise of the PIPE Warrants, as determined using the treasury stock method, as the average market prices of the Company's common stock during the respective period exceeded the exercise price of $10.00 per share for the PIPE Warrants, and (ii) excludes the incremental common shares issuable upon the exercise of the Settlement Warrants (as defined in Note 7, "– Common Stock – Settlement Warrants" below) and stock options as their effect would be anti-dilutive. In the year ended December 31, 2018, the average market prices of the Company's common stock were below the exercise price of $30.00 per share for Settlement Warrants.

The following tables summarizes the computation of basic and diluted net loss per share for the years ended December 31, 2020, 2019 and 2018, respectively (in thousands except per share amounts):

	Year Ended December 31,		
	2020	2019	2018
Basic net income (loss) attributable to Aveo common stockholders	$ (35,584)	$ 9,388	$ (5,329)
Less: non-cash gains attributable to the change in fair value of the PIPE Warrant liability	—	—	(19,919)
Diluted net income (loss) attributable to Aveo common stockholders	$ (35,584)	$ 9,388	$ (25,248)
Weighted-average shares of common stock outstanding	21,402	15,331	12,059
Dilutive securities:			
Incremental common shares issuable upon the exercise of the PIPE Warrants	—	—	1,014
Incremental common shares issuable upon the exercise of dilutive stock options	—	45	—
Weighted-average number of common shares outstanding and dilutive share equivalents outstanding	21,402	15,376	13,073
Basic net income (loss) per share	$ (1.66)	$ 0.61	$ (0.44)
Diluted net income (loss) per share	$ (1.66)	$ 0.61	$ (1.93)

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, 2020, 2019 and 2018, respectively:

	Years Ended December 31,		
	2020	2019	2018
Stock options outstanding	1,796,690	1,168,250	958,334
Offering Warrants Outstanding	2,500,000	2,500,000	—
PIPE Warrants outstanding	1,683,933	1,683,933	—
Settlement Warrants outstanding	—	—	200,000
Total	5,980,623	5,352,183	1,158,334

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 each award is recognized in the Company's statements of operations over the requisite service period for such award.

Awards that vest as the recipient provides service are expensed on a straight-line basis over the requisite service period. The Company uses the Black-Scholes option pricing model to value its stock option awards without market conditions, which requires the Company to make certain assumptions regarding the expected volatility of 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. The Company calculates volatility using its historical stock price data. 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 United States 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. During the years ended December 31, 2020, 2019 and 2018, the Company recorded the following stock-based compensation expense (in thousands):

	Years Ended December 31,		
	2020	2019	2018
	(in thousands)		
Research and development	$ 499	$ 662	$ 774
Selling, general and administrative	1,856	1,696	1,772
Total stock-based compensation expense	$ 2,355	$ 2,358	$ 2,546

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

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. The Company maintains a full valuation allowance on all deferred tax assets.

Segment and Geographic Information

Operating segments are defined as components of an enterprise engaging in business activities for which discrete financial information is available and regularly reviewed by the chief operating decision maker in deciding how to allocate resources and in assessing performance. The Company views its operations and manages its business in one operating segment principally in the United States. As of December 31, 2020, 2019 and 2018, the Company has no net assets located outside of the United States.

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, the assessment of the Company's ability to continue as a going concern, and the reported amounts of revenues and expenses during the reporting periods. Significant items subject to such estimates and assumptions include revenue recognition, clinical trial costs and contract research accruals, measurement of the PIPE Warrant liability, measurement of stock-based compensation, measurement of right-of-use assets and lease liabilities, and estimates of the Company's capital requirements over the next twelve months from the date of issuance of the consolidated financial statements. The Company bases its estimates on historical experience and various other assumptions that management believes to be reasonable under the circumstances. Material changes in these estimates could occur in the future. Changes in estimates are recorded or reflected in the Company's disclosures in the period in which they become known. Actual results could differ from those estimates if past experience or other assumptions do not turn out to be substantially accurate.

Accrued Clinical Trial Costs and Contract Research Liabilities

During the years ended December 31, 2020, 2019 and 2018, the Company had arrangements with multiple CROs whereby these organizations commit to performing services for the Company over multiple reporting periods. The Company recognizes the expenses associated with these arrangements based on its 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.

In addition to fees earned by the clinical research organizations to manage the Company's clinical trials, the clinical research organizations are also responsible for managing payments to the clinical trial sites on the Company's behalf. There can be significant lag time in clinical trial sites invoicing the clinical research organizations. The date on which services are performed, the level of services performed and the cost of such services are often determined based on subjective judgments. The Company makes these judgments based upon the facts and circumstances known to it, such as the terms of the contract and its knowledge of activity that has been incurred, including the number of active clinical sites, the number of patients enrolled, the activities to be performed for each patient, including patient treatment and any imaging, if applicable, the activities to be performed for each patient, and the duration for

which the patients will be enrolled in the trial. In the event that the Company does not identify some costs which have begun to be incurred, or the Company under or overestimates the level of services performed or the costs of such services in a given period, its reported expenses for such period would be understated or overstated. The Company currently reflects the effects of any changes in estimates based on changes in facts and circumstances directly in its operations in the period such change becomes known.

With respect to financial reporting periods presented in this Annual Report on Form 10-K, the timing of the Company's actual costs incurred have not differed materially from its estimated timing of such costs.

Recently Adopted Accounting Pronouncements

In June 2016, the Financial Accounting Standards Board ("FASB") issued ASU 2016-13, *Measurement of Credit Losses on Financial Instruments*, ("ASU 2016-13"). This standard requires that for most financial assets, losses be based on an expected loss approach which includes estimates of losses over the life of exposure that considers historical, current and forecasted information. Expanded disclosures related to the methods used to estimate the losses as well as a specific disaggregation of balances for financial assets are also required. The targeted transition relief standard allows filers an option to irrevocably elect the fair value option of ASC 825-10, Financial Instruments-Overall, applied on an instrument-by-instrument basis for eligible instruments. The Company adopted ASU 2016-13 effective January 1, 2020. The adoption of this standard did not have a material impact on the Company's consolidated financial statements.

In August 2018, the FASB issued ASU 2018-13, *Fair Value Measurement (Topic 820): Disclosure Framework-Changes to the Disclosure Requirements for Fair Value Measurement* ("ASU 2018-13"), which modifies the disclosure requirements for fair value measurements. The Company adopted ASU 2018-13 effective January 1, 2020. The adoption of this standard did not have a material impact on the Company's consolidated financial statements.

Recently Issued Accounting Pronouncements

In December 2019, the FASB issued ASU 2019-12, *Income Taxes (Topic 740): Simplifying the Accounting for Income Taxes* ("ASU 2019-12"), which is intended to simplify the accounting for income taxes. ASU 2019-12 removes certain exceptions to the general principles in Topic 740 and also clarifies and amends existing guidance to improve consistent application. The new standard will be effective beginning January 1, 2021. The Company is assessing the impact ASU 2019-12 will have on its consolidated financial statements.

(4) Collaborations and License Agreements

Collaboration Agreement

AstraZeneca

In December 2018, the Company entered into a clinical supply agreement (the "AstraZeneca Agreement") with a wholly-owned subsidiary of AstraZeneca PLC ("AstraZeneca") to evaluate the safety and efficacy of AstraZeneca's IMFINZI (durvalumab), a human monoclonal antibody directed against programmed death-ligand 1 (PD-L1), in combination with tivozanib as a first-line treatment for patients with advanced, unresectable HCC in an open-label, multi-center, randomized phase 1b/2 clinical trial (the "DEDUCTIVE trial"). The Company serves as the study sponsor; each party contributes the clinical supply of its study drug; key decisions are made by both parties by consensus; and external study costs are otherwise shared equally.

The Company is accounting for the joint development activities under the AstraZeneca Agreement as a joint risk-sharing collaboration in accordance with ASC 808 because both the Company and AstraZeneca are active participants in the oversight of the DEDUCTIVE trial via their participation on a joint steering committee and are exposed to significant risk and rewards in connection with the activity based on their obligation to share in the costs. AstraZeneca does not meet the definition of a customer, thus the joint development activities under the AstraZeneca Agreement are not accounted for under ASC 606.

Payments from AstraZeneca with respect to its share of the external costs for the DEDUCTIVE trial 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 that is not representative of a vendor-customer relationship.

The Company records reimbursements from AstraZeneca for external study costs as a reduction in research and development expense during the period that reimbursable expenses are incurred. As a result of the cost sharing provisions in the AstraZeneca Agreement, the Company's research and development expenses were reduced by approximately $1.1 million, $0.5 million and $0 in the years ended December 31, 2020, 2019 and 2018, respectively. The amount due to the Company from AstraZeneca pursuant to the cost-sharing provision was approximately $0.4 million as of December 31, 2020.

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 is a potent humanized IgG1 monoclonal antibody that targets ErbB3 (also known as HER3), for the diagnosis, treatment and prevention of disease in all countries outside of North America.

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 of foreign withholding taxes. CANbridge also reimbursed the Company for $1.0 million of certain AV-203 manufacturing costs incurred by the Company prior to entering into the CANbridge Agreement. CANbridge paid this manufacturing reimbursement in two installments of $0.5 million each, one in March 2017 and one in September 2017, net of foreign withholding taxes, following CANbridge's validation of the manufacturing process for AV-203 drug substance. In December 2017, CANbridge filed an investigative new drug ("IND") application with the National Medical Products Administration (formerly, the China Food and Drug Administration) (the "NMPA") for a clinical study of AV-203, which CANbridge refers to as CAN017, in esophageal squamous cell carcinoma ("ESCC"). In August 2018, CANbridge obtained regulatory approval of this IND application from the NMPA and, accordingly, the Company earned a $2.0 million development and regulatory milestone payment that was received from CANbridge in August 2018. No milestones had been achieved by CANbridge in the years ended December 31, 2020 and 2019, respectively.

A percentage of any milestone and royalty payments received by the Company pursuant to the CANbridge Agreement, excluding upfront and reimbursement payments, or under future partnership agreements related to the AV-203 program, 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. The $2.0 million development and regulatory milestone the Company earned in August 2018 for regulatory approval from the NMPA of an IND application for a clinical study of AV-203 in ESCC was subject to this sublicense fee, or $0.7 million, which was paid to Biogen in October 2018.

In March 2021, CANbridge exercised its right to terminate for convenience the CANbridge Agreement. Under the terms of the CANbridge Agreement, the Company expects the transfer of the AV-203 program to be complete in September 2021 and, at that time, the Company will regain worldwide rights to the AV-203 program.

Accounting Analysis Under ASC 606

The Company evaluated the CANbridge Agreement under ASC 606 and determined the CANbridge Agreement contained a single performance obligation related to the exclusive license to develop and commercialize AV-203 that was satisfied at the inception of the arrangement. The Company determined that the $1.0 million in upfront consideration received upon the execution of the CANbridge Agreement in March 2016 and the $1.0 million reimbursement received in the year ended December 31, 2017 for certain manufacturing costs incurred by the Company prior to the effective date constituted the amount of the consideration to be included in the transaction price upon the adoption of ASC 606 on January 1, 2018 and attributed these amounts to the Company's single performance obligation.

Because the Company satisfied the single performance obligation at the inception of the contract and had no remaining performance obligations, each of these amounts were recognized upon receipt. Upon adoption of ASC 606 on January 1, 2018, none of the development and regulatory milestones were included in the transaction price, as these milestone amounts were fully constrained. As part of its evaluation of the constraint, the Company considered multiple factors: (i) regulatory approvals are outside of the control of CANbridge, (ii) certain development and regulatory milestones are contingent upon the success of future clinical trials, if any, which is out of the control of CANbridge, and (iii) efforts by CANbridge.

Under the CANbridge Agreement, the Company had been eligible to receive milestone payments and royalties tied to the commencement of clinical trials, to regulatory approvals and to sales of such products upon commercialization. In the third quarter of 2018, the Company increased the transaction price to $4.0 million to include the $2.0 million development and regulatory milestone that was earned in August 2018 for regulatory approval from the NMPA of an IND application for a clinical study of AV-203 in ESCC. Accordingly, the Company recognized the full $2.0 million amount as collaboration and licensing revenue in the year ended December 31, 2018, as the Company did not have any ongoing performance obligations under the CANbridge Agreement. No additional milestones set forth in the CANbridge Agreement had been achieved prior to the termination of the CANbridge Agreement.

EUSA

In December 2015, the Company entered into the EUSA Agreement, 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 and Australasia (collectively, the "EUSA Licensed Territories") for all diseases and conditions in humans, excluding non-oncologic diseases or conditions of the eye.

EUSA made research and development reimbursement payments to the Company of $2.5 million upon the execution of the EUSA Agreement during the year ended December 31, 2015 and $4.0 million in September 2017 upon its receipt of marketing approval from the European Commission in August 2017 for FOTIVDA (tivozanib) for the treatment of RCC. In September 2017, EUSA elected to opt-in to co-develop the phase 2 clinical trial of tivozanib in combination with OPDIVO (nivolumab), a PD-1 inhibitor, in the first-line and the second-line treatment of RCC (the "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 50% of the total costs for the Company's phase 3 randomized, controlled, multi-center, open-label clinical trial comparing tivozanib to an approved therapy, sorafenib (Nexavar®), in 350 subjects in RCC patients whose disease had relapsed or become refractory to two or three prior systemic therapies, including subjects with prior checkpoint inhibitor therapy (the"TIVO-3 trial"), 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 (collectively, the "EU5"). The Company is also entitled to receive an additional $2.0 million for the grant of marketing approval for RCC, if any, in three of the licensed countries outside of the EU, as mutually agreed by the parties, of which approvals have been obtained in New Zealand in July 2019 and in South Africa in September 2020. In February 2018, November 2018 and February 2019, EUSA obtained reimbursement approval from the National Institute for Health and Care Excellence ("NICE") in the United Kingdom, the German Federal Association of the Statutory Health Insurances ("GKV-SV") in Germany and the Ministry of Health, Consumer Affairs and Social Welfare ("MSCBS") in Spain, respectively, for the first-line treatment of RCC. Accordingly, the Company earned a $2.0 million milestone payment with respect to reimbursement approval in the United Kingdom that was received in March 2018, a $2.0 million milestone payment with respect to reimbursement approval in Germany that was received in December 2018 and a $2.0 million milestone payment with respect to reimbursement approval in Spain that was received in May 2019. The Company is also eligible to receive a payment of $2.0 million per indication 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. No milestone payments nor research and development reimbursement payments were earned in the year ended December 31, 2020.

The research and development reimbursement payments under the EUSA Agreement are not subject to the 30% sublicensing payment payable to KKC, subject to certain limitations. The Company, however, would owe KKC 30% of other, non-research and development payments it may receive from EUSA pursuant to the EUSA Agreement, including reimbursement approvals for RCC in the EU5, marketing approvals for RCC in three specified non-EU licensed territories, EU marketing approval filings and corresponding marketing approvals by the EMA for up to three additional indications beyond RCC, and sales-based milestones and royalties, as set forth above. The $2.0 million milestone payments the Company earned in each of February 2018, November 2018 and February 2019 upon EUSA's reimbursement approval for FOTIVDA from the NICE in the United Kingdom, the GKV-SV in Germany and the MSCBS in Spain, respectively, for the first-line treatment of RCC were subject to the 30% KKC sublicense fee, or $0.6 million, each. The sublicense fees for EUSA's reimbursement approvals in the United Kingdom, Germany and Spain were paid in April 2018, January 2019 and June 2019, respectively.

EUSA is obligated to use commercially reasonable efforts to seek regulatory approval for and commercialize tivozanib throughout the EUSA Licensed Territories in RCC. 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.

Accounting Analysis Under ASC 606

Pursuant to ASC 606, the Company identified the following promised goods and services at the inception of the EUSA Agreement: (i) the Company's grant of an exclusive license to develop and commercialize tivozanib in the EUSA Licensed Territories, including the Company's obligation to transfer all technical knowledge and data useful in the development and manufacture of tivozanib; (ii) the Company's obligation to cooperate with EUSA and support its efforts to file for marketing approval in the EUSA Licensed Territories and in its commercialization efforts; (iii) 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 (iv) the Company's participation in a joint steering committee. The Company determined that the license to develop and commercialize tivozanib in the EUSA Licensed Territories was not distinct from the other promised goods and services and has accordingly accounted for these items as a single performance obligation. In reaching this conclusion, the Company concluded the remaining promises were essential to EUSA's use of the license.

The Company concluded at contract inception that EUSA's opt-in rights with respect to the TiNivo trial and the TIVO-3 trial did not represent material rights because at contract inception the Company had not yet initiated either trial and the option price (representing approximately 50% of the costs of the respective trial) was proportional to the value attributed to the EUSA Licensed Territories relative to the territorial rights retained by the Company. Accordingly, the Company accounts for each opt-in as a separate arrangement when such opt-ins occur.

The Company evaluated the promised goods and services at the inception of the EUSA Agreement under ASC 606. Based on this evaluation, the Company determined that $6.5 million in research and development payments by EUSA, including the $2.5 million upfront consideration received upon the execution of the EUSA Agreement in December 2015 and the $4.0 million payment upon the receipt of marketing approval from the EMA for FOTIVDA (tivozanib) for the treatment of RCC in August 2017, constituted the amount of the consideration that was included in the transaction price upon the adoption of ASC 606 on January 1, 2018 and attributed this amount to the Company's single performance obligation. Upon adoption of ASC 606 on January 1, 2018, none of the remaining regulatory-related milestones were included in the transaction price as these milestone amounts were fully constrained. As part of its evaluation of the constraint, the Company considered multiple factors: (i) the remaining reimbursement and marketing approvals in RCC are outside of the control of EUSA and vary on a country-by-country basis, (ii) milestones related to the submission filings for EMA approval of tivozanib in up to three additional indications are contingent upon the success of future clinical trials in additional indications, if any, and are outside of the control of EUSA, (iii) milestones related to the marketing approval by the EMA for tivozanib in up to three additional indications are contingent upon the success of the corresponding future clinical trials, if any, and are outside of the control of EUSA, and (iv) efforts by EUSA. Any consideration related to sales-based milestones (including royalties) will be recognized when the related sales occur as these amounts have been determined to relate predominantly to the license granted to EUSA and therefore are recognized at the later of when the performance obligation is satisfied (or partially satisfied) or the related sales occur. The Company will re-evaluate the transaction price, including its estimated variable consideration for milestones included in the transaction price and all constrained amounts, in each reporting period and as uncertain events are resolved or other changes in circumstances occur.

Under ASC 606, the upfront consideration and regulatory milestones included in the transaction price are being recognized as collaboration and licensing revenue over the Company's performance period from contract execution in December 2015 through the remaining patent life of tivozanib in April 2022. Under ASC 606, upon the achievement of a regulatory milestone, the amount that represents the cumulative catch-up for the period from contract execution in December 2015 through the date of the milestone achievement is recognized as collaboration and licensing revenue, with the balance classified as deferred revenue and recognized as collaboration and licensing revenue over the remainder of the performance period, currently estimated through April 2022.

In November 2017, the Company began earning sales royalties upon EUSA's commencement of the first commercial launch of FOTIVDA (tivozanib) with the initiation of product sales in Germany. EUSA has received reimbursement approval for and commercially launched FOTIVDA in Germany, the United Kingdom, and Spain as well as in some additional non-EU5 countries. EUSA is working to secure reimbursement approval in Italy and France and commercially launch FOTIVDA in additional European countries. The Company recognized royalty revenue of approximately $1.2 million, $0.9 million and $0.5 million in the years ended December 31, 2020, 2019 and 2018, respectively.

In the first quarter of 2018, the Company increased the transaction price to $8.5 million to include the $2.0 million milestone for reimbursement approval from the NICE in the United Kingdom in first-line RCC that was achieved in February 2018. Accordingly, the Company recognized approximately $0.7 million in collaboration and licensing revenue for the cumulative catch-up for the period from contract execution in December 2015 through the milestone achievement in February 2018, with the approximate $1.3 million balance classified as deferred revenue that is being recognized as collaboration and licensing revenue over the remainder of the performance period through April 2022.

In the fourth quarter of 2018, the Company increased the transaction price to $10.5 million to include the $2.0 million milestone for reimbursement approval from the GKV-SV in Germany in first-line RCC that was achieved in November 2018. Accordingly, the Company recognized approximately $0.9 million in collaboration and licensing revenue for the cumulative catch-up for the period from contract execution in December 2015 through the milestone achievement in November 2018, with the approximate $1.1 million balance classified as deferred revenue that is being recognized as collaboration and licensing revenue over the remainder of the performance period through April 2022.

In the first quarter of 2019, the Company increased the transaction price to $12.5 million to include the $2.0 million milestone for reimbursement approval from the MSCBS in Spain in first-line RCC that was achieved in February 2019. Accordingly, the Company recognized approximately $1.0 million in collaboration and licensing revenue for the cumulative catch-up for the period from contract execution in December 2015 through the milestone achievement in February 2019, with the approximate $1.0 million balance classified as deferred revenue that is being recognized as collaboration and licensing revenue over the remainder of the performance period through April 2022.

The Company recognized total revenues under the EUSA Agreement of approximately $3.2 million, $3.8 million and $3.4 million in the years ended December 31, 2020, 2019 and 2018, respectively. As of December 31, 2020, there was approximately $2.6 million in total deferred revenue that is expected to continue to be recognized as collaboration and licensing revenue, in the approximate amount of $0.5 million per quarter, over the duration of the Company's performance period through April 2022.

The following table summarizes the revenues earned in connection with the EUSA Agreement under ASC 606 for the year ended December 31, 2020, 2019 and 2018 (in thousands):

Revenue Type	Date Achieved	Year Ended December 31, 2020	Year Ended December 31, 2019	Year Ended December 31, 2018
Collaboration and Licensing Revenue:				
Amounts in contract liabilities at the beginning of the period:				
Upfront payment	December 2015	$ 395	$ 395	$ 395
R&D payment - EMA approval in RCC	August 2017	631	631	632
Milestone - UK reimbursement approval	February 2018	316	316	960
Milestone - German reimbursement approval	November 2018	316	316	960
Milestone - Spanish reimbursement approval	February 2019	316	1,276	—
		$ 1,974	$ 2,934	$ 2,947
Partnership Royalties		1,245	861	462
Total		$ 3,219	$ 3,795	$ 3,409

The following table summarizes changes in the Company's accounts receivable and contract liabilities (deferred revenue) in connection with the EUSA Agreement for the year ended December 31, 2020 (in thousands):

Contract Assets	Beginning Balance January 1, 2020	Additions	Deductions	Ending Balance December 31, 2020
Accounts Receivable	$ 270	$ 1,245	$ (1,123)	$ 392

				Deferred Revenue			
Contract Liabilities	Transaction Price	Date Achieved	Date Paid	Beginning Balance January 1, 2020	Additions	Deductions	Ending Balance December 31, 2020
Amounts in contract liabilities at the beginning of the period:							
Upfront payment	$ 2,500	December 2015	December 2015	$ 907	$ —	$ (395)	$ 512
R&D payment - EMA approval in RCC	4,000	August 2017	September 2017	1,448	—	(631)	817
Milestone - UK reimbursement approval	2,000	February 2018	March 2018	724	—	(316)	408
Milestone - German reimbursement approval	2,000	November 2018	December 2018	723	—	(316)	407
Milestone - Spanish reimbursement approval	2,000	February 2019	May 2019	724	—	(316)	408
Total	$ 12,500			$ 4,526	$ —	$ (1,974)	$ 2,552

Opt-In to the TiNivo Trial

In September 2017, EUSA elected to opt-in to co-develop the TiNivo trial. As previously described, the Company accounts for each opt-in as a separate arrangement. 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 the EUSA Licensed Territories. Upon the 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. 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 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 that is not representative of a vendor-customer relationship.

The Company recognized reductions in research and development expenses of approximately $0.1 million, $0.4 million and $0.5 million in the years ended December 31, 2020, 2019 and 2018, respectively. As of December 31, 2020, the Company had recognized $2.0 million in cumulative total reductions in research and development expenses related to EUSA's approximate 50% share of the cumulative study-to-date costs. EUSA paid the $2.0 million maximum amount of cost sharing per the EUSA Agreement in advance of the completion of the trial.

Novartis

In August 2015, the Company entered into a license agreement (the "Novartis Agreement") with Novartis International Pharmaceutical, Ltd. ("Novartis"), under which the Company granted Novartis the exclusive right to develop and commercialize AV-380 and the Company's related antibodies worldwide. On June 29, 2018, Novartis notified the Company that it would be terminating the Novartis Agreement without cause, following a change in strategic direction at Novartis. Effective August 28, 2018 the Company regained the rights to AV-380, and on December 19, 2018, the Company entered into a new agreement with Novartis (the "AV-380 Transfer Agreement") to further establish and clarify the terms on which Novartis would return the AV-380 program to the Company and to support the Company's continuing development of the AV-380 program. Pursuant to the AV-380 Transfer Agreement, Novartis made a one-time payment to the Company of $2.3 million in January 2019, which the Company used to cover the $2.3 million time-based milestone obligation due to St. Vincent's Hospital Sydney Limited ("St. Vincent's") in January 2019 under its license agreement as further described below under the heading "—In-License Agreements – St. Vincent's."

In connection with the AV-380 Transfer Agreement, the $2.3 million payment due from Novartis was not considered a revenue transaction due to the effective termination of the Novartis Agreement on August 28, 2018 and was instead considered other income. The Company evaluated the return of the AV-380 drug supply and determined that the inventory was not capitalizable as future economic benefit was not probable due to the AV-380 product candidate being in the pre-clinical development stage.

Biodesix

In April 2014, the Company entered into a worldwide co-development and collaboration agreement (the "Biodesix Agreement") with Biodesix, Inc. ("Biodesix") to develop and commercialize ficlatuzumab, the Company's potent humanized IgG1 monoclonal antibody that targets HGF. In September 2020, the Company regained full global rights to ficlatuzumab, effective December 2, 2020, when Biodesix exercised its "Opt-Out" rights (as defined below) under the Biodesix Agreement.

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 included the right to sublicense, subject to certain exceptions. The Company was designated to lead the clinical development of ficlatuzumab following approval of a development plan by a joint steering committee. The Company and Biodesix are currently funding an investigator-sponsored clinical trial for ficlatuzumab in combination with ERBITUX® (cetuximab) in HNSCC. The Biodesix Agreement generally provided for each party to contribute 50% of all clinical, regulatory, manufacturing and other costs to develop ficlatuzumab and to share equally in any future revenue from development or commercialization.

Under the Biodesix Agreement, prior to the first commercial sale of ficlatuzumab, each party had the right to elect to discontinue its funding obligation for further development or commercialization efforts with respect to ficlatuzumab in exchange for reduced economics in the program, which is referred to as an "Opt-Out." Pursuant to the terms of the Biodesix Agreement, as a result of Biodesix's election to Opt-Out, Biodesix will (i) continue to be responsible for reimbursement of development costs with respect to the ongoing open label Phase 2 investigator-sponsored clinical trial of ficlatuzumab in combination with ERBITUX® (cetuximab) in HNSCC (the "Phase 2 HNSCC Trial"), (ii) cease to be entitled to 50% sharing of profits resulting from commercialization of ficlatuzumab, (iii) be entitled to a low double digit royalty on future product sales and 25% of future licensing revenue (excluding contributions to research and development expenses) less approximately $2.5 million that Biodesix would be required to pay to the Company pursuant to the October 2016 amendment to the Biodesix Agreement and (iv) remain responsible for development obligations under the Biodesix Agreement with respect to VeriStrat. Biodesix and the Company also remain obligated to negotiate a commercialization agreement to delineate their rights and obligations in the event of any commercialization of VeriStrat with ficlatuzumab. As a result of Biodesix's decision to Opt-Out, the Company now has worldwide licensing rights and sole decision-making authority with respect to further development and commercialization of ficlatuzumab. The payment obligations between the parties under the Biodesix Agreement are in effect until completion of the Phase 2 HNSCC Trial.

The Company is accounting for the joint development activities under the Biodesix Agreement as a joint risk-sharing collaboration in accordance with ASC 808 because both the Company and Biodesix have been active participants in the ongoing development of ficlatuzumab via their participation on a joint steering committee that oversaw the development plans for ficlatuzumab and have been exposed to significant risk and rewards in connection with their activity based on their obligations to share in the costs, as defined above. Payments from Biodesix with respect to its share of ficlatuzumab 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 that is not representative of a vendor-customer relationship.

The Company records reimbursements from Biodesix for expenses related to these trials and drug manufacturing as a reduction in research and development expense during the period that reimbursable expenses are incurred. As a result of the cost sharing provisions in the Biodesix Agreement, the Company reduced research and development expenses by approximately $0.8 million, $0.9 million and $0.3 million in the years ended December 31, 2020, 2019 and 2018, respectively. The amount due to the Company from Biodesix pursuant to the cost-sharing provision was approximately $0.1 million as of December 31, 2020.

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, including AV-203, for the potential treatment and diagnosis of cancer and other diseases outside of North America (the "Biogen Agreement"). Under the Biogen 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, would generate data sufficient to support advancement to a phase 3 clinical trial.

In March 2014, the Company and Biogen amended the Biogen Agreement (the "Biogen Amendment"). Pursuant to the Biogen Amendment, Biogen agreed to the termination of its rights and obligations under the Biogen Agreement, including Biogen's option to (i) obtain a co-exclusive (with the Company) 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, the Company has worldwide rights to AV-203. Pursuant to the Biogen 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 the Company 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 a cumulative maximum amount of $50.0 million.

In March 2016, the Company entered into a collaboration and license agreement for AV-203 with CANbridge, which satisfied its obligation to seek a collaboration partner for the purpose of funding further development and commercialization of ErbB3 targeted antibodies. The $2.0 million development and regulatory milestone the Company earned in August 2018 in connection with CANbridge's regulatory approval from the NMPA of an IND application for a clinical study of AV-203 in ESCC was subject to this sublicense fee, or $0.7 million, which was paid to Biogen in October 2018. See "—*CANbridge*" within this Note 4 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 sublicensable right 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 (the "St. Vincent's Agreement"). Under the St. Vincent's 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 amended and restated the St. Vincent's Agreement and made an additional upfront payment to St. Vincent's of $1.5 million. As of December 31, 2020, the Company is required to make future milestone payments, up to an aggregate total of $14.4 million, upon the earlier of the 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 milestone payments made after the Company grants any sublicense, depending on the sublicensed territory. In February 2017, Novartis agreed to pay $1.8 million out of its then future payment obligations to the Company under the Novartis Agreement. These funds were used to satisfy a $1.8 million time-based milestone obligation that the Company owed to St. Vincent's in March 2017. The Company used the $2.3 million payment received from Novartis in January 2019, pursuant to the AV-380 Transfer Agreement, to cover a $2.3 million time-based milestone obligation that became due to St. Vincent's in January 2019. The Company will also be required to pay St. Vincent's tiered royalty payments equal to a low-single-digit percentage of any net sales it or its sublicensees make from licensed therapeutic products. The royalty rate escalates within the low-single-digit range during each calendar year based on increasing licensed therapeutic product sales during such calendar year.

Kyowa Kirin Co. (KKC)

In December 2006, the Company entered into the KKC Agreement with KKC, under which it obtained an exclusive, sublicensable license to develop, manufacture and commercialize tivozanib in all territories in the world except for Asia and the Middle East, where KKC retained the rights to tivozanib. Under the KKC Agreement, the Company obtained exclusive rights to tivozanib in its territory under certain KKC patents, patent applications and know-how for the diagnosis, prevention and treatment of all human diseases and conditions (the "Field"). On August 1, 2019, the Company entered into an amendment to the KKC Agreement pursuant to which KKC repurchased the non-oncology rights to tivozanib in the Company's territory, excluding the rights the Company has sublicensed to EUSA under the EUSA Agreement. The Company has upfront, milestone and royalty payment obligations to KKC under the KKC Agreement related to the amended Field for oncology development by the Company, and following the amendment, KKC also has upfront, milestone and royalty payment obligations to the Company related to non-oncology development by KKC in the Company's territory. Pursuant to the amendment to the KKC Agreement, KKC was required to make a non-refundable upfront payment to the Company in the amount of $25.0 million that was received in September 2019 and KKC waived a one-time milestone payment of $18.0 million otherwise payable by the Company upon obtaining marketing approval for tivozanib in the United States.

KKC Agreement

Upon entering into the KKC Agreement, the Company made an upfront payment in the amount of $5.0 million. In March 2010, the Company made a milestone payment to KKC in the amount of $10.0 million in connection with the dosing of the first patient in the Company's TIVO-1 trial. In December 2012, the Company made a $12.0 million milestone payment to KKC in connection with the acceptance by the FDA of the Company's 2012 NDA filing for tivozanib. Each milestone under the KKC Agreement is a one-time only payment obligation, accordingly, the Company did not owe KKC 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 KKC when the Company filed its then anticipated NDA with the FDA, which was subsequently filed on March 31, 2020. The Company has no remaining development and commercialization milestone payments due to KKC under the KKC Agreement.

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 KKC Agreement relating to rights the Company retains. The Company is required to pay KKC 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 receipt of marketing authorization from the European Commission for FOTIVDA (tivozanib) 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 KKC. In addition, if EUSA elects to opt-in to the TIVO-3 trial, the additional research and development reimbursement payment from EUSA of 50% of the total trial costs, up to $20.0 million, would also not be subject to a sublicense revenue payment to KKC, subject to certain limitations. The Company would, however, owe KKC 30% of other, non-research and development payments the Company may receive from EUSA pursuant to the EUSA Agreement, including reimbursement approvals for RCC in up to five specified EU countries, marketing approvals for RCC in three specified non-EU licensed territories, EU marketing approval filings and corresponding marketing approvals by the EMA for up to three additional indications beyond RCC, and sales-based milestones and royalties. The $2.0 million milestone payments the Company earned in each of February 2018, November 2018 and February 2019 upon EUSA's reimbursement approvals for FOTIVDA as a first-line treatment for RCC in the United Kingdom, Germany and Spain, respectively, were subject to the 30% KKC sublicense fee, or $0.6 million each. The sublicense fees for EUSA's reimbursement approvals in the United Kingdom, Germany and Spain were paid in April 2018, January 2019 and June 2019, respectively.

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 Company and KKC 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 KKC Agreement, as related to the amended Field for oncology development. Under the KKC Agreement, the Company is obligated to use commercially reasonable efforts to develop and commercialize tivozanib in its territory.

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

August 1, 2019 Amendment to the KKC Agreement

In addition to the non-refundable upfront payment to the Company pursuant to the amendment to the KKC Agreement in the amount of $25.0 million, KKC is also required to make milestone payments to the Company of up to an aggregate of $390.7 million upon the successful achievement of certain development and sales milestones of tivozanib in non-oncology indications. On August 2, 2020, KKC's IND application for a non-oncology formulation of tivozanib was accepted by the Pharmaceuticals and Medical Devices Agency of Japan. Accordingly, the Company earned a $2.8 million development milestone payment upon acceptance of the IND pursuant to the KKC Agreement that was received in August 2020. In addition, KKC is required to make tiered royalty payments to the Company on net sales of tivozanib in non-oncology indications in the Company's territory, which range from high single digit to low double digits as a percentage of net sales. The royalty rate escalates within this range based on increasing tivozanib sales, subject to certain adjustments. KKC's royalty payment obligations in a particular country in the Company's territory begin on the date of the first commercial sale of tivozanib in that country, and end on the later of the expiration date of the last valid claim of a patent application or patent owned by KKC covering tivozanib or 10 years after the date of first commercial sale of tivozanib in non-oncology indications in that country.

If KKC sublicenses any of its rights to tivozanib to a third-party, KKC is required to pay the Company a percentage of amounts received from the respective sublicensees related to the Company's territory, including upfront license fees, milestone payments and royalties, but excluding amounts received in respect of research and development reimbursement payments or equity investments, subject to certain limitations.

Accounting Analysis Under the August 1, 2019 Amendment to the KKC Agreement

Following the repurchase of non-oncology rights by KKC, the amended KKC Agreement is accounted for as two distinct agreements: (i) the KKC Agreement by which the Company has upfront, milestone and royalty payment obligations to KKC related to the Company's oncology development of tivozanib in the amended Field for the Company's territory that continues to be accounted for under ASC 730, *Research and Development*, and (ii) the amended KKC Agreement by which KKC has upfront, milestone and royalty payment obligations to the Company related to its non-oncology development of tivozanib for the Company's territory that will be accounted for under ASC 606.

The Company evaluated the amendment to the KKC Agreement under ASC 606 and determined that KKC met the definition of a customer as the Company considers the licensing or sale of intellectual property rights to be an output of the Company's ordinary activities and is central to the operations of the Company. The Company determined that the amendment to the KKC Agreement contained a single performance obligation related to the Company's transfer of rights to non-oncology intellectual property and know-how to KKC, excluding the rights the Company has sublicensed to EUSA under the EUSA Agreement. In addition, the Company determined that the $25.0 million non-refundable upfront payment received from KKC in September 2019 constituted the amount of the consideration to be included in the transaction price and attributed this amount to the Company's single performance obligation. The Company satisfied this performance obligation during the third quarter of 2019. Accordingly, the Company recognized the $25.0 million in consideration as revenue in the third quarter of 2019. The Company concluded the performance obligation was satisfied at a point in time because any know-how or clinical data generated from the Company's ongoing oncology development of tivozanib would not benefit KKC's non-oncology development of tivozanib.

In the third quarter of 2020, the Company increased the transaction price to $27.8 million to include the $2.8 million development milestone that was earned in August 2020 upon the acceptance of KKC's IND application for a non-oncology formulation of tivozanib by the Pharmaceuticals and Medical Devices Agency of Japan. Accordingly, the Company recognized the $2.8 million in consideration as revenue in the third quarter of 2020 as the Company did not have any ongoing performance obligations under the amendment to the KKC Agreement.

None of KKC's remaining development and regulatory milestones to the Company related to its non-oncology development of tivozanib for the Company's territory were included in the transaction price, as these milestone amounts were fully constrained. As part of its evaluation of the constraint, the Company considered multiple factors: (i) regulatory approvals are outside of the control of KKC, (ii) certain development and regulatory milestones are contingent upon the success of future clinical trials, if any, which is out of the control of KKC, and (iii) efforts by KKC. Any consideration related to development and regulatory milestones owed by KKC to the Company will be recognized when the corresponding milestones are no longer constrained as the Company does not have any ongoing performance obligations. Any consideration related to sales-based milestones (including royalties) will be recognized when the related sales occur as these amounts have been determined to relate predominantly to the intellectual property transferred to KKC and therefore are recognized at the later of when the performance obligation is satisfied or the related sales occur.

(5) Other Accrued Liabilities

Other accrued expenses consisted of the following:

	December 31, 2020	December 31, 2019
	(in thousands)	
Professional fees	$ 1,061	$ 806
Compensation and benefits	3,082	1,284
Other	320	246
Total	$ 4,463	$ 2,336

(6) Hercules Loan Facility

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

In December 2017, the Company entered into an amended and restated loan and security agreement (the "2017 Loan Agreement") to refinance the Company's prior loan facility with Hercules and to retire the $20.0 million in secured debt then-outstanding under the First Loan Agreement. Per the terms of the 2017 Loan Agreement, the $20.0 million loan facility had 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, the loan maturity date was revised from December 2019 to July 2021. The Company was not required to make principal payments until February 1, 2019, at which time the Company would have been 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. 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 the Company's TIVO-3 trial with results that are satisfactory to Hercules was removed. Per the 2017 Loan Agreement, the interest rate decreased from 11.9% to 9.45%. The Company incurred approximately $0.1 million in loan issuance costs paid directly to Hercules, which was accounted for as a loan discount. The 2017 Loan Agreement was accounted for as a loan modification in accordance with ASC 470-50, *Modifications and extinguishments* ("ASC 470-50").

The Company must make interest payments on the principal balance of the loan each month it remains outstanding. Per annum interest was 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%. In 2018, the interest rate increased to 9.70%, 9.95% and 10.20% in June 2018, September 2018 and December 2018, respectively, due to corresponding increases in the prime rate. In 2019, the interest rate decreased to 9.95%, 9.70% and 9.45% in August 2019, September 2019 and October 2019, respectively, due to corresponding decreases in the prime rate. The interest rate as of August 1, 2020 was 9.45%.

The interest-only period could be extended by two 6-month deferrals of principal payments upon the achievement of specified milestones relating to the development of tivozanib, subject to confirmation by Hercules at its reasonable discretion.

In November 2018, Hercules granted the first 6-month extension of the interest-only period. Accordingly, this resulted in the deferment of principal payments until August 1, 2019, at which time the Company resumed making 24 equal monthly payments of principal and interest, in the approximate amount of $0.9 million through July 2021. The outstanding principal balance as of August 1, 2020 was approximately $9.7 million.

On August 7, 2020, the Company entered into a first amendment to the 2017 Loan Agreement (the "2020 Loan Amendment") to provide the Company, subject to certain terms and conditions, with an additional term loan in an aggregate principal amount of up to $35.0 million (the "2020 Loan Facility") in up to four tranches to be used to refinance outstanding loans under the 2017 Loan Agreement, and for general working capital purposes.

The Company received the initial $15.0 million of the 2020 Loan Facility upon the closing of the 2020 Loan Amendment, of which approximately $9.7 million was used to retire the then outstanding balance under the 2017 Loan Agreement and of which approximately $5.3 million was new loan funding which was used for general working capital purposes.

The remainder of the loan amount will be available to the Company, at its option, subject to certain terms and conditions, including upon the achievement of the following milestones: (i) the second tranche of $10.0 million ("Tranche Two") would be available through June 30, 2021 upon achieving FDA approval of FOTIVDA ("Performance Milestone I"), (ii) the third tranche of $5.0 million ("Tranche Three") would be available from July 1, 2021 through January 31, 2022 assuming the Company achieves $20.0 million in net product revenues from sales of FOTIVDA, by no later than December 31, 2021 ("Performance Milestone II"), and (iii) the fourth tranche of $5.0 million would be available through June 30, 2022 contingent upon the achievement of both Performance Milestone I and Performance Milestone II, and subject to the consent of Hercules.

The 2020 Loan Amendment also amends the 2017 Loan Agreement by: (i) extending maturity until September 1, 2023, which is extendable to September 1, 2024 at the Company's option assuming the Tranche Three funding has occurred, (ii) providing for an interest-only period beginning on the closing date of 2020 Loan Amendment and ending on September 30, 2021, which period may be extended through September 30, 2022 provided the Company achieved Performance Milestone I and further extendable through March 31, 2023 after the Tranche Three funding has occurred, if at all, and (iii) revising the per annum interest rate to the greater of (x) 9.65% and (y) an amount equal to 9.65% plus the prime rate as reported in the Wall Street Journal minus 3.25% as determined daily, provided however, that the per annum interest rate shall not exceed 15%. Principal payments are scheduled to commence on October 1, 2021, at the earliest, as described above. The interest rate as of December 31, 2020 was 9.65%.

Per the terms of the 2020 Loan Facility, principal will be repaid in equal monthly installments following the conclusion of the interest-only period. The Company may prepay all of the outstanding principal and accrued interest under the 2020 Loan Facility, subject to a prepayment charge up to 3.0% in the first year following the closing of the 2020 Loan Amendment, decreasing to 2.0% in year two and 1.0% in year three. The Company is obligated to make an end-of-term payment of 6.95% of the aggregate amount of loan funding received under the 2020 Loan Facility on the earlier of the maturity of the loan or the date on which the Company prepays any outstanding loan balance. The approximate $0.8 million end-of-term payment under the 2017 Loan Agreement continues to be due on July 1, 2021. In connection with the 2020 Loan Amendment, the Company incurred approximately $0.3 million in loan issuance costs paid directly to Hercules, which are accounted for as a loan discount. The 2020 Loan Amendment was accounted for as a loan modification in accordance with ASC 470-50.

The unamortized discount to be recognized over the remainder of the loan period was approximately $1.2 million and $0.4 million as of December 31, 2020 and December 31, 2019, respectively.

The 2020 Loan Facility includes various financial and operating covenants, including that the Company maintain an unrestricted cash position of at least $10.0 million through the date the Third Tranche funding is received and at least $5.0 million thereafter through the maturity of the loan. The Company is also required to achieve greater than or equal to 75% of its forecasted net product revenues from its sales of tivozanib over a 6-month trailing period, as defined and measured on a monthly basis, effective upon the Third Tranche funding and continuing through the maturity of the loan. The net product revenue covenant will not apply at any time the Third Tranche funding has not been provided nor such advance has been prepaid in full.

On February 1, 2021, the Company entered into the second amendment to the 2017 Loan Agreement (the “2021 Loan Amendment”), which increases the 2020 Loan Facility from up to $35.0 million to up to $45.0 million following FDA approval of FOTIVDA. The 2021 Loan Amendment makes certain changes to the 2020 Loan Amendment, including, among other things, (i) increasing Tranche Two funding upon achieving Performance Milestone I from $10.0 million to $20.0 million, thereby increasing the total amount of unfunded term loan commitments under the 2020 Loan Facility from $20.0 million to $30.0 million, (ii) increasing the amount of net product revenues from sales of FOTIVDA required to achieve Performance Milestone II from $20.0 million to $35.0 million and changing the deadline for achieving Performance Milestone II from December 31, 2021 to April 1, 2022 and (iii) increasing the amount of the financial covenant for the maintenance of an unrestricted cash position from at least $10.0 million to at least $15.0 million from the date the Tranche Two funding is received until the date the Tranche Three funding is received and at least $10.0 million thereafter through the maturity of the Loan Agreement.

On March 11, 2021, the Company completed the $20.0 million drawdown of Tranche Two funding under the 2021 Loan Amendment that was made available in connection with the achievement of Performance Milestone I upon FDA approval of FOTIVDA on March 10, 2021. The achievement of Performance Milestone I extended the interest-only period by twelve months from September 30, 2021 to September 30, 2022 and increased the amount of unrestricted cash required for the Company to satisfy the minimum financial covenant during the period between receiving Tranche Two funding and Tranche Three funding from $10.0 million to $15.0 million.

The 2020 Loan Facility is secured by substantially all of the Company’s assets, excluding intellectual property. The 2020 Loan Facility provides that certain events shall constitute a default by the Company, including failure by the Company to pay amounts under the 2020 Loan Amendment when due; breach or default in the performance of any covenant under the 2020 Loan Amendment by the Company, subject to certain cure periods; insolvency of the Company and certain other bankruptcy proceedings involving the Company; default by the Company of obligations involving indebtedness in excess of $500,000; and the occurrence of an event or circumstance that would have a material adverse effect upon the business of the Company. As of December 31, 2020, 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 effect as defined in the 2020 Loan Amendment.

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 as a long-term liability based on the timing of scheduled principal payments.

Future minimum payments under the loans payable outstanding as of December 31, 2020 are as follows (amounts in thousands):

Year Ending December 31:	
2021	3,961
2022	8,277
2023	7,272
	19,510
Less amount representing interest	(2,678)
Less unamortized discount	(1,228)
Less deferred charges	(1,832)
Less loans payable current, net of discount	(1,056)
Loans payable, net of current portion and discount	$ 12,716

(7) Common Stock

As of December 31, 2020, the Company had 50,000,000 authorized shares of common stock, $0.001 par value, of which 26,882,696 shares were issued and outstanding.

Reverse Stock Split – February 2020

On February 13, 2020, the holders of a majority of the Company's outstanding shares of common stock approved the reverse stock split and gave the Company's board of directors discretionary authority to select a ratio for the split ranging from 1-for-5 to 1-for-15. The Company's board of directors approved the reverse stock split at a ratio of 1-for-10 on February 13, 2020. On February 19, 2020, the Company effected a reverse stock split of its outstanding shares of common stock at a ratio of one-for-ten pursuant to a Certificate of Amendment to its Certificate of Incorporation filed with the Secretary of State of the State of Delaware. The reverse stock split was reflected on Nasdaq beginning with the opening of trading on February 20, 2020. The primary purpose of the reverse stock split was to enable the Company to regain compliance with the $1.00 minimum bid price requirement for continued listing on Nasdaq.

The reverse stock split affected all issued and outstanding shares of the Company's common stock, as well as the number of authorized shares of the Company's common stock and the number of shares of common stock available for issuance under the Company's equity incentive plans. The reverse stock split reduced the number of shares of the Company's issued and outstanding common stock from approximately 160.8 million to approximately 16.1 million. In addition, the reverse stock split effected a reduction in the number of shares of the Company's common stock issuable upon the exercise of stock options and warrants outstanding immediately prior to the reverse stock split, with a proportional increase in the respective exercise prices. The reverse stock split proportionately reduced the number of authorized shares of the Company's common stock from 500.0 million shares to 50.0 million shares. The reverse stock split did not change the par value of the Company's common stock or the authorized number of shares of the Company's preferred stock. All share and per share amounts give effect to the reverse stock split on a retroactive basis.

Public Offering – June 2020

On June 19, 2020, the Company completed an underwritten public offering of 9,725,000 shares of its common stock, including the partial exercise by the underwriters of their option to purchase an additional 1,225,000 shares, at the public offering price of $5.25 per share for gross proceeds of approximately $51.1 million. Three stockholders beneficially holding more than 5% of the Company's voting securities, including an entity affiliated with New Enterprise Associates and two other stockholders, purchased an aggregate of 4,503,571 shares in this offering at the same public offering price per share as the other investors. At such time, entities affiliated with New Enterprise Associates (collectively) beneficially held more than 5% of the Company's voting securities. The net offering proceeds to the Company were approximately $47.7 million after deducting underwriting discounts and commissions and estimated offering expenses payable by the Company.

Universal Shelf Registration Statement

On November 9, 2020, the Company filed a shelf registration statement on Form S-3 with the U.S. Securities and Exchange Commission, which covers the offering, issuance and sale of up to $300.0 million of its common stock, preferred stock, debt securities, warrants and/or units (the "2020 Shelf"). The 2020 Shelf (File No. 333-249982) was declared effective by the SEC on November 18, 2020 and was filed to replace the Company's then existing shelf registration statement, which was terminated. As of December 31, 2020, there was approximately $268.2 million available for future issuance of common stock, preferred stock, debt securities, warrants and/or units.

Public Offering – April 2019

In April 2019, the Company completed an underwritten public offering of 2,173,913 shares of its common stock and warrants to purchase an aggregate of 2,500,000 shares of its common stock ("the Offering Warrants"), including warrants to purchase an aggregate of 326,086 shares of its common stock sold pursuant to the underwriter's partial exercise of its overallotment option, at the public offering price of $11.40 per share and $0.10 per warrant for gross proceeds of approximately $25.0 million. The Offering Warrants were immediately exercisable upon issuance at an exercise price of $12.50 per share, subject to adjustment in certain circumstances, and will expire two years from the date of issuance upon their scheduled expiration on April 8, 2021. Any Offering Warrants that have not been exercised for cash prior to their expiration shall be automatically exercised via cashless exercise on the expiration date. The shares and warrants were issued separately and are separately transferable. An entity affiliated with New Enterprise Associates purchased 434,782 shares and warrants to purchase an aggregate of 434,782 shares in this offering at the same public offering price per share as the other investors. At such time, entities affiliated with New Enterprise Associates (collectively) beneficially held more than 5% of the Company's voting securities. The net offering proceeds to the Company were approximately

$22.8 million after deducting underwriting discounts and commissions and estimated offering expenses payable by the Company. As of December 31, 2020, Offering Warrants to purchase 2,500,000 shares of the Company's common stock were outstanding. The Company determined the shares of common stock and the Offering Warrants represented freestanding financial instruments. In addition, the Company conducted an assessment of the classification of the Offering Warrants and, based on their terms, concluded the Offering Warrants are equity-classified. Accordingly, the net offering proceeds of $22.8 million have been recorded within stockholders' equity (deficit).

In March 2021, Offering Warrants exercisable for 247,391 shares of common stock had been exercised, for approximately $3.1 million in cash proceeds, and Offering Warrants exercisable for 2,252,609 shares of common stock were outstanding.

Sales Agreement with SVB Leerink

In February 2018, the Company entered into a sales agreement with SVB Leerink (the "SVB Leerink Sales Agreement") pursuant to which the Company may issue and sell shares of its common stock from time to time up to an aggregate amount of $50.0 million, at its option, through SVB Leerink as its sales agent, with any sales of common stock through SVB 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"), or in other transactions pursuant to an effective shelf registration statement on Form S-3. The Company agreed to pay SVB Leerink a commission of up to 3% of the gross proceeds of any sales of common stock pursuant to the SVB Leerink Sales Agreement. In the fourth quarter of 2018, the Company sold 470,777 shares pursuant to the SVB Leerink Sales Agreement, resulting in approximately $10.3 million in proceeds, net of commissions. In February 2019, the Company sold 1,251,555 shares pursuant to the SVB Leerink Sales Agreement, resulting in proceeds of approximately $7.5 million, net of commissions. In November 2020, the Company sold 1,070,175 shares pursuant to the SVB Leerink Sales Agreement, resulting in proceeds of approximately $5.9 million, As of December 31, 2020, approximately $25.7 million was available for issuance in connection with future stock sales pursuant to the SVB Leerink Sales Agreement.

Public Offering – August 2018

On August 21, 2018, the Company completed an underwritten public offering of 250,000 shares of its common stock at the public offering price of $22.60 per share for gross proceeds of approximately $5.7 million. Two greater than 5% stockholders, including an entity affiliated with New Enterprise Associates and another stockholder purchased approximately 200,000 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 $5.1 million after deducting underwriting discounts and estimated offering expenses payable by the Company.

Settlement Warrants

On July 16, 2018, the Company issued and delivered 200,000 warrants to purchase shares of its common stock that the Company agreed to issue in connection with the settlement of the former 2013 class action lawsuit (the "Settlement Warrants"). The Settlement Warrants were exercisable for a one-year period after the date of issuance at an exercise price equal to $30.00 per share. All 200,000 Settlement Warrants expired on July 15, 2019 as none of the warrants had been exercised during the one-year exercise period.

Private Placement – May 2016

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 1,764,242 units, at a price of $9.65 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 $10.00 per share and are exercisable for a period of five years from the date of issuance until their scheduled expiration on May 16, 2021. Certain of the Company's directors and executive officers purchased an aggregate of 54,402 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. As of December 31, 2020, PIPE Warrants exercisable for 80,309 shares of common stock had been exercised, for approximately $0.8 million in cash proceeds, and PIPE Warrants exercisable for 1,683,933 shares of common stock were outstanding.

(8) Stock-based Compensation

Stock Incentive Plan

The Company previously maintained the 2010 Stock Incentive Plan (the "2010 Plan") for employees, consultants, advisors, and directors, as amended in March 2013, June 2014 and June 2017.

In April 2019, the Company's board of directors adopted the 2019 Equity Incentive Plan (the "2019 Plan") and on June 12, 2019 the stockholders approved the 2019 Plan at the Annual Meeting of Stockholders. The 2019 Plan provides similar terms as the 2010 Plan, including: (i) a provision for the grant of equity awards such as stock options and restricted stock, (ii) 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 grant 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, (iii) that options and restricted stock granted under the 2019 Plan vest over periods as determined by the board of directors, which generally are equal to four years, and (iv) that options granted under the 2019 Plan expire over periods as determined by the board of directors, which generally are ten years from the date of grant. In April 2020, the board of directors adopted an amendment to the 2019 Plan to increase the total number of shares reserved under the Plan by 1,300,000 shares, among other things. The amendment was approved by stockholders at the Annual Meeting of Stockholders held on June 10, 2020.

Awards may be made under the 2019 Plan for up to the sum of (i) 2,300,000 shares of common stock and (ii) such additional number of shares of common stock (up to 1,068,901 shares) as is equal to (x) the number of shares of common stock reserved for issuance under the 2010 Plan that were available for grant under the 2010 Plan immediately prior to the date the 2019 Plan was approved by the Company's stockholders and (y) the number of shares of common stock subject to awards outstanding under the 2010 Plan, which awards expire, terminate or are otherwise surrendered, cancelled, forfeited or repurchased by the Company pursuant to a contractual repurchase right. As of December 31, 2020, there were 1,563,282 shares of common stock available for future issuance under the 2019 Plan and no shares of common stock available for future issuance under the 2010 Plan.

The following table summarizes stock option activity during the year ended December 31, 2020:

	Options	Weighted-Average Exercise Price	Weighted-Average Remaining Contractual Term	Aggregate Intrinsic Value
Outstanding at January 1, 2020	1,168,222	$ 16.77		
Granted	740,522	$ 5.83		
Exercised	(934)	$ 5.60		
Forfeited	(111,120)	$ 36.45		
Outstanding at December 31, 2020	1,796,690	$ 11.05	7.53	$ 170,000
Exercisable at December 31, 2020	909,963	$ 14.56	6.14	$ 12,000

The aggregate intrinsic value is based upon the Company's closing stock price of $5.77 on December 31, 2020.

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,		
	2020	2019	2018
Volatility factor	94.37% - 102.48%	88.27% - 98.81%	80.18% - 83.61%
Expected term (in years)	5.50 - 6.25	5.50 - 6.25	5.50 - 6.25
Risk-free interest rates	0.31% - 1.67%	1.43% - 2.55%	2.64% - 3.10%
Dividend yield	—	—	—

The risk-free interest rate is determined based upon the United States Treasury's rates for U.S. Treasury zero-coupon bonds with maturities similar to those of the expected term of the options being valued. The Company does not expect to pay dividends in the foreseeable future.

Based upon these assumptions, the weighted-average grant date fair value of stock options granted was $4.54, $5.70 and $21.40 during the years ended December 31, 2020, 2019 and 2018, respectively.

As of December 31, 2020, there was $4.9 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 2.8 years. The intrinsic value of options exercised was $1,000, $7,000 and $0.4 million in the years ended December 31, 2020, 2019 and 2018, respectively.

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 25,000 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 76,400 shares of common stock under the ESPP. As of December 31, 2020, there were 23,859 shares available for future issuance under the ESPP.

Pursuant to the ESPP, the Company sold a total of 5,971 shares of common stock during the year ended December 31, 2020 at purchases prices of $6.46 and $4.57, which represents 85% of the closing price of the Company's common stock on December 1, 2019 and November 30, 2020, respectively. Pursuant to the ESPP, the Company sold a total of 897 shares of common stock during the year ended December 31, 2018 at purchases prices of $18.80 and $17.60, which represents 85% of the closing price of the Company's common stock on May 31, 2018 and November 30, 2018, respectively. The Company did not sell any shares of common stock during the year ended December 31, 2019. The total stock-based compensation expense recorded as a result of the ESPP was approximately $25,000, $2,000 and $8,000 during the years ended December 31, 2020, 2019 and 2018, respectively.

(9) Commitments and Contingencies

Operating Leases

On March 5, 2020, the Company entered into the Winter Street Sublease to relocate the Company's corporate headquarters previously located at One Broadway in Cambridge, Massachusetts. Under the terms of the Winter Street Sublease, the Company leases 10,158 square feet of office space for $47.00 per square foot, or approximately $0.5 million per year in base rent subject to certain operating expenses, taxes and annual base rent increases of approximately 3%. Previously, the Company leased office space under a month-to-month lease. Rent expense under the operating leases amounted to $0.6 million, $0.8 million and $0.7 million for the years ended December 31, 2020, 2019 and 2018, respectively.

Manufacturing Commitments

The Company has entered into a contract with a clinical manufacturing organization for the manufacture of clinical drug supply for tivozanib and commercial drug supply for FOTIVDA in the United States, which includes minimum annual purchase requirements, in the approximate amount of $1.4 million for the next few years. In addition, the Company has entered into contracts with another clinical manufacturing organization for the manufacture of clinical drug supply for ficlatuzumab and AV-380, for which we have manufacturing commitments in 2021, in the aggregate amount of approximately $10.3 million.

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.

(10) Income Taxes

The Company accounts for income taxes under the provisions of ASC 740. The Company recorded no tax provision for each of the years ended December 31, 2020 and 2019. For the year ended December 31, 2020, 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, 2020, 2019 and 2018:

	Years Ended December 31,		
	2020	2019	2018
Income tax computed at federal statutory tax rate	21.0%	21.0%	21.0%
State taxes, net of federal benefit	6.7%	1.3%	27.2%
Research and development credits	1.5%	(4.2)%	5.2%
PIPE Warrants	2.9%	(25.9)%	78.5%
Other permanent differences	(0.5)%	1.8%	(3.5)%
Other	(1.1)%	5.7%	(2.0)%
Change in valuation allowance	(30.5)%	0.3%	(126.4)%
Total	—	—	—

With limited exceptions, the Company has incurred net operating losses from inception. At December 31, 2020, the Company had domestic federal, state, and United Kingdom (UK) net operating loss carryforwards of approximately $565.8 million, $420.9 million, and $6.0 million respectively, available to reduce future taxable income. The federal net operating loss carryforwards expire beginning in 2022 and continue through 2037 and the state loss carryforwards begin to expire in 2030 and continue through 2040. The Company's federal net operating losses include $63.2 million, which do not expire. 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 $11.8 million and $4.3 million, respectively, available to reduce future tax liabilities and which expire at various dates. The federal credits expire beginning in 2023 through 2040 and the state credits expire beginning in 2021 through 2035. 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, 2020 and 2019 are as follows (in thousands):

	December 31,	
	2020	2019
	(in thousands)	
Deferred tax assets:		
NOL carryforwards	$ 148,689	$ 138,105
Research and development credits	15,271	14,666
Deferred revenue and R&D reimbursements	742	1,262
Other temporary differences	5,001	4,820
Total deferred tax assets:	169,703	158,853
Valuation allowance	(169,703)	(158,853)
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 and expected future losses. The valuation allowance increased by $10.9 million and $27 thousand during the years ended December 31, 2020 and 2019, respectively, which was primarily due to the generation of net operating losses and tax credits.

The Company applies the provisions of 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 2017 through 2020. 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.

Utilization of the net operating loss carryforwards and research and development tax credit carryforwards may be subject to an annual limitation under Section 382 of the Internal Revenue Code of 1986, as amended (the "Internal Revenue Code"), and corresponding provisions of state law, due to ownership changes that have occurred previously or that could occur in the future. These ownership changes may limit the amount of carryforwards that can be utilized annually to offset future taxable income. In general, an ownership change, as defined by Section 382, results from transactions increasing the ownership of certain shareholders or public

groups in the stock of a corporation by more than 50% over a three-year period. The Company has not recently conducted a study to assess whether a change of control has occurred or whether there have been multiple changes of control since the last study was completed due to the significant complexity and cost associated with such a study. If the Company has experienced a change of control, as defined by Section 382, at any time since the last study was completed, utilization of the net operating loss carryforwards or research and development tax credit carryforwards would be subject to an annual limitation under Section 382, which is determined by first multiplying the value of the Company's stock at the time of the ownership change by the applicable long-term tax-exempt rate, and then could be subject to additional adjustments, as required. Any limitation may result in expiration of a portion of the net operating loss carryforwards or research and development tax credit carryforwards before utilization.

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, 2020, 2019 and 2018:

	Years Ended December 31,		
	2020	2019	2018
	(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	(122)	—	—
Balance as of end of year	$ 1,078	$ 1,200	$ 1,200

(11) 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 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, 2020, 2019 and 2018.

(12) Quarterly Results (Unaudited)

	Three Month Ended			
	March 31, 2020	June 30, 2020	September 30, 2020	December 31, 2020
	(in thousands, expect per share data) (unaudited)			
Revenues	$ 784	$ 749	$ 3,600	$ 886
Operating expenses	11,498	8,156	11,660	13,582
Loss from operations	(10,714)	(7,407)	(8,060)	(12,696)
Change in fair value of PIPE Warrant liability	2,648	450	86	1,714
Other income (expense), net	(315)	(349)	(419)	(522)
Net income (loss)	$ (8,381)	$ (7,306)	$ (8,393)	$ (11,504)
Basic net income (loss) per share				
Net income (loss) per share	$ (0.52)	$ (0.42)	$ (0.33)	$ (0.44)
Weighted average number of common shares outstanding	16,081	17,364	25,808	26,252
Diluted net income (loss) per share				
Net income (loss) per share	$ (0.52)	$ (0.42)	$ (0.33)	$ (0.44)
Weighted average number of common shares and dilutive common share equivalents outstanding	16,081	17,364	25,808	26,252

	Three Month Ended			
	March 31, 2019	June 30, 2019	September 30, 2019	December 31, 2019
	(in thousands, expect per share data) (unaudited)			
Revenues	$ 1,611	$ 703	$ 25,717	$ 764
Operating expenses	9,307	5,597	6,867	7,398
Loss from operations	(7,696)	(4,894)	18,850	(6,634)
Change in fair value of PIPE Warrant liability	8,815	2,210	(1,954)	2,506
Other income (expense), net	(564)	(451)	(467)	(333)
Net income (loss)	$ 555	$ (3,135)	$ 16,429	$ (4,461)
Basic net income (loss) per share				
Net income (loss) per share	$ 0.04	$ (0.20)	$ 1.02	$ (0.28)
Weighted average number of common shares outstanding	13,230	15,902	16,074	16,077
Diluted net income (loss) per share				
Net income (loss) per share	$ (0.62)	$ (0.20)	$ 1.02	$ (0.28)
Weighted average number of common shares and dilutive common share equivalents outstanding	13,283	15,902	16,083	16,077

(13) Legal Proceedings

As of the date of filing this Annual Report on Form 10-K, there are no outstanding legal proceedings against the Company or its current officers or directors.

On July 24, 2020, the District Court for the District of Massachusetts dismissed a purported class action filed against the Company in 2019. This purported class action lawsuit (the “2019 Class Action”) was filed against the Company and certain of its present and former officers, Michael Bailey, Matthew Dallas, and Keith Ehrlich, in the Southern District of New York for the District of New York, captioned *David Hackel v. AVEO Pharmaceuticals, Inc., et al*, No. 1:19-cv-01722-AT. On April 12, 2019, the court granted the defendants’ motion to transfer the action to the District of Massachusetts (Case No. 1:19-cv-10783-JCB). On May 6, 2019, the court appointed Andrej Hornak as lead plaintiff and approved Pomerantz LLP as lead counsel and Andrews DeValerio LLP as liaison counsel. On July 24, 2019, the plaintiffs filed an amended complaint naming Michael Needle as an additional defendant. The amended complaint purported to be brought on behalf of shareholders who purchased the Company’s common stock between May 4, 2017 through January 31, 2019. It generally alleged that the Company and its officers violated Sections 10(b) and/or 20(a) of the Securities Exchange Act of 1934 and Rule 10b-5 promulgated thereunder by failing to disclose and/or making allegedly false and/or misleading statements about the estimated dates by which the Company would report the topline results from the TIVO-3 trial, the preliminary overall survival results from the TIVO-3 trial, the sufficiency of the overall survival data from the TIVO-3 trial, the timing of the NDA submission, and the risk of FDA approval. The complaint sought unspecified damages, interest, attorneys’ fees, and other costs. On September 27, 2019, the defendants filed a motion to dismiss the amended complaint. On July 24, 2020, the District Court granted the Company’s motion to dismiss. The time for appeal expired in August 2020 without appeal

In connection with the filing of the 2019 Class Action, two derivative lawsuits were filed on July 8, 2019 and July 10, 2019 against the Company, certain of its present and former officers and its directors in the Suffolk Superior Court, Commonwealth of Massachusetts, captioned *Stephen Favre v. Michael P. Bailey, et al*. 19-2169-BLS2 and *Jianbin Yu v. Michael P. Bailey, et al.* 19-2188-BLS2, respectively. The complaints generally alleged breach of fiduciary duty, unjust enrichment, and waste of corporate assets due to the 2019 Class Action and the actions alleged therein. On July 26, 2019, the court granted the parties’ joint motion to consolidate the cases and stay the consolidated matter pending the dismissal of, or filing of an answer to, the complaint in the 2019 Class Action. After the 2019 Class Action was dismissed and the time for appeal had expired, the parties’ filed a joint stipulation to voluntarily dismiss the derivative lawsuit without prejudice. On December 8, 2021, the court entered an order dismissing the derivative action.

In June 2018, the Company settled a consolidated class action lawsuit (the "2013 Class Action"), *In re AVEO Pharmaceuticals, Inc. Securities Litigation et al., No. 1:13-cv-11157-DJC*, that had been filed in 2013 against the Company and certain of its former officers (Tuan Ha-Ngoc, David N. Johnston, William Slichenmyer, and Ronald DePinho) in the United States District Court for the District of Massachusetts (the "District Court"). The 2013 Class Action had been dismissed without prejudice in March 2015, and the lead plaintiffs then filed a second amended complaint bringing similar allegations, but which no longer named Mr. DePinho as a defendant. The Company moved to dismiss again, and the District Court ruled in the Company's favor and dismissed the second amended complaint with prejudice in November 2015. The lead plaintiffs appealed the District Court's decision and also filed a motion to vacate and reconsider the District Court's judgment. In January 2017, the District Court granted the plaintiffs' motion to vacate the dismissal and judgment. In February 2017, the plaintiffs filed a third amended complaint, on behalf of stockholders who purchased common stock between May 16, 2012 and May 1, 2013 (the "2013 Class") 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 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. In July 2017, the District Court entered an order referring the case to alternative dispute resolution. The parties mediated during the fall of 2017.

On December 26, 2017, the parties entered into a binding memorandum of understanding (the "MOU") to settle the 2013 Class Action. Under the terms of the MOU, the Company agreed to cause certain of the Company's and the individual defendants' insurance carriers to provide the 2013 Class with a cash payment of $15.0 million, which included the cash amount of any attorneys' fees or litigation expenses that the District Court may award. Additionally, the Company agreed to issue to the 2013 Class the Settlement Warrants, for the purchase of 0.2 million shares of the Company's common stock, which, subject to certain conditions, are exercisable from the date of issue until the expiration of a one-year period after the date of issue at an exercise price of $3.00 per share, equal to the closing price on December 22, 2017, the trading day prior to the execution of the MOU. On January 29, 2018, the parties entered into a definitive Stipulation of Settlement (the "Stipulation"), which was filed with the District Court on February 2, 2018. On February 8, 2018, the District Court issued an order preliminarily approving the terms of the Stipulation. In February 2018, the insurance carriers funded the settlement escrow account for the $15.0 million cash settlement. On May 30, 2018, the District Court held the final approval hearing and approved the settlement and the plaintiffs' request for attorneys' fees and expenses, subject to the final judgment. Upon the conclusion of a standard 30-day appeal period, the effective date was deemed to be June 29, 2018. On July 16, 2018, the Company issued and delivered the Settlement Warrants in accordance with the Stipulation and filed a corresponding shelf registration statement to register the shares of common stock underlying the Settlement Warrants which was declared effective by the SEC on July 25, 2018. All 0.2 million Settlement Warrants expired on July 15, 2019 as none of the warrants had been exercised during the one-year exercise period.

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, the Company's liability related to 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. Pursuant to the Final Judgment, all claims against the Company were released upon the Effective Date. In addition, pursuant to the Stipulation, the Company has no interest in the settlement escrow account subsequent to the Effective Date. Accordingly, the Company reversed the $15.0 million cash portion of the settlement from both the contingent liability and the corresponding insurance recovery as of the Effective Date.

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, 2020. 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 for the Company. 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, 2020. 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, 2020, our internal control over financial reporting was 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

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, 2020, 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, 2020, 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, 2020 and 2019, the related consolidated statements of operations, comprehensive income (loss), stockholders' equity (deficit), and cash flows for each of the three years in the period ended December 31, 2020, and the related notes and our report dated March 16, 2021 expressed an unqualified opinion thereon.

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 16, 2021

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 2020 that have materially affected, or is reasonably likely to materially affect, our internal control over financial reporting.

ITEM 9B. Other Information

Bristol-Myers Squibb Company Clinical Trial Collaboration and Supply Agreement

On January 26, 2021, or the Effective Date, we entered into a Clinical Trial Collaboration and Supply Agreement, or the Agreement, with Bristol-Myers Squibb Company, or BMS. Under the terms of the Agreement, BMS agreed to supply OPDIVO® (nivolumab), its anti-PD-1 therapy, for a combined therapy clinical trial, which we refer to as the TiNivo-2 Trial, with FOTIVDA® (tivozanib) in patients with advanced relapsed or refractory renal cell carcinoma following prior immunotherapy exposure, which we agreed to conduct in accordance with a specified protocol. In connection with the TiNivo-2 Trial, BMS granted us a non-exclusive,

worldwide (other than within certain territories specified therein), non-transferable, royalty-free license under certain BMS patent rights, technology and regulatory documentation to use OPDIVO in research and development, solely to the extent necessary to conduct the TiNivo-2 Trial. Additionally, BMS granted us a non-exclusive, worldwide (other than within certain territories specified therein), non-transferable, irrevocable, royalty-free license under certain patent rights, technology and regulatory documentation, to seek regulatory approval of FOTIVDA for use in a combined therapy in the field, and, upon any such regulatory approval, to market and promote FOTIVDA solely for use in a combined therapy in the field in any manner that is consistent with the regulatory approval for FOTIVDA. Finally, BMS granted us a non-exclusive, worldwide (other than within certain territories specified therein), non-transferable, irrevocable, royalty-free license in the field under certain inventions and patent rights relating to OPDIVO for all purposes in the field except to research, develop, make, have made, use, sell offer for sale, export or import OPDIVO or any biosimilar version. We and BMS shall jointly own all inventions, or the Combined Therapy Inventions, and patent rights, or the Combined Therapy Patent Rights, relating to the combined therapy used in the TiNivo-2 Trial. We and BMS each may freely exploit the Combined Therapy Inventions and Combined Therapy Patent Rights, and the parties will share equally in costs relating to maintaining and prosecuting the Combined Therapy Patent Rights.

Each party will be responsible for expenses relating to the manufacturing and supply of its respective products. For expenses related to conduct of the TiNivo-2 Trial: (i) we will be responsible for all out-of-pocket costs associated with the performance of the TiNivo-2 Trial, and (ii) each party will be responsible for its own internal costs associated with the TiNivo-2 Trial. If the conduct of the TiNivo-2 Trial requires a third-party license payment, then the party required to make such payment shall be determined in accordance with the prior sentence.

The parties' obligations under the Agreement are conditioned upon our execution of an agreement with a clinical research organization to conduct the TiNivo-2 Trial.

The term of the Agreement commenced on the Effective Date and will continue, unless earlier terminated in accordance with the Agreement, until completion of the TiNivo-2 Trial by all centers participating in the TiNivo-2 Trial, delivery of all study data, including all completed case report forms, all final analyses and all final clinical study reports contemplated by the TiNivo-2 Trial to both parties, and the completion of any statistical analyses and bioanalyses contemplated by the protocol or otherwise agreed to by the Parties to be conducted under the Agreement.

Either party may terminate the Agreement in the event of a material breach of the Agreement by the other party or in the event of a material safety issue present in the TiNivo-2 Trial.

This agreement became material to us on March 10, 2021 upon approval by the FDA of FOTIVDA in the United States for the treatment of adult patients with relapsed or refractory advanced RCC following two or more prior systemic therapies.

Drawdown of Tranche Two funding under the 2021 Loan Amendment

On February 1, 2021, the Company entered into the 2021 Loan Amendment, which increases the 2020 Loan Facility from up to $35.0 million to up to $45.0 million following FDA approval of FOTIVDA. The 2021 Loan Amendment makes certain changes to the 2020 Loan Amendment, including, among other things, increasing Tranche Two funding upon achieving Performance Milestone I from $10.0 million to $20.0 million and increasing the amount of the financial covenant for the maintenance of an unrestricted cash position from at least $10.0 million to at least $15.0 million from the date the Tranche Two funding is received until the date the Tranche Three funding is received and at least $10.0 million thereafter through the maturity of the Loan Agreement.

On March 11, 2021, we completed the $20.0 million drawdown of Tranche Two funding under the 2021 Loan Amendment that was made available in connection with the achievement of Performance Milestone I upon FDA approval of FOTIVDA on March 10, 2021. The achievement of Performance Milestone I increased the amount of unrestricted cash required for us to satisfy the minimum financial covenant during the period between receiving Tranche Two funding and Tranche Three funding from $10.0 million to $15.0 million and extended the interest-only period by twelve months from September 30, 2021 to September 30, 2022.

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 “Delinquent Section 16(a) Reports,” if applicable, appearing in the definitive proxy statement we will file in connection with our 2021 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 Annual Report on Form 10-K under the heading “Business—Information about our Executive Officers” and is incorporated herein by reference.

We post our Code of Business Conduct and Ethics, which applies to all of our directors, officers and employees, including our principal executive officer, principal financial officer, principal accounting officer or controller, or persons performing similar functions, in the “Corporate Governance” sub-section of the “Investors” section of our website at www.aveooncology.com. We intend to disclose on our website any amendments to, or waivers from, the Code of Business Conduct and Ethics that are required to be disclosed pursuant to the disclosure requirements of Item 5.05 of Form 8-K.

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 2021 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 2021 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 2021 Annual Meeting of Stockholders and is incorporated by reference herein.

ITEM 14. Principal Accountant 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 2021 Annual Meeting of Stockholders and is incorporated by reference herein.

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 Income (Loss)

Consolidated Statements of Stockholders' Equity (Deficit)

Consolidated Statements of Cash Flows

Notes to Consolidated Financial Statements

(2) Schedules

Schedules have been omitted as all required information has been disclosed in the financial statements and related footnotes.

(3) Exhibits

The Exhibits listed in the Exhibit Index are filed as a part of this Form 10-K.

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, as amended					X
3.2	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	10-K	001-34655	03/16/2020	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	
4.3	Warrant Agreement, dated July 16, 2018, by and among the Company and Computershare Inc. and Computershare Trust Company, N.A., acting jointly as Warrant Agent	8-K	001-34655	07/16/2018	4.1	
4.4	Form of Offering Warrant	8-K	001-34655	04/04/2019	4.1	
4.5	Description of Registered Securities	10-K	001-34655	03/16/2020	4.5	
	Material Contracts—Management Contracts and Compensatory Plans					
10.1	Second Amended and Restated 2010 Stock Incentive Plan	8-K	001-34655	06/27/2017	99.1	
10.2	Form of Incentive Stock Option Agreement under 2010 Stock Incentive Plan	S-1/A	333-163778	02/08/2010	10.6	
10.3	Form of Nonqualified Stock Option Agreement under 2010 Stock Incentive Plan	S-1/A	333-163778	02/08/2010	10.7	
10.4	Form of Restricted Stock Agreement under 2010 Stock Incentive Plan	10-K	001-34655	03/30/2012	10.8	
10.5	2019 Equity Incentive Plan	DEF-14A	001-34655	04/30/2019	Appendix A	
10.6	Amendment No.1 to 2019 Equity Incentive Plan	DEF-14A	001-34655	04/28/2020	Appendix A	
10.7	Key Employee Change in Control Severance Benefits Plan	S-1	333-163778	12/16/2009	10.8	
10.8	2010 Employee Stock Purchase Plan, as amended	S-1/A	333-163778	02/23/2010	10.17	
10.9	Amendment No. 1 to 2010 Employee Stock Purchase Plan	8-K	001-34655	06/04/2013	99.2	
10.10	Offer Letter by Registrant to Michael Bailey, dated as of January 6, 2015	10-Q	001-34655	05/07/2015	10.1	
10.11	Severance Agreement, dated September 13, 2010, by and between the Registrant and Michael Bailey	10-Q	001-34655	11/05/2010	10.1	
10.12	Letter Agreement regarding Retention Bonus Award and Severance Agreement, dated February 3, 2014, by and between the Company and Michael Bailey	10-K	001-34655	3/13/2014	10.22	
10.13	Offer Letter by the Registrant to Michael Needle, dated January 8, 2015	10-Q	001-34655	05/07/2015	10.4	
10.14	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	
10.15	Offer Letter by and between the Registrant and Erick Lucera, dated December 12, 2019	10-K	001-34655	03/16/2020	10.16	

Exhibit Number	Description of Exhibit	Incorporated by Reference				Filed Herewith
		Form	File Number	Date of Filing	Exhibit Number	
10.16	Severance and Change in Control Agreement, dated January 6, 2020, by and between the Registrant and Erick Lucera	10-K	001-34655	03/16/2020	10.17	
10.17	Separation and Release of Claims Agreement, dated January 25, 2021, by and between the Registrant and Karuna Rubin	8-K	001-34655	01/29/2021	10.1	
	Material Contracts—Financing Agreements					
10.18	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	
10.19	Form of Warrant to Purchase Common Stock	8-K	001-34655	05/13/2016	10.2	
10.20	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	
10.21	First Amendment to Amended and Restated Loan and Security Agreement, dated as of August 7, 2020, by and among the Registrant, Hercules Capital, Inc. and the other lenders named therein	10-Q	001-34655	08/10/2020	10.1	
10.22	Second Amendment to Amended and Restated Loan and Security Agreement, dated February 1, 2021, by and among the Registrant, the several banks and other financial institutions or entities from time to time parties thereto and Hercules Capital, Inc.	8-K	001-34655	02/02/2021	10.1	
10.23	Sales Agreement dated February 16, 2018, by and between the Company and Leerink Partners LLC	8-K	001-34655	02/16/2018	1.1	
10.24	Amendment No.1 to the Sales Agreement dated November 9, 2020, by and between the Registrant and SVB Leerink LLC	S-3	333-249982	11/09/2020	1.3	
	Material Contracts—License and Strategic Partnership Agreements					
10.25†	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	
10.26††	Amendment to License Agreement, dated as of August 1, 2019, by and between the Registrant and Kyowa Kirin Co., Ltd.	8-K	001-34655	8/01/2019	10.1	
10.27††	Option and License Agreement, dated as of March 18, 2009, by and between the Registrant and Biogen Idec International GmbH					X
10.28††	Amendment No. 1 to Option and License Agreement, dated as of March 18, 2014 by and between the Registrant and Biogen Idec MA Inc.					X
10.29†	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	
10.30†	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	
10.31†	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	
10.32†	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	

Exhibit Number	Description of Exhibit	Incorporated by Reference				Filed Herewith
		Form	File Number	Date of Filing	Exhibit Number	
10.33†	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					
10.34	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	
10.35	Stipulation of Settlement, dated January 29, 2018, by and among the Company and the parties named therein	10-Q	001-34655	5/8/2018	10.2	
10.36	Sublease, dated March 5, 2020, by and between the Registrant and Commonwealth Care Alliance, Inc.	10-Q	001-34655	4/30/2020	10.2	
21.1	Subsidiaries of the Registrant					X
23.1	Consent of Ernst & Young LLP					X
31.1	Certification of principal executive officer pursuant to Rule 13a-14(a)/15d-14(a) of the Securities Exchange Act of 1934, as amended.					X
31.2	Certification of principal financial officer pursuant to Rule 13a-14(a)/15d-14(a) of the Securities Exchange Act of 1934, as amended.					X
32.1	Certification of principal executive officer pursuant to 18 U.S.C. §1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.					X
32.2	Certification of principal financial officer pursuant to 18 U.S.C. §1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.					X
101.INS	XBRL Instance Document.					X
101.SCH	XBRL Taxonomy Extension Schema Document.					X
101.CAL	XBRL Taxonomy Calculation Linkbase Document.					X
101DEF	XBRL Taxonomy Extension Definition Linkbase Document.					X
101.LAB	XBRL Taxonomy Label Linkbase Document.					X
101.PRE	XBRL Taxonomy Presentation Linkbase Document.					X
104	Cover Page Interactive Data File (embedded within the Inline XBRL document).					

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

†† Portions of this exhibit have been omitted pursuant to Item 601(b)(10)(iv) of Regulation S-K.

SIGNATURES

Pursuant to the requirements of Section 13 or 15(d) of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned, thereunto duly authorized.

AVEO PHARMACEUTICALS, INC.

Date: March 16, 2021

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 16, 2021
/s/ ERICK LUCERA **Erick Lucera**	Chief Financial Officer *Principal Financial and Accounting Officer*	March 16, 2021
/s/ KENNETH M. BATE **Kenneth M. Bate**	Director	March 16, 2021
/s/ CORINNE EPPERLY **Corinne Epperly**	Director	March 16, 2021
/s/ ANTHONY B. EVNIN **Anthony B. Evnin**	Director	March 16, 2021
/s/ GREGORY T. MAYES **Gregory T. Mayes**	Director	March 16, 2021
/s/ SCARLETT SPRING **Scarlett Spring**	Director	March 16, 2021
/s/ ROBERT C. YOUNG **Robert C. Young**	Director	March 16, 2021

Delaware

The First State

I, JEFFREY W. BULLOCK, SECRETARY OF STATE OF THE STATE OF DELAWARE, DO HEREBY CERTIFY THE ATTACHED ARE TRUE AND CORRECT COPIES OF ALL DOCUMENTS FILED FROM AND INCLUDING THE RESTATED CERTIFICATE OR A MERGER WITH A RESTATED CERTIFICATE ATTACHED OF "AVEO PHARMACEUTICALS, INC." AS RECEIVED AND FILED IN THIS OFFICE.

THE FOLLOWING DOCUMENTS HAVE BEEN CERTIFIED:

RESTATED CERTIFICATE, FILED THE SEVENTEENTH DAY OF MARCH, A.D. 2010, AT 8 O'CLOCK A.M.

CERTIFICATE OF AMENDMENT, FILED THE TWENTY-EIGHTH DAY OF MAY, A.D. 2015, AT 5 O'CLOCK P.M.

CERTIFICATE OF AMENDMENT, FILED THE TWENTY-SIXTH DAY OF JUNE, A.D. 2017, AT 8:33 O'CLOCK A.M.

CERTIFICATE OF AMENDMENT, FILED THE THIRTEENTH DAY OF JUNE, A.D. 2019, AT 11:47 O'CLOCK A.M.

CERTIFICATE OF AMENDMENT, FILED THE NINETEENTH DAY OF FEBRUARY, A.D. 2020, AT 8:20 O'CLOCK A.M.

3444819 8100X
SR# 20210801026

Authentication: 202653462
Date: 03-04-21

You may verify this certificate online at corp.delaware.gov/authver.shtml

Delaware

The First State

Jeffrey W. Bullock, Secretary of State

3444819 8100X
SR# 20210801026

Authentication: 202653462
Date: 03-04-21

You may verify this certificate online at corp.delaware.gov/authver.shtml

State of Delaware
Secretary of State
Division of Corporations
Delivered 07:50AM 03/17/2010
FILED 08: 00 AM 03/17/2010
SRV 100286912 - 3444819 FILE

RESTATED CERTIFICATE OF INCORPORATION

OF

AVEO PHARMACEUTICALS, INC.

(originally incorporated on October 19, 2001 under the name GenPath Pharmaceuticals, Inc.)

FIRST: The name of the Corporation is Aveo Pharmaceuticals, Inc.

SECOND: The address of the Corporation's registered office in the State of Delaware is Corporation Trust Center, 1209 Orange Street, in the City of Wilmington, County of New Castle. The name of its registered agent at that address is The Corporation Trust Company.

THIRD: The nature of the business or purposes to be conducted or promoted by the Corporation is to engage in any lawful act or activity for which corporations may be organized under the General Corporation Law of the State of Delaware.

FOURTH: The total number of shares of all classes of stock which the Corporation shall have authority to issue is 105,000,000 shares, consisting of (i) 100,000,000 shares of Common Stock, $0.001 par value per share ("Common Stock"), and (ii) 5,000,000 shares of Preferred Stock, $0.001 par value per share ("Preferred Stock").

The following is a statement of the designations and the powers, privileges and rights, and the qualifications, limitations or restrictions thereof in respect of each class of capital stock of the Corporation.

A COMMON STOCK.

1. General. The voting, dividend and liquidation rights of the holders of the Common Stock are subject to and qualified by the rights of the holders of the Preferred Stock of any series as may be designated by the Board of Directors upon any issuance of the Preferred Stock of any series.

2. Voting. The holders of the Common Stock shall have voting rights at all meetings of stockholders, each such holder being entitled to one vote for each share thereof held by such holder; provided, however, that, except as otherwise required by law, holders of Common Stock shall not be entitled to vote on any amendment to this Certificate of Incorporation (which, as used herein, shall mean the certificate of incorporation of the Corporation, as amended from time to time, including the terms of any certificate of designations of any series of Preferred Stock) that relates solely to the terms of one or more outstanding series of Preferred Stock if the holders of such affected series are entitled, either separately or together as a class with the holders of one or more other such series, to vote thereon pursuant to this Certificate of Incorporation. There shall be no cumulative voting.

The number of authorized shares of Common Stock may be increased or decreased (but not below the number of shares thereof then outstanding) by the affirmative vote of the holders of a majority of the stock of

the Corporation entitled to vote, irrespective of the provisions of Section 242(b)(2) of the General Corporation Law of the State of Delaware.

3. Dividends. Dividends may be declared and paid on the Common Stock from funds lawfully available therefor as and when determined by the Board of Directors and subject to any preferential dividend or other rights of any then outstanding Preferred Stock.

4. Liquidation. Upon the dissolution or liquidation of the Corporation, whether voluntary or involuntary, holders of Common Stock will be entitled to receive all assets of the Corporation available for distribution to its stockholders, subject to any preferential or other rights of any then outstanding Preferred Stock.

B PREFERRED STOCK.

Preferred Stock may be issued from time to time in one or more series, each of such series to have such terms as stated or expressed herein and in the resolution or resolutions providing for the issue of such series adopted by the Board of Directors of the Corporation as hereinafter provided. Any shares of Preferred Stock which may be redeemed, purchased or acquired by the Corporation may be reissued except as otherwise provided by law.

Authority is hereby expressly granted to the Board of Directors from time to time to issue the Preferred Stock in one or more series, and in connection with the creation of any such series, by adopting a resolution or resolutions providing for the issuance of the shares thereof and by filing a certificate of designations relating thereto in accordance with the General Corporation Law of the State of Delaware, to determine and fix the number of shares of such series and such voting powers, full or limited, or no voting powers, and such designations, preferences and relative participating, optional or other special rights, and qualifications, limitations or restrictions thereof, including without limitation thereof, dividend rights, conversion rights, redemption privileges and liquidation preferences, as shall be stated and expressed in such resolutions, all to the full extent now or hereafter permitted by the General Corporation Law of the State of Delaware. Without limiting the generality of the foregoing, the resolutions providing for issuance of any series of Preferred Stock may provide that such series shall be superior or rank equally or be junior to any other series of Preferred Stock to the extent permitted by law.

The number of authorized shares of Preferred Stock may be increased or decreased (but not below the number of shares then outstanding) by the affirmative vote of the holders of a majority of the voting power of the capital stock of the Corporation entitled to vote thereon, voting as a single class, irrespective of the provisions of Section 242(b)(2) of the General Corporation Law of the State of Delaware.

FIFTH: Except as otherwise provided herein, the Corporation reserves the right to amend, alter, change or repeal any provision contained in this Certificate of Incorporation, in the manner now or hereafter prescribed by statute and this Certificate of Incorporation, and all rights conferred upon stockholders herein are granted subject to this reservation.

SIXTH: In furtherance and not in limitation of the powers conferred upon it by the General Corporation Law of the State of Delaware, and subject to the terms of any series of Preferred Stock, the Board of Directors shall have the power to adopt, amend, alter or repeal the By-laws of the Corporation by the affirmative vote of a majority of the directors present at any regular or special meeting of the Board of Directors at which a quorum is present. The stockholders may not adopt, amend, alter or repeal the By-laws of the Corporation, or adopt any provision inconsistent therewith, unless such action is approved, in addition to any other vote required by this Certificate of Incorporation, by the affirmative vote of the holders of at least seventy-five percent (75%) of the votes that all the stockholders would be entitled to cast in any annual election of directors. Notwithstanding any other provisions of law, this Certificate of Incorporation or the By-laws of the Corporation, and notwithstanding

the fact that a lesser percentage may be specified by law, the affirmative vote of the holders of at least seventy-five percent (75%) of the votes which all the stockholders would be entitled to cast in any annual election of directors shall be required to amend or repeal, or to adopt any provision inconsistent with, this Article SIXTH.

SEVENTH: Except to the extent that the General Corporation Law of the State of Delaware prohibits the elimination or limitation of liability of directors for breaches of fiduciary duty, no director of the Corporation shall be personally liable to the Corporation or its stockholders for monetary damages for any breach of fiduciary duty as a director, notwithstanding any provision of law imposing such liability. No amendment to or repeal of this provision shall apply to or have any effect on the liability or alleged liability of any director of the Corporation for or with respect to any acts or omissions of such director occurring prior to such amendment or repeal. If the General Corporation Law of the State of Delaware is amended to permit further elimination or limitation of the personal liability of directors, then the liability of a director of the Corporation shall be eliminated or limited to the fullest extent permitted by the General Corporation Law of the State of Delaware as so amended.

EIGHTH: The Corporation shall provide indemnification as follows:

1. Actions, Suits and Proceedings Other than by or in the Right of the Corporation. The Corporation shall indemnify each person who was or is a party or threatened to be made a party to any threatened, pending or completed action, suit or proceeding, whether civil, criminal, administrative or investigative (other than an action by or in the right of the Corporation) by reason of the fact that he or she is or was, or has agreed to become, a director or officer of the Corporation, or is or was serving, or has agreed to serve, at the request of the Corporation, as a director, officer, partner, employee or trustee of, or in a similar capacity with, another corporation, partnership, joint venture, trust or other enterprise (including any employee benefit plan) (all such persons being referred to hereafter as an "Indemnitee"), or by reason of any action alleged to have been taken or omitted in such capacity, against all expenses (including attorneys' fees), liabilities, losses, judgments, fines (including excise taxes and penalties arising under the Employee Retirement Income Security Act of 1974), and amounts paid in settlement actually and reasonably incurred by or on behalf of Indemnitee in connection with such action, suit or proceeding and any appeal therefrom, if Indemnitee acted in good faith and in a manner which Indemnitee reasonably believed to be in, or not opposed to, the best interests of the Corporation, and, with respect to any criminal action or proceeding, had no reasonable cause to believe his or her conduct was unlawful. The termination of any action, suit or proceeding by judgment, order, settlement, conviction or upon a plea of nolo contendere or its equivalent, shall not, of itself, create a presumption that Indemnitee did not act in good faith and in a manner which Indemnitee reasonably believed to be in, or not opposed to, the best interests of the Corporation, and, with respect to any criminal action or proceeding, had reasonable cause to believe that his or her conduct was unlawful.

2. Actions or Suits by or in the Right of the Corporation. The Corporation shall indemnify any Indemnitee who was or is a party to or threatened to be made a party to any threatened, pending or completed action or suit by or in the right of the Corporation to procure a judgment in its favor by reason of the fact that Indemnitee is or was, or has agreed to become, a director or officer of the Corporation, or is or was serving, or has agreed to serve, at the request of the Corporation, as a director, officer, partner, employee or trustee of, or in a similar capacity with, another corporation, partnership, joint venture, trust or other enterprise (including any employee benefit plan), or by reason of any action alleged to have been taken or omitted in such capacity, against all expenses (including attorneys' fees) and, to the extent permitted by law, amounts paid in settlement actually and reasonably incurred by or on behalf of Indemnitee in connection with such action, suit or proceeding and any appeal therefrom, if Indemnitee acted in good faith and in a manner which Indemnitee reasonably believed to be in, or not opposed to, the best interests of the Corporation, except that no indemnification shall be made under this Section 2 in respect of any claim, issue or matter as to which Indemnitee shall have been adjudged to be liable to the Corporation, unless, and only to the extent, that the

Court of Chancery of Delaware or the court in which such action or suit was brought shall determine upon application that, despite the adjudication of such liability but in view of all the circumstances of the case, Indemnitee is fairly and reasonably entitled to indemnity for such expenses (including attorneys' fees) which the Court of Chancery of Delaware or such other court shall deem proper.

3. Indemnification for Expenses of Successful Party. Notwithstanding any other provisions of this Article EIGHTH, to the extent that an Indemnitee has been successful, on the merits or otherwise, in defense of any action, suit or proceeding referred to in Sections 1 and 2 of this Article EIGHTH, or in defense of any claim, issue or matter therein, or on appeal from any such action, suit or proceeding, Indemnitee shall be indemnified against all expenses (including attorneys' fees) actually and reasonably incurred by or on behalf of Indemnitee in connection therewith. Without limiting the foregoing, if any action, suit or proceeding is disposed of, on the merits or otherwise (including a disposition without prejudice), without (i) the disposition being adverse to Indemnitee, (ii) an adjudication that Indemnitee was liable to the Corporation, (iii) a plea of guilty or nolo contendere by Indemnitee, (iv) an adjudication that Indemnitee did not act in good faith and in a manner he or she reasonably believed to be in or not opposed to the best interests of the Corporation, and (v) with respect to any criminal proceeding, an adjudication that Indemnitee had reasonable cause to believe his or her conduct was unlawful, Indemnitee shall be considered for the purposes hereof to have been wholly successful with respect thereto.

4. Notification and Defense of Claim. As a condition precedent to an Indemnitee's right to be indemnified, such Indemnitee must notify the Corporation in writing as soon as practicable of any action, suit, proceeding or investigation involving such Indemnitee for which indemnity will or could be sought. With respect to any action, suit, proceeding or investigation of which the Corporation is so notified, the Corporation will be entitled to participate therein at its own expense and/or to assume the defense thereof at its own expense, with legal counsel reasonably acceptable to Indemnitee. After notice from the Corporation to Indemnitee of its election so to assume such defense, the Corporation shall not be liable to Indemnitee for any legal or other expenses subsequently incurred by Indemnitee in connection with such action, suit, proceeding or investigation, other than as provided below in this Section 4. Indemnitee shall have the right to employ his or her own counsel in connection with such action, suit, proceeding or investigation, but the fees and expenses of such counsel incurred after notice from the Corporation of its assumption of the defense thereof shall be at the expense of Indemnitee unless (i) the employment of counsel by Indemnitee has been authorized by the Corporation, (ii) counsel to Indemnitee shall have reasonably concluded that there may be a conflict of interest or position on any significant issue between the Corporation and Indemnitee in the conduct of the defense of such action, suit, proceeding or investigation or (iii) the Corporation shall not in fact have employed counsel to assume the defense of such action, suit, proceeding or investigation, in each of which cases the fees and expenses of counsel for Indemnitee shall be at the expense of the Corporation, except as otherwise expressly provided by this Article EIGHTH. The Corporation shall not be entitled, without the consent of Indemnitee, to assume the defense of any claim brought by or in the right of the Corporation or as to which counsel for Indemnitee shall have reasonably made the conclusion provided for in clause (ii) above. The Corporation shall not be required to indemnify Indemnitee under this Article EIGHTH for any amounts paid in settlement of any action, suit, proceeding or investigation effected without its written consent. The Corporation shall not settle any action, suit, proceeding or investigation in any manner which would impose any penalty or limitation on Indemnitee without Indemnitee's written consent. Neither the Corporation nor Indemnitee will unreasonably withhold or delay its consent to any proposed settlement.

5. Advance of Expenses. Subject to the provisions of Section 6 of this Article EIGHTH, in the event of any threatened or pending action, suit, proceeding or investigation of which the Corporation receives notice under this Article EIGHTH, any expenses (including attorneys' fees) incurred by or on behalf of Indemnitee in defending an action, suit, proceeding or investigation or any appeal therefrom shall be paid by the Corporation in advance of the final disposition of such matter; provided, however, that the payment of such expenses

incurred by or on behalf of Indemnitee in advance of the final disposition of such matter shall be made only upon receipt of an undertaking by or on behalf of Indemnitee to repay all amounts so advanced in the event that it shall ultimately be determined that Indemnitee is not entitled to be indemnified by the Corporation as authorized in this Article EIGHTH; and provided further that no such advancement of expenses shall be made under this Article EIGHTH if it is determined (in the manner described in Section 6) that (i) Indemnitee did not act in good faith and in a manner he or she reasonably believed to be in, or not opposed to, the best interests of the Corporation, or (ii) with respect to any criminal action or proceeding, Indemnitee had reasonable cause to believe his or her conduct was unlawful. Such undertaking shall be accepted without reference to the financial ability of Indemnitee to make such repayment.

6. Procedure for Indemnification and Advancement of Expenses. In order to obtain indemnification or advancement of expenses pursuant to Section 1, 2, 3 or 5 of this Article EIGHTH, an Indemnitee shall submit to the Corporation a written request. Any such advancement of expenses shall be made promptly, and in any event within 60 days after receipt by the Corporation of the written request of Indemnitee, unless (i) the Corporation has assumed the defense pursuant to Section 4 of this Article EIGHTH (and none of the circumstances described in Section 4 of this Article EIGHTH that would nonetheless entitle the Indemnitee to indemnification for the fees and expenses of separate counsel have occurred) or (ii) the Corporation determines within such 60-day period that Indemnitee did not meet the applicable standard of conduct set forth in Section 1, 2 or 5 of this Article EIGHTH, as the case may be. Any such indemnification, unless ordered by a court, shall be made with respect to requests under Section 1 or 2 only as authorized in the specific case upon a determination by the Corporation that the indemnification of Indemnitee is proper because Indemnitee has met the applicable standard of conduct set forth in Section 1 or 2, as the case may be. Such determination shall be made in each instance (a) by a majority vote of the directors of the Corporation consisting of persons who are not at that time parties to the action, suit or proceeding in question ("disinterested directors"), whether or not a quorum, (b) by a committee of disinterested directors designated by majority vote of disinterested directors, whether or not a quorum, (c) if there are no disinterested directors, or if the disinterested directors so direct, by independent legal counsel (who may, to the extent permitted by law, be regular legal counsel to the Corporation) in a written opinion, or (d) by the stockholders of the Corporation.

7. Remedies. The right to indemnification or advancement of expenses as granted by this Article EIGHTH shall be enforceable by Indemnitee in any court of competent jurisdiction. Neither the failure of the Corporation to have made a determination prior to the commencement of such action that indemnification is proper in the circumstances because Indemnitee has met the applicable standard of conduct, nor an actual determination by the Corporation pursuant to Section 6 of this Article EIGHTH that Indemnitee has not met such applicable standard of conduct, shall be a defense to the action or create a presumption that Indemnitee has not met the applicable standard of conduct. Indemnitee's expenses (including attorneys' fees) reasonably incurred in connection with successfully establishing Indemnitee's right to indemnification, in whole or in part, in any such proceeding shall also be indemnified by the Corporation. Notwithstanding the foregoing, in any suit brought by Indemnitee to enforce a right to indemnification hereunder it shall be a defense that the Indemnitee has not met any applicable standard for indemnification set forth in the General Corporation Law of the State of Delaware.

8. Limitations. Notwithstanding anything to the contrary in this Article EIGHTH, except as set forth in Section 7 of this Article EIGHTH, the Corporation shall not indemnify an Indemnitee pursuant to this Article EIGHTH in connection with a proceeding (or part thereof) initiated by such Indemnitee unless the initiation thereof was approved by the Board of Directors of the Corporation. Notwithstanding anything to the contrary in this Article EIGHTH, the Corporation shall not indemnify an Indemnitee to the extent such Indemnitee is reimbursed from the proceeds of insurance, and in the event the Corporation makes any indemnification payments to an Indemnitee and such Indemnitee is subsequently reimbursed from the proceeds of insurance,

such Indemnitee shall promptly refund indemnification payments to the Corporation to the extent of such insurance reimbursement.

9. Subsequent Amendment. No amendment, termination or repeal of this Article EIGHTH or of the relevant provisions of the General Corporation Law of the State of Delaware or any other applicable laws shall adversely affect or diminish in any way the rights of any Indemnitee to indemnification under the provisions hereof with respect to any action, suit, proceeding or investigation arising out of or relating to any actions, transactions or facts occurring prior to the final adoption of such amendment, termination or repeal.

10. Other Rights. The indemnification and advancement of expenses provided by this Article EIGHTH shall not be deemed exclusive of any other rights to which an Indemnitee seeking indemnification or advancement of expenses may be entitled under any law (common or statutory), agreement or vote of stockholders or disinterested directors or otherwise, both as to action in Indemnitee's official capacity and as to action in any other capacity while holding office for the Corporation, and shall continue as to an Indemnitee who has ceased to be a director or officer, and shall inure to the benefit of the estate, heirs, executors and administrators of Indemnitee. Nothing contained in this Article EIGHTH shall be deemed to prohibit, and the Corporation is specifically authorized to enter into, agreements with officers and directors providing indemnification rights and procedures different from those set forth in this Article EIGHTH. In addition, the Corporation may, to the extent authorized from time to time by its Board of Directors, grant indemnification rights to other employees or agents of the Corporation or other persons serving the Corporation and such rights may be equivalent to, or greater or less than, those set forth in this Article EIGHTH.

11. Partial Indemnification. If an Indemnitee is entitled under any provision of this Article EIGHTH to indemnification by the Corporation for some or a portion of the expenses (including attorneys' fees), liabilities, losses, judgments, fines (including excise taxes and penalties arising under the Employee Retirement Income Security Act of 1974) or amounts paid in settlement actually and reasonably incurred by or on behalf of Indemnitee in connection with any action, suit, proceeding or investigation and any appeal therefrom but not, however, for the total amount thereof, the Corporation shall nevertheless indemnify Indemnitee for the portion of such expenses (including attorneys' fees), liabilities, losses, judgments, fines (including excise taxes and penalties arising under the Employee Retirement Income Security Act of 1974) or amounts paid in settlement to which Indemnitee is entitled.

12. Insurance. The Corporation may purchase and maintain insurance, at its expense, to protect itself and any director, officer, employee or agent of the Corporation or another corporation, partnership, joint venture, trust or other enterprise (including any employee benefit plan) against any expense, liability or loss incurred by him or her in any such capacity, or arising out of his or her status as such, whether or not the Corporation would have the power to indemnify such person against such expense, liability or loss under the General Corporation Law of the State of Delaware.

13. Savings Clause. If this Article EIGHTH or any portion hereof shall be invalidated on any ground by any court of competent jurisdiction, then the Corporation shall nevertheless indemnify each Indemnitee as to any expenses (including attorneys' fees), liabilities, losses, judgments, fines (including excise taxes and penalties arising under the Employee Retirement Income Security Act of 1974) and amounts paid in settlement in connection with any action, suit, proceeding or investigation, whether civil, criminal or administrative, including an action by or in the right of the Corporation, to the fullest extent permitted by any applicable portion of this Article EIGHTH that shall not have been invalidated and to the fullest extent permitted by applicable law.

14. Definitions. Terms used herein and defined in Section 145(h) and Section 145(i) of the General Corporation Law of the State of Delaware shall have the respective meanings assigned to such terms in such Section 145(h) and Section 145(i).

NINTH: In furtherance of and not in limitation of powers conferred by law, it is further provided:

1. General Powers of Board. The business and affairs of the Corporation shall be managed by or under the direction of the Board of Directors.

2. Election of Directors. Election of directors need not be by written ballot, except as and to the extent provided in the By-laws of the Corporation.

TENTH: Stockholders of the Corporation may not take any action by written consent in lieu of a meeting. Notwithstanding any other provisions of law, this Certificate of Incorporation or the By-laws of the Corporation, and notwithstanding the fact that a lesser percentage may be specified by law, the affirmative vote of the holders of at least seventy-five percent (75%) of the votes which all the stockholders would be entitled to cast in any annual election of directors shall be required to amend or repeal, or to adopt any provision inconsistent with, this Article TENTH.

ELEVENTH: Special meetings of stockholders for any purpose or purposes may be called at any time by only the Board of Directors, the Chairman of the Board or the Chief Executive Officer, and may not be called by any other person or persons. Business transacted at any special meeting of stockholders shall be limited to matters relating to the purpose or purposes stated in the notice of meeting. Notwithstanding any other provisions of law, this Certificate of Incorporation or the By-laws of the Corporation, and notwithstanding the fact that a lesser percentage may be specified by law, the affirmative vote of the holders of at least seventy-five percent (75%) of the votes which all the stockholders would be entitled to cast in any annual election of directors shall be required to amend or repeal, or to adopt any provision inconsistent with, this Article ELEVENTH.

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IN WITNESS WHEREOF, this Restated Certificate of Incorporation, which restates, integrates and amends the certificate of incorporation of the Corporation, and which has been duly adopted in accordance with Sections 228, 242 and 245 of the General Corporation Law of the State of Delaware, has been executed by its duly authorized officer this 17th day of March, 2010.

AVEO PHARMACEUTICALS, INC.

By: /s/ Tuan Ha-Ngoc
Tuan Ha-Ngoc
President and Chief Executive Officer

State of Delaware
Secretary of State
Division of Corporations
Delivered 02:03 PM 05/28/2015
FILED 01:50 PM 05/28/2015
SRV 150805039 - 3444819 FILE

CERTIFICATE OF AMENDMENT
OF
RESTATED CERTIFICATE OF INCORPORATION
OF
AVEO PHARMACEUTICALS, INC.

Aveo Pharmaceuticals, Inc., a corporation organized and existing under the laws of the State of Delaware (the "Corporation"), does hereby certify as follows:

1. The name of the Corporation is Aveo Pharmaceuticals, Inc.

2. Article 4 of the Restated Certificate of Incorporation of the Corporation, is hereby amended by replacing the first paragraph thereof with the following:

"FOURTH: The total number of shares of all classes of stock which the Corporation shall have authority to issue is 205,000,000 shares, consisting of (i) 200,000,000 shares of Common Stock, $0.001 par value per share ("Common Stock") and (ii) 5,000,000 shares of Preferred Stock, $0.001 par value per share ("Preferred Stock").

3. This Certificate of Amendment has been duly adopted by the Board of Directors and stockholders of the Corporation in accordance with Section 242 of the General Corporation Law of the State of Delaware.

4. This Certificate of Amendment shall become effective at 5:00 p.m. Eastern Time on May 28, 2015.

IN WITNESS WHEREOF, the Corporation has caused its duly authorized officer to execute this Certificate of Amendment on this 28th day of May, 2015.

AVEO PHARMACEUTICALS, INC.

By: /s/ Michael Bailey
Name: Michael Bailey
Title: President and Chief Executive Officer

State of Delaware
Secretary of State
Division of Corporations
Delivered 08:33 AM 06/26/2017
FILED 08:33AM 06/26/2017
SR 20174935494 - File Number 3444819

CERTIFICATE OF AMENDMENT
OF
RESTATED CERTIFICATE OF INCORPORATION
OF
AVEO PHARMACEUTICALS, INC.

AVEO Pharmaceuticals, Inc. (the "Corporation"), a corporation organized and existing under and by virtue of the provisions of the General Corporation Law of the State of Delaware (the "General Corporation Law"), does hereby certify as follows:

1. The name of the Corporation is AVEO Pharmaceuticals, Inc.

2. Article FOURTH of the Restated Certificate of Incorporation of the Corporation, is hereby amended by replacing the first paragraph thereof with the following:

"FOURTH: The total number of shares of all classes of stock which the Corporation shall have authority to issue is 255,000,000 shares, consisting of (i) 250,000,000 shares of Common Stock, $0.001 par value per share ("Common Stock") and (ii) 5,000,000 shares of Preferred Stock, $0.001 par value per share ("Preferred Stock")."

3. This Certificate of Amendment has been duly adopted by the Board of Directors and stockholders of the Corporation in accordance with Section 242 of the General Corporation Law.

* * *

IN WITNESS WHEREOF, the Corporation has caused its duly authorized officer to execute this Certificate of Amendment on this 26th day of June, 2017.

AVEO PHARMACEUTICALS, INC.

By: /s/ Michael Bailey
Name: Michael Bailey
Title: President and Chief Executive Officer

State of Delaware
Secretary of State
Division of Corporations
Delivered 11:47 AM 06/13/2019
FILED 11:47 AM 06/l3/2019
SR 20195416931 – File Number 3444819

CERTIFICATE OF AMENDMENT
OF
RESTATED CERTIFICATE OF INCORPORATION
OF
AVEO PHARMACEUTICALS, INC.

AVEO Pharmaceuticals, Inc. (the "Corporation"), a corporation organized and existing under and by virtue of the provisions of the General Corporation Law of the State of Delaware (the "General Corporation Law"), does hereby certify as follows:

1. The name of the Corporation is AVEO Pharmaceuticals, Inc.

2. Article FOURTH of the Restated Certificate of Incorporation of the Corporation, is hereby amended by replacing the first paragraph thereof with the following:

"FOURTH: The total number of shares of all classes of stock which the Corporation shall have authority to issue is 505,000,000 shares, consisting of (i) 500,000,000 shares of Common Stock, $0.001 par value per share ("Common Stock") and (ii) 5,000,000 shares of Preferred Stock, $0.001 par value per share ("Preferred Stock")."

3. This Certificate of Amendment has been duly adopted by the Board of Directors and stockholders of the Corporation in accordance with Section 242 of the General Corporation Law.

IN WITNESS WHEREOF, the Corporation has caused its duly authorized officer to execute this Certificate of Amendment on this 13th day of June, 2019.

AVEO PHARMACEUTICALS, INC.

By: /s/ Michael Bailey
Name: Michael Bailey
Title: President and Chief Executive Officer

State of Delaware
Secretary of State
Division of Corporations
Delivered 08:20 AM 02/19/2020
FILED 08:20AM 02/19/2020
SR 20201234599 - File Number 3444819

CERTIFICATE OF AMENDMENT
OF
RESTATED CERTIFICATE OF INCORPORATION
OF
AVEO PHARMACEUTICALS, INC.

AVEO Pharmaceuticals, Inc. (the "Corporation"), a corporation organized and existing under and by virtue of the provisions of the General Corporation Law of the State of Delaware (the "General Corporation Law"), does hereby certify as follows:

1. The current name of the Corporation is AVEO Pharmaceuticals, Inc.

2. The Board of Directors of the Corporation duly adopted resolutions pursuant to Section 242 of the General Corporation Law proposing the amendment set forth in this Certificate of Amendment of the Restated Certificate of Incorporation of the Corporation, (as amended, the "Restated Certificate"), declaring the advisability of the amendment set forth in this Certificate of Amendment of the Restated Certificate and authorizing the appropriate officers of the Corporation to solicit the consent of the stockholders therefor, which resolution setting forth the proposed amendment is as follows:

RESOLVED, that Article FOURTH of the Restated Certificate be amended by replacing the first paragraph thereof with the following:

"FOURTH: Effective at 5:00p.m., Eastern Time, on the date of filing of this Certificate of Amendment of the Restated Certificate of Incorporation with the Secretary of State of the State of Delaware (the "Effective Time"), each five (5) to fifteen (15) shares of the Corporation's common stock, par value $0.001 per share (the "Common Stock"), issued and outstanding or held by the Corporation in treasury immediately prior to the Effective Time shall be reclassified and combined into one validly issued, fully paid and nonassessable share of outstanding Common Stock or treasury share, as applicable, automatically and without any action by the holder thereof upon the Effective Time and shall represent one share of Common Stock from and after the Effective Time (such reclassification and combination of shares, the "Reverse Stock Split"). The exact ratio of the Reverse Stock Split within such five (5) to fifteen (15) range shall be determined by the Board of Directors of the Corporation and publicly announced by the Corporation prior to the Effective Time. The par value of the Common Stock following the Reverse Stock Split shall remain at $0.001 par value per share. No fractional shares of Common Stock shall be issued as a result of the Reverse Stock Split and, in lieu thereof, upon surrender after the Effective Time of a certificate which formerly represented shares of Common Stock that were issued and outstanding immediately prior to the Effective Time, any person who would otherwise be entitled to a fractional share of Common Stock as a result of the Reverse Stock Split, following the Effective Time, shall be entitled to receive a cash payment (without interest) equal to the fraction of a share of Common Stock to which such holder would otherwise be entitled multiplied by the average (after taking into account the exact ratio of the Reverse Stock Split determined by the Board of Directors of the Corporation) of the high and low trading prices of the Common Stock on The Nasdaq Capital Market during regular trading hours for the five trading days immediately preceding the Effective Time.

Each stock certificate that, immediately prior to the Effective Time, represented shares of Common Stock that were issued and outstanding immediately prior to the Effective Time shall, from and after the Effective Time, automatically and without the necessity of presenting the same for exchange, represent that number of whole shares of Common Stock after the Effective Time into which the shares formerly represented by such certificate have been reclassified (as well as the right to receive cash in lieu of fractional shares of Common Stock after the Effective Time); provided, however, that each person of record holding a certificate that represented shares of Common Stock that were issued and outstanding immediately prior to the Effective Time shall receive, upon surrender of such certificate, a new certificate evidencing and representing the number of whole shares of Common Stock after the Effective Time into which the shares of Common Stock formerly represented by such certificate shall have been reclassified.

The total number of shares of all classes of stock which the Corporation shall have authority to issue is 55,000,000 shares, consisting of

(i) 50,000,000 shares of Common Stock, $0.001 par value per share ("Common Stock") and

(ii) 5,000,000 shares of Preferred Stock, $0.001 par value per share ("Preferred Stock")."

This Certificate of Amendment of the Restated Certificate has been duly adopted by the stockholders of the Corporation in accordance with the provisions of Section 242 of the Delaware General Corporation Law.

IN WITNESS WHEREOF, the Corporation has caused its duly authorized officer to execute this Certificate of Amendment on this l9th day of February 2020.

AVEO PHARMACEUTICALS, INC.

By: /s/ Michael Bailey
Name: Michael Bailey
Title: President and Chief Executive Officer

Execution Copy
Exhibit 10.27

Certain identified information has been excluded from the exhibit because it is both (i) not material and (ii) is the type of information that the registrant treats as private or confidential. Double asterisks denote omissions.

OPTION AND LICENSE AGREEMENT
BY AND BETWEEN

AVEO PHARMACEUTICALS, INC.

AND

BIOGEN IDEC INTERNATIONAL GMBH

OPTION AND LICENSE AGREEMENT

This Option and License Agreement, made this 18th day of March, 2009 (the "Effective Date"), is by and between AVEO Pharmaceuticals, Inc., a Delaware corporation, with principal offices located at 75 Sidney St., Cambridge, MA 02139 ("AVEO") and Biogen Idec International GmbH, with principal offices located at Landis+Gyr-Strasse 3, 6300 Zug, Switzerland ("Biogen Idec"). Each of AVEO and Biogen Idec shall be referred to, individually, as a "Party", and, collectively, as the "Parties".

RECITALS

WHEREAS, AVEO has a broad pipeline of preclinical stage novel antibodies directed at targets with potential utility in the oncology area, including antibodies targeting erbB3;

WHEREAS, Biogen Idec is in the business of researching, developing and commercializing biopharmaceutical products, and has an interest in the area of oncology; and

WHEREAS, Biogen Idec is interested in obtaining an option to commercialize AVEO's antibodies to erbB3 outside of North America, and AVEO is willing to grant Biogen Idec such an option on the terms and conditions set forth in this Agreement.

NOW, THEREFORE, in consideration of the foregoing and the mutual covenants contained in this Agreement, AVEO and Biogen Idec, intending to be legally bound, hereby agree as follows:

ARTICLE I.
DEFINITIONS

When used in this Agreement, each of the following capitalized terms, whether used in the singular or plural, shall have the meanings set forth in this Article I.

1.1 "Affiliate" of a Person means any other Person which, directly or indirectly, controls, is controlled by or is under common control with such Person. For the purposes of this definition, "control" refers to any of the following: (i) direct or indirect ownership of fifty percent (50%) or more of the voting securities entitled to vote for the election of directors in the case of a corporation, or of fifty percent (50%) or more of the equity interest with the power to direct management in the case of any other type of legal entity; (ii) status as a general partner in any partnership; or (iii) any other arrangement where a Person possesses, directly or indirectly, the power to direct the management or policies of an entity, whether through ownership of voting securities, by contract or otherwise.

1.2 "Agreement" means this Option and License Agreement, including any and all schedules, appendices, exhibits and other addenda to it, as it may be added to or amended from time to time in accordance with the provisions of this document.

1.3 "Agreement Term" shall mean the period commencing on the Effective Date and ending on the expiration of the Agreement in accordance with the provisions of Section 14.1.

1.4 "Antibody" means any immunoglobulin molecule (such as IgG) whether in monospecific, bispecific or any other form, and shall include any immunoglobulin fragment (such as Fv, Fab, F(ab')2) of any such immunoglobulin molecule containing one or more complementarity determining regions, any fusion protein comprising any such immunoglobulin molecule or immunoglobulin fragment and any single chain antibody (such as scFv), and any truncation or derivative of any of the foregoing.

1.5 "AVEO Collaboration Know-how" means, subject to Sections 3.6, 5.11, 5.12 and 5.13, any Know-how that is owned or otherwise Controlled by AVEO or any of its Affiliates, patentable or otherwise, first identified, discovered, or developed solely by employees of AVEO or its Affiliates, or other persons not employed by AVEO or any of its Affiliates but acting on behalf of AVEO or any of its Affiliates, in the conduct of Development, Manufacture or Commercialization of Licensed Product under this Agreement during the License Term, but not including AVEO's interest in Joint Collaboration Know-how.

1.6 "AVEO Collaboration Patent Rights" means, subject to Sections 3.6 and 3.9, any Patent Rights Covering AVEO Collaboration Know-how that are owned or otherwise Controlled by AVEO or any of its Affiliates, but not including AVEO's interest in Joint Collaboration Patent Rights.

1.7 "AVEO In-License" means, subject to Section 3.9, any agreement between AVEO or any of its Affiliates, on the one hand, and a Third Party, on the other hand, entered into prior to the Option Exercise Date subject to the provisions of Section 2.6 or during the License Term in compliance with the provisions of Section 3.6, pursuant to which AVEO or any of its Affiliates acquires or obtains a license or other right to use, any Know-how and/or Patent Rights that are necessary or reasonably useful to Develop, Commercialize or Manufacture Licensed Product in the Field in the Territory.

1.8 "AVEO Know-how" means any Know-how owned or otherwise Controlled by AVEO or any of its Affiliates as of the Effective Date or, subject to Sections 3.6, 3.9, 5.11, 5.12 and 5.13, any Know-how as to which Control is obtained (whether by ownership, license or otherwise) by AVEO or any of its Affiliates during the Agreement Term, in each case to the extent such Know-how is necessary or reasonably useful in the Development, Manufacture or Commercialization of Licensed Product in the Field, but not including AVEO Collaboration Know-how or AVEO's interest in Joint Collaboration Know-how.

1.9 "AVEO Patent Rights" means Patent Rights Covering AVEO Know-how that are owned or otherwise Controlled by AVEO or any of its Affiliates as of the Effective Date or, subject to Sections 3.6 and 3.9, Patent Rights covering AVEO Know-how as to which Control is obtained (whether by ownership, license or otherwise) by AVEO or any of its Affiliates at any time after the Effective Date, including the Patent Rights in the Territory described in Exhibit A, but not including AVEO Collaboration Patent Rights or AVEO's interest in Joint Collaboration Patent Rights.

1.10 "AVEO Proprietary Composition Licensed Product" means a Licensed Product the composition of matter of which is Covered by AVEO Patent Rights.

1.11 "AVEO Technology" means, collectively, AVEO Know-how, AVEO Patent Rights, AVEO Collaboration Know-how, AVEO Collaboration Patent Rights and AVEO's interest in Joint Collaboration IP.

1.12 "AVEO Territory" means North America.

1.13 "Biogen Idec Collaboration Know-how" means, subject to Sections 3.6, 5.11, 5.12 and 5.13, any Know-how that is owned or otherwise Controlled by Biogen Idec or any of its Affiliates, patentable or otherwise, first identified, discovered, or developed solely by employees of Biogen Idec or its Affiliates, or other persons not employed by Biogen Idec or any of its Affiliates but acting on behalf of Biogen Idec or any of its Affiliates, in the conduct of Development, Manufacture or Commercialization of Licensed Product under this Agreement during the License Term, but not including Biogen Idec's interest in Joint Collaboration Know-how.

1.14 "Biogen Idec Collaboration Patent Rights" means, subject to Sections 3.6 and 3.9, Patent Rights Covering Biogen Idec Collaboration Know-how that are owned or otherwise Controlled by Biogen Idec or any of its Affiliates, but not including Biogen Idec's interest in Joint Collaboration Patent Rights.

1.15 "Biogen Idec Collaboration Technology" means, collectively, Biogen Idec Collaboration Know-how, Biogen Idec Collaboration Patent Rights and Biogen Idec's interest in Joint Collaboration IP

1.16 "Biogen Idec In-License" means, subject to Section 3.9, an agreement between Biogen Idec or any of its Affiliates, on the one hand, and a Third Party, on the other hand, entered into during the License Term in compliance with the provisions of Section 3.6, pursuant to which Biogen Idec or any of its Affiliates acquires or obtains title to, or a license or other right to use, any Know-how and/or Patent Rights that are necessary or reasonably useful to Develop, Commercialize or Manufacture the Licensed Product in the Field in the Territory.

1.17 "BLA" means a biologics license application or equivalent application that is filed with the FDA to obtain Regulatory Approval for a Licensed Product in the United States or any comparable application filed with a Regulatory Authority of a country or group of countries in the Territory other than the United States to obtain Regulatory Approval for Licensed Product in that country or in that group of countries.

1.18 "Business Day" means a day that is not a Saturday or Sunday and not a federal holiday in the United States or a state holiday in the Commonwealth of Massachusetts.

1.19 "Calendar Quarter" means each of the three month periods ending on March 31, June 30, September 30 and December 31 of any year.

1.20 "Calendar Year" means each successive period of twelve (12) months commencing on January 1 and ending on December 31; provided that the first Calendar Year of the License Term shall begin on the Option Exercise Date and end on the following December 31, and the last Calendar Year of the License Term shall end on the last day of the License Term.

1.21 "Commercialization", "Commercializing" or "Commercialize" means all activities related to pre-marketing, launching, marketing, promotion (including advertising and detailing), labeling, pricing and reimbursement, distribution, storage, handling, offering for sale, selling, importing and exporting for sale, distribution, customer service and support, and post-marketing safety surveillance and reporting, but not including Manufacturing.

1.22 "Collaboration Know-how" means AVEO Collaboration Know-how, Biogen Idec Collaboration Know-how and Joint Collaboration Know-how.

1.23 "Collaboration Patent Rights" means AVEO Collaboration Patent Rights, Biogen Idec Collaboration Patent Rights and Joint Collaboration Patent Rights.

1.24 "Combination Product" means any pharmaceutical product containing a Licensed Product and one or more other significantly active pharmaceutical ingredients.

1.25 "Commercially Reasonable Efforts" in respect of a Party means efforts and resources (measured as of the time that such efforts are required to be used under this Agreement) commonly used by a company in the industry of a similar size and profile as such Party to Develop, Manufacture or Commercialize, as the case may be, a product owned by such company or to which it has rights, which product is at a similar stage in its development or product life and is of a similar market and profitability potential to Licensed Product and taking into account all relevant factors including the patent and other proprietary position of the product, product labeling or anticipated labeling, market potential, financial return, medical and clinical considerations, regulatory environments and competitive market conditions, and other technical, legal, scientific, medical or commercial factors that such a company would deem to be relevant.

1.26 "Confidential Information" means any and all information, data and materials of a confidential or proprietary nature, including information, data and materials regarding or included within AVEO Technology or Biogen Idec Collaboration Technology and all other scientific, pre-clinical, clinical, regulatory, manufacturing, marketing, financial or commercial information or data, whether communicated in writing or orally or by any other method, which is provided by one Party or any of its Affiliates to the other Party or any of its Affiliates in connection with this Agreement. AVEO Technology is Confidential Information of AVEO, and Biogen Idec Collaboration Technology is Confidential Information of Biogen Idec, provided that Joint Collaboration IP is the Confidential Information of both Parties.

1.27 "Control" or "Controlled", other than for purposes of Section 1.1, means the possession of the right to grant licenses or sublicenses or to disclose proprietary or trade secret information without violating the terms of any agreement or other arrangement with a Third Party.

1.28 "Cost of Goods Sold" means, with respect to Licensed Product in bulk form manufactured for use as an active pharmaceutical ingredient or in finished final packaged and labeled product form, or in intermediate states, as the case may be, Manufactured by or on behalf of a Party under this Agreement, the reasonable internal and external costs of such Party or any of its Affiliates incurred in Manufacturing such Licensed Product, including: (a) to the extent that such Licensed Product is Manufactured by such Party or any of its Affiliates, the cost of

goods sold of such Licensed Product, consisting of direct materials and direct labor costs, plus Manufacturing overhead directly attributable to Licensed Product supplied (excluding facilities start-up costs, corporate administrative overhead, depreciation and costs associated with excess capacity), all calculated in accordance with GAAP in the United States consistently applied, (b) to the extent that such Licensed Product is Manufactured by a Third Party manufacturer, the actual fees paid by such Party or any of its Affiliates to the Third Party for the Manufacture, supply, testing, packaging, labeling and shipping of such Licensed Product, and any reasonable out-of-pocket and direct labor costs actually incurred by such Party or any of its Affiliates in managing or overseeing the Third Party relationship, and (c) royalties, license or other fees paid by such Party or any of its Affiliates to Third Parties in respect of Manufacture of such Licensed Product.

1.29 "Cover", "Covering" or "Covered" means, with respect to whether an invention or Know-how is "Covered" by a Patent Right, that, in the absence of ownership of, or a license under, such Patent Right, the practice by such Person of such invention or Know-how would infringe a Valid Claim of such Patent Right (including in the case of a Patent Right that is a patent application, a Valid Claim of such patent application as if such patent application were an issued patent).

1.30 "CPI" means the Consumer Price Index for all Urban Consumers Northeastern Urban (Boston, Brockton, Nashua, NH, ME, CT) City Average for all Items, 1982, 84-100, published by the United States Department of Labor, Bureau of Labor Statistics (or its successor equivalent index) in the United States.

1.31 "Data Exclusivity" means, with respect to a Licensed Product in a country, that period during which a Party or any of its Affiliates or Sublicensees has been granted the exclusive legal right by a Regulatory Authority (or is otherwise entitled to the exclusive legal right by operation of applicable Law) in such country to market and sell such Licensed Product in such country in the approved indication in the Field.

1.32 "Data Package" means a complete, detailed, data-cleaned, unbiased and unblended data package that contains the results of the first Proof of Concept Study in the following form: (i) a statistical analysis of results; (ii) analysis tables, data listings and illustrative figures; (iii) the table of adverse events; (iv) case report forms (CRFs) in hard copy or electronic form, or, alternatively, available for review by Biogen Idec employees during normal business hours at the principal office of AVEO in the United States, commencing upon delivery of the other parts of the Data Package; and (v) a narrative description of serious adverse events, in each case in the format compiled by AVEO, which shall be cGCP compliant and otherwise consistent with industry standards. The Data Package shall also contain (x) a copy (or rights of access for purposes of clause (iv) above) of the relevant IND and the information specified in clauses (i) – (v) for any Phase 1 Clinical Trial or any other Phase 2 Clinical Trial completed prior to completion of the first Proof of Concept Study, as well as all regulatory correspondence relating thereto, (y) copies of all AVEO In-Licenses entered into between the period commencing after the Effective Date through the date of delivery of the Data Package and (z) a copy of the initial Development Plan.

1.33 "Development" or "Develop" means any and all non-clinical and clinical drug research and development activities, whether before or after Regulatory Approval, including discovery efforts, toxicology and pharmacology work, test method development, stability testing, process development, formulation development, delivery system development, quality assurance and quality control development, statistical analysis, clinical studies (including pre-approval studies and Post-Approval Clinical Studies), regulatory affairs, and product approval and clinical study regulatory activities (excluding regulatory activities directed to obtaining pricing and reimbursement approvals).

1.34 "Development Costs" means all costs incurred by AVEO or any of its Affiliates in Developing the Licensed Product in the Field, in accordance with this Agreement and GAAP, whether incurred before or after Regulatory Approval, provided that except as otherwise specifically set forth in this Agreement, such activities and costs are consistent with the then current Development Plan and included in the related budget (pursuant to the provisions of Section 5.4 and 5.5 below), including without duplication:

(i) all out-of-pocket costs and expenses actually incurred;

(ii) the costs of internal personnel engaged in such efforts, which costs shall be determined based on the FTE Cost, unless another basis is otherwise agreed by the Parties in writing;

(iii) (a) the Cost of Goods Sold and distribution costs and expenses for pre-clinical and clinical supplies needed for such efforts as set forth in the Development Plan, including the Cost of Goods Sold for clinical supplies of the Licensed Product; (b) the costs of comparator or combination drugs, placebo or devices; (c) costs and expenses of disposal of clinical samples; (d) costs and expenses incurred in connection with (1) manufacturing process, formulation or delivery system development or validation; (2) manufacturing scale-up and improvements; (3) stability testing; and (4) quality assurance/quality control development; and (e) internal and Third Party costs and expenses incurred in connection with qualification, validation or auditing of Third Party contract manufacturers, in each case to the extent specific to Licensed Product, and not including the purchase of capital equipment for the purposes of building manufacturing facilities and capabilities;

(iv) subject to Section 5.5(b), (a) costs associated with threatened or pending claims or actions by a Third Party for product liability resulting from those Development activities under this Agreement as to which Development Costs are shared by the Parties or paid fully by Biogen Idec under Section 5.4, other than those claims or actions for which Biogen Idec is entitled to indemnification under Article XII or pursuant to a Supply Agreement, provided that if there is a bona fide dispute as to whether a Party is entitled to indemnification for any such costs, the determination as to whether such costs are Development Costs shall not be made until such dispute is resolved; and (b) product liability insurance premiums for policies related to Development of Licensed Product in the Licensed Territory under which Biogen Idec is named as an additional insured; and

(v) other costs incurred that are explicitly included in the budgets that are approved by the JDC and included in the Development Plan.

In addition to the foregoing, "Development Costs" shall also include Pre-Option Exercise Phase 3 Manufacturing Costs, to the extent not otherwise captured by this definition. For purposes of clarity, the FTE Cost does not include travel and lodging expenses incurred by an FTE in connection with Development activities which such expenses shall be separately included as Development Costs. The term "Development Costs" shall in no event include any payments made by either Party or its Affiliates in connection with an AVEO In-License or a Biogen Idec In-License or in connection with any Third Party Technology Agreement, except to the extent that such payments are in respect of the Manufacture of Licensed Product and are included in Costs of Goods Sold for pre-clinical and clinical supplies needed for such efforts as set forth in the Development Plan. Section 8.9 sets forth the Parties' respective obligations regarding payments under AVEO In-Licenses and Biogen Idec In-Licenses, as well as the Parties' respective rights to offset certain payment obligations under other Third Party Technology Agreements against royalty payments obligations, that the Parties would otherwise have under this Agreement.

1.35 "Development Plan" means the written work-plan and budget for AVEO's Development efforts, agreed upon by the Parties after the Option Exercise Date in accordance with Section 5.2, and as amended from time to time in accordance with this Agreement or, if none, the Delivered Initial Development Plan.

1.36 "Directly Competitive Product" means any product comprising or containing an ERBB3 Antibody that is not a Licensed Product.

1.37 "Drug Regulations Laws" means Laws regulating drugs and pharmaceutical products, including the United States Federal Food, Drug, and Cosmetic Act, 21 U.S.C. §301 *et seq.*, the Prescription Drug Marketing Act of 1987, the federal Controlled Substances Act, 21 U.S.C. §801 *et seq*., and policies issued by the FDA, and similar Laws of the EMEA or other countries or jurisdictions in the Territory, each as in effect and as amended from time to time.

1.38 "Drug Safety Information Exchange Agreement" means an agreement between the Parties which outlines the requirements and responsibilities for drug safety reporting and monitoring within the Territory, as described in Section 5.8.

1.39 "ERBB3" means the human erbB3 (aka HER3) polypeptide, including: (i) any species variants or homologs thereof; (ii) any amino acid sequence variants or mutations of the foregoing, (iii) any post-translational modifications of the foregoing; and (iv) any derivative or fragment of the foregoing; provided that the derivative or fragment elicits an antibody that reacts with native human erbB3, when used as an antigen.

1.40 "ERBB3 Antibody" means an Antibody that binds to ERBB3.

1.41 "EMEA" means the European Medicines Agency or any successor agency.

1.42 "European Union" or "EU" means the countries of the European Union, as it is constituted as of the Effective Date and as it may be expanded from time to time.

1.43 "FDA" means the United States Food and Drug Administration or any successor agency thereto.

1.44 "Field" means all diagnostic, therapeutic and prophylactic uses in humans.

1.45 "First Commercial Sale" as to a particular country in the applicable Territory means the first commercial sale of a Licensed Product by a Party or its Affiliates or permitted Sublicensee to a Third Party in an arm's length transaction in such country after approval of the BLA, or if approval of a BLA is not required in such country, then following receipt of Regulatory Approval required to market such Licensed Product in such country. Sales for test marketing, clinical study purposes or compassionate, named patient or similar use shall not constitute a First Commercial Sale, but may constitute a sale under the definition of Net Sales if the recipient is billed.

1.46 "FTE" means a full-time-equivalent person year of scientific, technical, regulatory or professional work. An FTE shall consist of a total of [**], with any portion of an FTE calculated based upon hours worked divided by such annual total.

1.47 "FTE Cost" means, for any period, the product of (i) the actual total FTEs (and/or portion thereof) during such period, and (ii) the FTE Rate.

1.48 "FTE Rate" means [**] Dollars ($[**]) increased or decreased on the Option Exercise Date by the cumulative percentage increase or decrease in the CPI as of the Option Exercise Date over the level of the CPI as of the Effective Date, and thereafter further increased or decreased annually during the Agreement Term by the percentage increase in the CPI as of December 31st of each year over the level of the CPI as of December 31st of the prior year; provided, however, that in no event shall the FTE Rate exceed [**] Dollars ($[**]) or be less than [**] Dollars ($[**]) at any time during the Agreement Term.

1.49 "GAAP" means United States generally accepted accounting principles applied on a consistent basis, or any successor accounting principles generally accepted for public companies in the United States (such as International Financial Reporting Standards ("IFRS")).

1.50 "Governmental Authority" means any United States federal, state or local government or any foreign national, state, provincial, county, or city government or political subdivision thereof or any multinational organization or authority or any authority, agency, or commission entitled to exercise any administrative, executive, judicial, legislative, police, regulatory, or taxing authority or power, any court or tribunal (or any department, bureau or division thereof) or any governmental arbitrator or arbitral body.

1.51 "ICH" means the International Conference on Harmonization of Technical Requirements for Registration of Pharmaceuticals for Human Use.

1.52 "IND" means an Investigational New Drug Application filed with FDA or a similar application filed with an applicable Regulatory Authority outside of the United States such as a clinical trial application (CTA).

1.53 "Joint Collaboration Know-how" means Know-how, patentable or otherwise, first identified, discovered or developed jointly by the Parties or their Affiliates or others acting on behalf of the Parties or their Affiliates in the conduct of Development, Manufacturing or Commercialization of Licensed Product under this Agreement during the Agreement Term.

1.54 "Joint Collaboration Patent Rights" means Patent Rights that Cover Joint Collaboration Know-how.

1.55 "Joint Collaboration IP" means, collectively Joint Collaboration Know-how and Joint Collaboration Patent Rights.

1.56 "Know-how" means all biological materials and other tangible materials, inventions, practices, methods, protocols, formulae, knowledge, know-how, trade secrets, processes, procedures, assays, skills, experience, techniques, data and results of experimentation and testing, including pharmacological, toxicological and pre-clinical and clinical test data and analytical and quality control data, patentable or otherwise.

1.57 "Law" or "Laws" means all laws, statutes, rules, codes, regulations, orders, decrees, judgments or ordinances of any Governmental Authority, or any license, permit or similar right granted under any of the foregoing, or any similar provision having the force or effect of law.

1.58 "Licensed Product" means any product comprising or containing an ERBB3 Antibody (A) that is (i) discovered, Developed or Controlled by or on behalf of AVEO or any of its Affiliates prior to or during the Agreement Term or (ii) derived from an ERBB3 Antibody discovered, Developed or Controlled by or on behalf of AVEO or any of its Affiliates prior to or during the Agreement Term, or (B) the Development, Manufacture or Commercialization of which is Covered by Patent Rights owned or Controlled by AVEO or any of its Affiliates, but, in each case, not including any product excluded from the definition of Licensed Product under Section 3.9.

1.59 "License Term" means the period commencing upon the Option Exercise Date and ending on the date of expiration of the Agreement in accordance with the provisions of Section 14.1.

1.60 "Licensed Territory" means the entire world except North America.

1.61 "Losses" means any and all damages (including all incidental, consequential, statutory and treble damages), awards, deficiencies, settlement amounts, defaults, assessments, fines, dues, penalties, costs, fees, liabilities, obligations, liens, losses, and expenses (including court costs, interest and reasonable fees of attorneys, accountants and other experts) required to be paid to Third Parties with respect to a claim as to which a Party is entitled to indemnification under Article XII, by reason of any judgment, order, decree, stipulation or injunction, or any settlement entered into in accordance with the provisions of this Agreement, together with all documented reasonable out-of-pocket costs and expenses incurred in complying with any judgments, orders, decrees, stipulations and injunctions that arise from or relate to a claim of a Third Party.

1.62 "Manufacture" or "Manufacturing" means all activities related to the manufacturing of any Licensed Product, in bulk form manufactured for use as an active pharmaceutical ingredient or in finished final packaged and labeled product form, or in intermediate states, including but not limited to formulation, manufacturing scale-up, manufacturing for use in non-clinical and clinical studies, manufacturing for commercial sale, packaging, release of product, manufacturing quality assurance/quality control testing (including in-process release and stability testing), release, storage and shipping of product or any component or ingredient thereof, regulatory activities related to all of the foregoing, and data management and recordkeeping related to all of the foregoing.

1.63 "Net Sales" means the gross amount invoiced on sales of the Licensed Product by a Party, its Affiliates or Sublicensees to any Third Party, less the following reasonable deductions to the extent included in the gross invoiced sales price for the Licensed Product or otherwise directly paid, allowed, accrued, or incurred by such Party, its Affiliates or Sublicensees with respect to the sale of such Licensed Product:

(i) reasonable, normal and customary trade, cash and quantity discounts actually given; coupons for price reductions, actually taken; credits, price adjustments or allowances for damaged products, recalls, returns or rejections of products;

(ii) reasonable price adjustments, allowances, credits, chargeback payments and rebates (or the equivalent thereof) for the Licensed Product granted to and actually used by group purchasing organizations or other buying groups, managed health care organizations, pharmacy benefit management companies, health maintenance organizations and any other providers of health insurance coverage, health care organizations or other health care institutions (including hospitals), Third Party health care administrators or patient assistance or other similar programs, or to federal, state/provincial, local and other governments, including their agencies, or to wholesalers, distributors or other trade customers;

(iii) reasonable and customary freight, shipping, insurance and other transportation expenses (if actually borne by such Party or its Affiliates or Sublicensees without reimbursement from any Third Party);

(iv) required distribution commissions/fees payable to Third Party wholesalers for distribution of Licensed Product;

(v) sales, value-added, excise taxes, tariffs and duties, and other taxes and government charges directly related to the sale, to the extent that such items are included in the gross invoice price of the Licensed Product and actually borne by such Party, its Affiliates or Sublicensees without reimbursement from any Third Party (but not including taxes assessed against the income derived from such sale); and

(vi) a reasonable amount for bad debts actually written off which are attributable to sales of Licensed Product not to exceed [**] of Net Sales.

The transfer of a Licensed Product by a Party or one of its Affiliates to another Affiliate or Sublicensee for resale shall not be considered a sale.

Disposal of the Licensed Product for, or use of the Licensed Product in, clinical trials, as free samples, or under compassionate use, patient assistance, or test marketing programs or non-registrational studies or other similar programs or studies where a Licensed Product is supplied without charge, shall not result in any Net Sales, however if a Party or its Affiliates or Sublicensees charges for such Licensed Product, the amount billed will be included in the calculation of Net Sales.

Net Sales will include the cash consideration received on a sale and the fair market value of all non-cash consideration. In the event Licensed Product is sold, other than in an arm's length transaction, Net Sales for such sale will be determined using the average per unit Net Sales amount for the preceding Calendar Quarter.

Net Sales shall be determined on an accrual basis from books and records maintained in accordance with GAAP, consistently applied throughout the organization and across all products of the entity whose sales of Licensed Product are giving rise to Net Sales.

In the event a Licensed Product is sold in the form of a Combination Product, then the Net Sales for any such Combination Product shall be determined by [**].

1.64 "North America" or "N.A." means the United States, Canada and Mexico and their respective territories and possessions.

1.65 "Patent Rights" means (i) all national, regional and international patents and patent applications, including provisional patent applications; (ii) all patent applications filed either from such patents, patent applications or provisional applications or from an application claiming priority from any of these, including divisionals, continuations, and continuations-in-parts; (iii) any and all patents that have issued or issue in the future from the foregoing patent applications, including author certificates, inventor certificates, utility models, petty patents and design patents and certificates of invention; (iv) any and all extensions or restorations by existing or future extension or restoration mechanisms, including revalidations, reissues, re-examinations and extensions (including any supplementary protection certificates and the like) of the foregoing patents or patent applications; and (v) any similar rights, including pipeline protection (where the subject matter previously disclosed was not previously patentable in a particular jurisdiction but subsequently becomes patentable subject matter in such jurisdiction), or any importation, revalidation, confirmation or introduction patent or registration patent or patent of additions to any such foregoing patent applications and patents.

1.66 "Person" means any natural person, corporation, firm, business trust, joint venture, association, organization, company, partnership or other business entity, or any government, or any agency or political subdivisions thereof.

1.67 "Phase 1 Clinical Trial" means a human clinical trial that is intended to initially evaluate the safety and/or pharmacological effect of Licensed Product or that would otherwise satisfy the requirements of 21 C.F.R. 312.21(a) or an equivalent clinical trial in a country in the Territory other than the United States.

1.68 "Phase 2 Clinical Trial" means a human clinical trial, for which the primary endpoints include a determination of dose ranges or an indication of efficacy in patients being studied as described in 21 C.F.R. §312.21(b), or an equivalent clinical trial in a country in the Territory other than the United States.

1.69 "Phase 3 Clinical Trial" means a human clinical trial that is prospectively designed to demonstrate statistically whether a product is safe and effective for use in humans in the indication being investigated in a manner sufficient to obtain Regulatory Approval to market such product in patients having the disease or condition being studied as described in 21 C.F.R. §312.21(c), or an equivalent clinical trial in a country in the Territory other than the United States.

1.70 "Post-Approval Clinical Study" means (A) with respect to AVEO, any human clinical trial or registry either (i) required to be carried out by a Regulatory Authority in the AVEO Territory for the purpose of post-marketing surveillance of Licensed Product in the AVEO Territory or (ii) otherwise requested by Regulatory Authorities in the AVEO Territory after Regulatory Approval of Licensed Product in the AVEO Territory in an indication, designed to obtain additional information regarding Licensed Product's risks, benefits and optimal use of that Licensed Product in such indication, and (B) with respect to Biogen Idec, any human clinical trial or registry either (i) required to be carried out by a Regulatory Authority in the Licensed Territory for the purpose of post-marketing surveillance of Licensed Product in the Licensed Territory or (ii) otherwise requested by Regulatory Authorities in the Licensed Territory after Regulatory Approval of Licensed Product in the Licensed Territory in an indication, designed to obtain additional information regarding Licensed Product's risks, benefits and optimal use of that Licensed Product in such indication. For purposes of clarity, a clinical trial of Licensed Product in an indication for which such Licensed Product is not approved shall not be considered Post-Approval Clinical Study even if such trial occurs after such Licensed Product is approved in another indication.

1.71 "Pre-Option Exercise Phase 3 Manufacturing Costs" means the out-of-pocket costs and expenses incurred by AVEO or any of its Affiliates prior to the Option Exercise Date to obtain quantities of Licensed Product (including drug substance, drug product, validation batches and material for stability and other testing) for a Phase 3 Clinical Trial or for Commercialization or for testing of Licensed Product for any such Phase 3 Clinical Trial.

1.72 "Proof of Concept Development Plan" means the written work-plan for AVEO's Development efforts in connection with the Proof of Concept Study (including a description of the Proof of Concept Study itself), prepared and finalized by AVEO in accordance with Section 2.5, and as amended from time to time in accordance with this Agreement.

1.73 "Proof of Concept Study" means a Phase 2 Clinical Trial that is appropriately designed (i) to demonstrate efficacy in the disease to be studied through relevant primary and/or secondary efficacy endpoints as described in the Proof of Concept Development Plan and (ii) to allow dose selection and support generation of efficacy data that would allow movement of the product into a Phase 3 Clinical Trial that would support the regulatory strategy of seeking Regulatory Approval in both the AVEO Territory and the EU. For purpose of clarity, a clinical

study meeting the requirements of this definition will be considered a Proof of Concept Study when completed whether or not the endpoints of the study are actually met.

1.74 "Regulatory Approval" means any approval, including price approval, registration, license or authorization from any Governmental Authority or Regulatory Authority required for the Manufacture, Development or Commercialization of a Licensed Product in the Territory, and shall include, without limitation, an approval, registration, license or authorization granted in connection with the BLA.

1.75 "Regulatory Authority" means any federal, national, multinational, state, county, city, provincial, or local regulatory agency, department, bureau or other governmental entity with authority over the Marketing, Commercialization, Manufacture or sale of a pharmaceutical product in the Territory, including the FDA in the United States and the EMEA in the EU.

1.76 "Safety Data" means adverse event information and other information (if any) required by one or more Regulatory Authorities to be collected or to be reported to such Regulatory Authorities under applicable Laws.

1.77 "Sales Representative" means an individual, who engages in or manages sales calls and other promotional efforts with respect to the Licensed Product and who is employed by a Party or an Affiliate of a Party.

1.78 "Sublicensee" means a Third Party to whom a Party, as permitted under this Agreement, grants a license or sublicense, as the case may be, under the AVEO Technology, Biogen Idec Collaboration Technology or Joint Collaboration IP, to Develop, Manufacture, Commercialize or use Licensed Product in the Field, or otherwise grants rights to distribute, promote or sell Licensed Product in the Field, but does not include wholesale distributors of a Party or its Affiliates who purchase Licensed Product from such Party or its Affiliates in an arm's length transaction. For purposes of clarity, the term "wholesale distributors" does not include those distributors whose obligations to a Party or any of its Affiliates include responsibility for sales or marketing efforts in such country or sharing of costs and expenses with respect to sales or marketing on behalf of a Party or its Affiliates, which such distributors shall be deemed Sublicensees for purposes of this definition.

1.79 "Territory" means, collectively, the AVEO Territory and the Licensed Territory.

1.80 "Territory-Specific Clinical Trial" means, with respect to AVEO, a human clinical trial specifically required in the AVEO Territory which will generate data that will not be applicable to Licensed Product in the Licensed Territory (other than the applicability of safety data) and, except with respect to safety data, will not be included in a filing for Regulatory Approval for Licensed Product in the Licensed Territory, and, with respect to Biogen Idec, a human clinical trial specifically required in the Licensed Territory which will generate data that will not be applicable to Licensed Product in the AVEO Territory (other than the applicability of safety data) and, except with respect to safety data, will not be included in a filing for Regulatory Approval for Licensed Product in the AVEO Territory.

1.81 "Third Party" means any Person other than a Party or any of its Affiliates or their respective employees.

1.82 "United States" or "U.S." means the United States of America and its territories and possessions.

1.83 "Valid Claim" means (i) a claim of an issued and unexpired patent, which has not been held permanently revoked or held unenforceable or invalid by a decision of a court or other governmental agency of competent jurisdiction, unappealable or un-appealed within the time allowed for appeal, and which has not been admitted to be invalid or unenforceable through reissue or disclaimer or otherwise or been dedicated to the public or (ii) a claim in a pending patent application that (A) is being prosecuted in good faith, (B) has not been abandoned or disclaimed or finally determined to be unallowable by the applicable Governmental Authority in a decision from which no appeal is or can be taken, and (C) has not been pending for more than five (5) years from the date of issuance of the first substantive patent office action considering the patentability of such claim by the applicable Governmental Authority in such country (at which time such pending claim shall cease to be a Valid Claim for purposes of this Agreement unless and until such claim becomes a claim of an issued patent).

1.84 Additional Definitions. Each of the following definitions is set forth in the Section of this Agreement indicated below:

Defined Term	Section
Audited Party	§8.16(a)
Auditing Party	§8.16(a)
AVEO	Preamble
AVEO Control Assumption Date	§14.6(a)
AVEO Indemnities	§12.1
AVEO Group	§3.2(b)
Bankruptcy Code	§13.3
Biogen Idec	Preamble
Biogen Idec Control Assumption Date	§14.6(b)
Biogen Idec Indemnitees	§12.2
Breached Licensed Product	§14.5(a)
[**]	§8.3(b)
Collaboration Manager	§4.5
Commercially Viable Indication	§5.12(a)
Competing Acquiror	§13.1
Competitive Infringement	§9.6(a)
Contract Manufacturer Notice	§7.2
Control Assumption Option	§13.1
Cost Payment	§5.5
Cure Plan	§14.3(b)
Delivered Initial Development Plan	§2.9
Development Plan Guidelines	§4.8(a)
Divestiture Period	§13.1
Effective Date	Preamble
Event Milestone	§8.4
Event Milestone Payment	§8.4

Defined Term	Section
Force Majeure Event	§16.2
Funding Party	§5.11(a)
[**]	§8.3(c)
Indication Specific Royalty	§5.13(a)
Indemnitee	§12.3
Initial Development Plan	§2.9
Initial Release	§10.3
Insolvency Control Assumption Option	§13.3
Insolvency Event	§13.3
JCT	§6.2(a)
JCT Chairperson	§6.2(b)
JDC	§4.1
JDC Chairperson	§4.2
M&A Control Assumption Option	§13.1
M&A Event	§3.9
Manufacturing Party	§14.7
New Indication Existing Licensed Product	§5.12(a)
New Indication Funding Party	§5.12(a)
New Licensed Product	§5.11(a)
Non-Manufacturing Party	§14.7
Non-performing Manufacturing Party	§7.6
Notified Party	§14.3(b)
Notifying Party	§14.3(b)
Opt-in Indication	§5.13(a)
Opt-in Effective Date	§5.13(a)
Opt-in New Indication Existing Licensed Product	§5.13(a)
Opt-in Notice	§5.13(a)
Opt-in Notice Date	§5.13(a)
Opting-out Party	§5.11
Option	§2.1
Option Exercise Date	§2.3
Option Exercise Fee	§8.3(d)
Option Exercise Notice	§2.3
Option Exercise Period	§2.2
Panel Identification	§8.3(a)
Parties	Preamble
Party	Preamble
Patent Expenses	§9.5
Pre-Exercise Milestone	§8.3
Pre-Exercise Milestone Payment	§8.3
Product Opt-out Effective Date	§5.11
Product Trademarks	§9.9(b)
Promotional Materials	§6.4
Quarterly Cost Notice	§5.5
Royalty Term	§8.8

Defined Term	Section
Royalty-paying Party	§8.10
Section 5.11 Opt-out Effective Date	§5.11(a)
Section 5.12 Opt-out Effective Date	§5.12(a)
Senior Representative	§4.1
Supplemental Information	§2.2
Supply Agreement	§7.7
Tax/Taxes	§8.11
Third Party Technology	§3.6(a)
Third Party Technology Agreements	§3.6(a)

ARTICLE II.
OPTION GRANT AND DEVELOPMENT DURING OPTION PERIOD

2.1. Grant of Option. AVEO hereby grants to Biogen Idec an exclusive option, exercisable during the Option Exercise Period, as defined in Section 2.2, to acquire from AVEO the licenses set forth in Section 3.1, subject to the terms and conditions of this Agreement (the "Option").

2.2. Option Exercise Period. AVEO shall deliver the Data Package from the first Proof of Concept Study to Biogen Idec and an initial Development Plan no later than [**] after the last visit of the last patient to be dosed in such Proof of Concept Study. During the [**] following delivery of the Data Package, (i) Biogen Idec may request, and AVEO will provide to Biogen Idec, any other data and information in AVEO's possession and Control (and AVEO shall make reasonable efforts to procure or produce such other data and information that is not in AVEO's possession and Control) as Biogen Idec may reasonably request in connection with its review of the Data Package (the "Supplemental Information"), (ii) the Parties shall meet in good faith to discuss Biogen Idec's comments to the initial Development Plan in accordance with Section 2.9, (iii) AVEO will deliver to Biogen Idec copies of any AVEO In-Licenses entered into after the Effective Date, and (iv) AVEO will deliver to Biogen Idec a reasonably detailed statement of Pre-Option Exercise Phase 3 Manufacturing Costs actually incurred by AVEO and its Affiliates as of such date and reasonably expected to be incurred prior to the end of the Option Exercise Period. The Option shall be exercisable by Biogen Idec at any time during the period commencing on the Effective Date and ending on the later of (i) [**]after delivery of the Data Package, or (ii) [**] after the last to be delivered of the Supplemental Information (the "Option Exercise Period").

2.3. Option Exercise. In the event Biogen Idec elects to exercise the Option, it shall, no later than the [**] of the [**] of the Option Exercise Period, deliver to AVEO (i) written notice specifying that Biogen Idec has elected to exercise the Option (the "Option Exercise Notice"), and (ii) payment of the Option Exercise Fee. The date, if any, on which Biogen Idec has properly exercised the Option in accordance with the preceding sentence shall be the "Option Exercise Date" for purposes of this Agreement. The Option Exercise Period will be deemed to have ended, and the License Term will be deemed to have commenced, on the Option Exercise Date.

2.4. Effectiveness of License. Upon the exercise by Biogen Idec of the Option in accordance with this Article II, the provisions set forth in Article I and Articles III - XVI of this Agreement shall constitute the terms and conditions of the license and sublicense rights granted by AVEO to Biogen Idec with respect to the AVEO Technology in the Field, and by Biogen Idec to AVEO with respect to Biogen Idec Collaboration Technology, related to all Licensed Products in the Field. During the period commencing on the Effective Date and ending on the expiration of the Option Exercise Period, AVEO will not grant a license or other rights to any Third Party or take any other action that would prevent AVEO from being able to grant to Biogen Idec the license set forth in Section 3.1. In the event Biogen Idec does not exercise the Option during the Option Exercise Period, the licenses and other rights granted under Articles III shall have no force or effect.

2.5. Proof of Concept Development Plan. As promptly as practicable after AVEO has prepared the Proof of Concept Development Plan, AVEO shall provide a copy thereof to Biogen Idec for its review and comment. Biogen Idec shall have a period of [**] to review and comment on the Proof of Concept Development Plan. AVEO shall consider in good faith all reasonable comments made by Biogen Idec to the Proof of Concept Development Plan. If and to the extent requested by Biogen Idec, appropriate members of the clinical development and regulatory teams of AVEO shall meet with appropriate members of the clinical development and regulatory teams of Biogen Idec to discuss the Proof of Concept Study, including the design thereof as well as the Licensed Product and indication being studied in the Proof of Concept Study, and the Development activities and timelines contemplated under the Proof of Concept Development Plan. AVEO may amend, modify, supplement or update the Proof of Concept Development Plan at any time and from time to time in its discretion, provided that AVEO complies with the foregoing provisions of this Section 2.5 (but with Biogen Idec having a [**] review period instead of [**]) with respect to any such amendment, modification, supplement or update of the Proof of Concept Development Plan to the same extent as AVEO is required in connection with the initial Proof of Concept Development Plan, and any such amendment, modification, supplement or update of the Proof of Concept Development Plan is consistent with the parameters set forth in the next sentence. The Proof of Concept Development Plan proposed by AVEO hereunder, including any amendment, modification, supplement or update, shall meet the following parameters: [**].

2.6. Development During Option Period. During the Option Exercise Period, AVEO shall have sole responsibility for Development and Manufacture of Licensed Product, at AVEO's sole cost and expense, and AVEO shall use Commercially Reasonable Efforts to perform its Development activities as contemplated under the Proof of Concept Development Plan and to Develop Licensed Product through completion of the first Proof of Concept Study. For purposes of clarity, Biogen Idec shall have no right to Develop or Manufacture Licensed Product during the Option Exercise Period. During the Option Exercise Period, AVEO shall not enter into any AVEO In-License with respect to any Know-how or Patent Rights as to which (x) rights thereto in both the AVEO Territory and Licensed Territory will be necessary, (y) such Know-how is incorporated in any Licensed Product or such Patent Rights Cover any Licensed Product or (z) such Know-how or Patent Rights are owned or licensed by a Sublicensee (or any of such Sublicensee's Affiliates) to whom AVEO has granted a license or sublicense under AVEO Technology or Biogen Idec Collaboration Technology to Commercialize Licensed Product in the AVEO Territory, unless either (i) such AVEO In-License includes rights with respect to such

Know-how and Patent Rights in both the AVEO Territory and the Licensed Territory and such rights are Controlled by AVEO during the Agreement Term or (ii) to the extent Control cannot be obtained, licenses are available, as a matter of course, separately from the licensor of such Know-how or Patent Rights for Development, Manufacture or Commercialization, as the case may be, of Licensed Product in both the AVEO Territory and the Licensed Territory on terms that, at the time AVEO enters into such license, would be substantially the same as the terms obtained by AVEO with respect to the AVEO Territory, and AVEO provides written notice to Biogen Idec that Control could not be obtained. For purposes of clarification and not by way limitation, it is understood and agreed that the term "necessary" as used in this Section 2.6 shall be deemed to include any Know-how or Patent Rights as to which rights in both the AVEO Territory and Licensed Territory would be necessary for Biogen Idec to Develop, Manufacture or Commercialize, as the case may be, Licensed Product in both the AVEO Territory and the Licensed Territory under this Agreement, including, without limitation, under Sections 5.11, 5.12, 7.5, 13.1, 13.3 or 14.5(b).

2.7. Decision-making during Option Period. During the Option Exercise Period, AVEO shall have sole decision-making authority with respect to Development and Manufacture of Licensed Product, provided that AVEO complies with the provisions of Section 2.5 hereof.

2.8. Development Updates. On a quarterly basis during the Option Exercise Period, AVEO and Biogen Idec will hold an in-person meeting, at either AVEO's or Biogen Idec's headquarters in Massachusetts, at such time as the Parties shall mutually agree, during which AVEO shall present the results of its Development activities related to Licensed Product since the last update, and shall describe its Development plans with respect to Licensed Product for the following three months and the remainder of the then Calendar Year.

2.9. Initial Development Plan. As soon as AVEO has prepared the initial Development Plan (even if prior to delivery of the Data Package), AVEO shall deliver to Biogen Idec the initial Development Plan. During the period between Data Package delivery by AVEO and Option Exercise Date, AVEO and Biogen Idec, including appropriate members of the clinical development and regulatory teams of both AVEO and Biogen Idec shall meet to discuss the initial Development Plan, including the design thereof as well as the indication being studied, and the Development activities and timelines contemplated thereunder. In anticipation of Biogen Idec's exercise of the Option, AVEO shall (x) consider in good faith all reasonable Biogen Idec proposals to such initial Development Plan and (y) deliver to Biogen Idec a revised initial Development Plan (or if no revised initial Development Plan is delivered, the initial Development Plan shall be deemed re-delivered) no less than thirty (30) days prior to the end of the Option Exercise Period (the "Delivered Initial Development Plan"). The Delivered Initial Development Plan shall meet the following criteria: (i) such Delivered Initial Development Plan shall be directed only to the indication that was the subject of the Proof of Concept Study; (ii) the size of the pivotal trial included in such Delivered Initial Development Plan shall be reasonable given the scope of the indication, in light of then prevailing industry standards and regulatory guidance; (iii) such Delivered Initial Development Plan shall in addition include, at a minimum, study designs, assignment of responsibilities (both among the Parties and Third Parties), timelines, decision criteria, supply plans, quality standards, expected resources, costs and a budget for Development Costs; and (iv) the budget for Development Costs in such Delivered

Initial Development Plan shall be for no longer than through the end of completion of the pivotal trial for the indication that was the subject of the Proof of Concept Study.

ARTICLE III.
LICENSE GRANTS

3.1. AVEO Grant to Biogen Idec. Subject to the terms and conditions of this Agreement, effective immediately upon the Option Exercise Date, AVEO and its Affiliates grant the following licenses to Biogen Idec: (i) co-exclusive (with AVEO and its Affiliates), royalty-free license, with the right to grant sublicenses, to the extent set forth under Section 3.3(a), and subject to AVEO's rights under Section 3.3(b), under AVEO Technology, including AVEO's interest in Joint Collaboration IP, solely to Develop, have Developed, Manufacture and have Manufactured, Licensed Product anywhere in the world pursuant to, and in accordance with, this Agreement, and (ii) an exclusive (including with respect to AVEO and its Affiliates), royalty-bearing license, with the right to grant sublicenses, to the extent set forth under Section 3.3(a), under AVEO Technology solely to Commercialize, have Commercialized, import, and have imported Licensed Product in the Licensed Territory within the Field.

3.2. Biogen Idec Grant to AVEO.

(a) License. Subject to the terms and conditions of this Agreement, effective immediately upon the Option Exercise Date, Biogen Idec and its Affiliates grant the following licenses to AVEO: (i) a co-exclusive (with Biogen Idec and its Affiliates), royalty-free license, with the right to grant sublicenses, to the extent set forth under Section 3.3(b), and subject to Biogen Idec's rights under Section 3.3(a), under Biogen Idec Collaboration Technology, including Biogen Idec's interest in Joint Collaboration IP, solely to Develop, have Developed, Manufacture and have Manufactured, Licensed Product anywhere in the world pursuant to, and in accordance with, this Agreement, and (ii) an exclusive (including with respect to Biogen Idec and its Affiliates), royalty-bearing license, with the right to grant sublicenses, to the extent set forth under Section 3.3(b), under Biogen Idec Collaboration Technology, including Biogen Idec's interest in Joint Collaboration IP, solely to Commercialize, have Commercialized, import, and have imported Licensed Product in the AVEO Territory within the Field.

(b) Covenant Not to Sue. In further consideration of the licenses granted to Biogen Idec under this Agreement and subject to Section 3.9, Biogen Idec and its Affiliates grant to AVEO and its present and future Affiliates and Sublicensees (the "AVEO Group") a covenant not to sue or bring action against any member of the AVEO Group claiming or asserting that the Development, Manufacture or Commercialization of any AVEO Proprietary Composition Licensed Product by any member of the AVEO Group in the AVEO Territory within the Field pursuant to, and in accordance with, the provisions of this Agreement infringes any Patent Rights owned and Controlled by Biogen Idec or any of its Affiliates (other than any such Patent Rights that are included in Biogen Idec Collaboration Patent Rights or Joint Collaboration Patent Rights) that Cover the composition of matter or method of use of such AVEO Proprietary Composition Licensed Product and that are necessary to the Development, Manufacture or Commercialization of such AVEO Proprietary Composition Licensed Product in the AVEO Territory. Notwithstanding anything express or implied in the foregoing provisions of this Section 3.2(b) to the contrary, the provisions of this Section 3.2(b) shall not apply with respect to

any AVEO Proprietary Composition Licensed Product that Biogen Idec does not have the right to Develop or Commercialize under the terms of this Agreement. The provisions of this Section 3.2(b) shall not apply with respect of Patent Rights or Know-how under Third Party Technology Agreements entered into by either Party or any of its Affiliates pursuant to Section 3.6 hereof.

3.3. Licenses and Sublicenses; Contractors.

(a) Biogen Idec Rights. Biogen Idec shall have the right to grant any licenses or sublicenses under Biogen Idec Collaboration Technology to Develop, have Developed, Manufacture or have Manufactured Licensed Product anywhere in the world under the terms of this Agreement or to Commercialize, have Commercialized, import and have imported Licensed Products in the Licensed Territory, provided that any such licenses or sublicenses comply with the provisions set forth in Sections 3.3(c), 3.3(d) and 3.3(e) below, as applicable, and that Biogen Idec provides prior written notice to AVEO of any such licenses or sublicenses to any Third Party. In addition, Biogen Idec may sublicense the rights granted to it by AVEO under Section 3.1, in whole or in part, (i) to any of its Affiliates or (ii) to a Third Party with prior written notice to AVEO.

(b) AVEO Rights. AVEO shall have the right to grant any licenses or sublicenses under AVEO Technology to Develop, have Developed, Manufacture or have Manufactured Licensed Products anywhere in the world under the terms of this Agreement or to Commercialize, have Commercialized, import and have imported Licensed Product in the AVEO Territory, provided that (i) during the Option Exercise Period, AVEO and its Affiliates shall not grant any license or sublicense to Develop Licensed Product, (ii) after the Option Exercise Period, AVEO and its Affiliates shall retain final decision-making authority under such license or sublicense for Development of Licensed Product, (iii) any license or sublicense granted to a Third Party with respect to Manufacture of Licensed Product shall be subject to the terms of Article VII, (iv) in no event shall AVEO grant any such license or sublicense to any Third Party that is Developing or Commercializing a Directly Competitive Product, (v) AVEO provides prior written notice to Biogen Idec of such licenses or sublicenses, (vi) AVEO shall have complied with the provisions of Section 3.7 hereof prior to granting such license or sublicense, and (vii) such license or sublicense complies with the provisions set forth in Sections 3.3(c), 3.3(d) and 3.3(e) below. AVEO may only sublicense the rights granted it by Biogen Idec under Section 3.2(a), in whole or in part, (x) to any of its Affiliates or (y) to a Third Party to whom AVEO has granted licenses or sublicenses under AVEO Technology pursuant to this Section 3.3(b), provided that AVEO provides prior written notice to Biogen Idec of any sublicense granted under clause (y).

(c) Sublicense Terms. Each permitted license or sublicense and agreement with a Sublicensee (i) must be consistent with the terms and conditions of this Agreement, (ii) must contain a provision under which the licensing Party shall obtain an exclusive or non-exclusive license, with the right to grant a sublicense to the other Party as set forth under this Agreement, to Develop, have Developed, Manufacture, have Manufactured, to Commercialize and have Commercialized Licensed Product in the Territory under Know-how and Patent Rights owned or licensed by such Sublicensee or any of its Affiliates, that are (A) necessary to Develop, Manufacture or Commercialize Licensed Product, (B) incorporated in any Licensed Product, in

the case of such Know-how, or that Cover any Licensed Product, in the case of such Patent Rights, and (C) reasonably useful to Develop, Manufacture or Commercialize Licensed Product, provided, however, that notwithstanding the foregoing provisions of this clause (ii), if the applicable Sublicensee is not granted the right under such license or sublicense to Commercialize or have Commercialized Licensed Product in the AVEO Territory or the Licensed Territory, the provisions of the foregoing subclauses (A) and (B) shall be limited only to Know-how and Patent Rights generated by such Sublicensee or any of its Affiliates that arise directly out of the Development or Manufacture of Licensed Product under such license or sublicense agreement and the provisions of the foregoing subclause (C) shall not apply, and (iii) must not contain provisions that result in the licensing Party not having the ability to license or sublicense to the other Party as set forth in this Agreement any Patent Rights or Know-how owned, licensed, used or practiced by the licensing Party or any of its Affiliates. Each permitted license or sublicense by AVEO or any of its Affiliates must contain a provision that the applicable Sublicensee and its Affiliates shall not Develop, Manufacture or Commercialize a Directly Competitive Product or collaborate with, or grant to, any other Third Party any license or right to Develop, Manufacture or Commercialize a Directly Competitive Product.

(d) Performance by Sublicensees. Each Party shall be responsible for the performance of all of its Sublicensees, and shall remain fully responsible for all of its Sublicensees' obligations under this Agreement. Each license or sublicense granted by a Party pursuant to this Article III shall be subject and subordinate to the terms and conditions of this Agreement, and shall contain terms and conditions consistent with those in this Agreement. Each Party shall promptly provide the other Party with a copy of the fully executed license or sublicense agreement covering any license or sublicense granted hereunder, and such license or sublicense agreement shall contain the following provisions: (i) a requirement that such Sublicensee submit applicable sales or other reports to the Party granting the license or sublicense to the extent necessary or relevant to the reports required to be made or records required to be maintained under this Agreement; (ii) an audit requirement consistent with that set forth in Section 8.16; (iii) a requirement that such Sublicensee comply with the confidentiality provisions and restrictions on use of Confidential Information contained in Article X with respect to both Parties' Confidential Information; and (iv) any other provisions required under any AVEO In-License or Biogen Idec In-License, as the case may be. If a granting Party becomes aware of a material breach of any license or sublicense by a Sublicensee of the rights granted to such Party or the other Party under this Agreement, the granting Party shall promptly notify the other Party of the particulars of the same and use Commercially Reasonable Efforts to enforce the terms of such license or sublicense.

(e) Performance by Contractors. If, and to the extent that, either Party has the right or obligation pursuant to, and in accordance with, the provisions of this Agreement to Develop, Manufacture or Commercialize any Licensed Product, such Party shall be entitled to utilize the services of Third Parties (including Third Party contract research organizations, Third Party contract manufacturing organizations ("CMOs") and Third Party contract sales organizations ("CSOs")) to perform the Development, Manufacturing or Commercialization activities that such Party has the right or obligation to perform under this Agreement with respect to such Licensed Product; provided that the contracting Party shall remain at all times fully liable for its responsibilities under this Agreement. Neither Party shall use Third Party contract resources to perform any activities that the contracting Party has the right or obligation to

perform under this Agreement unless the contracting Party's rights under the agreement with the Third Party contractor guarantee to the other Party the same rights under this Agreement as if the contracting Party had performed such activities itself, and any such Third Party contractor agreement includes a requirement that such Third Party contractor comply with the confidentiality provisions and restrictions on use of Confidential Information contained in Article X with respect to both Parties' Confidential Information and a requirement that such Third Party contractor comply with any other provisions required under any AVEO In-License or Biogen Idec In-License, as the case may be. Notwithstanding anything in this Agreement to the contrary, the contracting Party under this Section 3.3(e) shall (A) obtain from any Third Party performing any activities of the contracting Party under this Agreement a license to any Know-how and Patent Rights generated by such Third Party arising directly out of the contracting activities to the extent necessary for the Development, Manufacture and Commercialization of Licensed Product or to the extent such Know-how is incorporated in any Licensed Product or such Patent Rights Cover any Licensed Product, (B) if such Third Party or any of its Affiliates is a Sublicensee of the contracting Party to whom the contracting Party has granted rights to Commercialize Licensed Product in the contracting Party's Territory, obtain from such Third Party a license to any Know-how and Patent Rights generated by such Third Party arising directly out of the contracting activities to the extent reasonably useful for the Development, Manufacture and Commercialization of Licensed Product and (C) use Commercially Reasonable Efforts to obtain from such Third Party (other than a Third Party referred to in the foregoing clause (B)) a license to any Know-how and Patent Rights generated by such Third Party arising directly out of the contracting activities to the extent reasonably useful for the Development, Manufacture and Commercialization of Licensed Product. Each such license referred to in the foregoing clause (A), (B) or (C) of this Section 3.3(e) shall include rights to both the AVEO Territory and the Licensed Territory to the extent such Know-how and Patent Rights are necessary for the Development, Manufacture or Commercialization of Licensed Product in each such Territory or to the extent such Know-how is incorporated in any Licensed Product or such Patent Rights Cover any Licensed Product. Each such license referred to in the foregoing clause (A), clause (B) or clause (C) of this Section 3.3(e) shall include the right to sublicense to the other Party consistent with this Agreement. For purposes of clarification and not by way of limitation, it is understood and agreed that the term "necessary" as used in this Section 3.3(e) shall be deemed to include any Know-how or Patent Rights as to which rights in both the AVEO Territory and Licensed Territory would be necessary for the contracting Party to Develop, Manufacture or Commercialize, as the case may be, Licensed Product in both the AVEO Territory and the Licensed Territory under this Agreement, including, without limitation, under Sections 5.11, 5.12, 7.5, 13.1, 13.3 or 14.5(b).

3.4. Restrictive Covenants. Except for the Development, Manufacture and Commercialization of Licensed Products pursuant to, and in accordance with, the terms and conditions set forth in this Agreement and except for the grant of any licenses or sublicenses by AVEO with respect to Licensed Products pursuant to Section 3.3(b) above and except as set forth in Section 3.9, during the Agreement Term neither AVEO nor any of its Affiliates (i) shall Develop, Manufacture or Commercialize any ERBB3 Antibody in the AVEO Territory or the Licensed Territory within the Field, (ii) shall collaborate with any Third Party, shall grant to any Third Party the right, or shall engage in activities on behalf of any Third Party, to Develop, Manufacture or Commercialize any ERBB3 Antibody in the AVEO Territory or the Licensed Territory within the Field, (iii) shall grant to any Third Party any license or other right under any

AVEO Technology to Develop, Manufacture or Commercialize any ERBB3 Antibody in the AVEO Territory or the Licensed Territory within the Field or (iv) subject to Section 16.5 hereof, shall sell, assign, convey or otherwise transfer any right, title or interest in and to any AVEO Technology or any ERBB3 Antibody (including, without limitation, any Licensed Product), provided that the foregoing clause (iv) shall not be deemed a restriction on AVEO's right to license AVEO Technology for any and all uses other than the Development, Manufacture or Commercialization of ERBB3 Antibodies or for any and all uses outside the Field.

3.5. Retained Rights. Subject to Section 3.3(b) and Section 3.4, any rights of a Party not expressly granted under this Agreement shall be retained by such Party.

3.6. Third Party Technology.

(a) Process. The Parties agree that it may be necessary or desirable at any time and from time to time during the License Term to enter into agreements with a Third Party to acquire, in-license or otherwise obtain or use technology, intellectual property rights, information, materials, data or know-how, patentable or otherwise, owned or Controlled by such Third Party ("Third Party Technology") in order for either Party to Develop, Manufacture or Commercialize Licensed Product under this Agreement (such Third Party agreements being hereinafter referred to, collectively, as the "Third Party Technology Agreements"). Such Third Party Technology Agreements shall not conflict with the terms and conditions of this Agreement. In the event that either Party believes that entering into a Third Party Technology Agreement is necessary or desirable in connection with the Development, Manufacture or Commercialization of Licensed Product pursuant to this Agreement, such Party shall notify the JDC and the other Party promptly and include in such notification a summary of the Third Party Technology that would be covered by such Third Party Technology Agreement, the anticipated commercial terms of such Third Party Technology Agreement and any other relevant information. The JDC shall discuss (i) whether the Third Party Technology that would be the subject of such Third Party Technology Agreement is necessary or desirable in connection with the Development, Manufacture or Commercialization of Licensed Product pursuant to this Agreement, (ii) the anticipated commercial terms of such Third Party Technology Agreement, (iii) the advantages and disadvantages associated with entering into such Third Party Technology Agreement at that time or at a later point in time and (iv) any other factors the JDC deems relevant. If the JDC determines that such Third Party Technology Agreement should be pursued, AVEO shall be responsible for negotiating, in consultation with the JDC and Biogen Idec, any such Third Party Technology Agreements and, upon final approval of the JDC as provided below, for entering into such Third Party Technology Agreements. AVEO shall use Commercially Reasonable Efforts to negotiate as promptly as possible such Third Party Technology Agreements that the JDC has determined to pursue and throughout such negotiation AVEO shall consider in good faith and use Commercially Reasonable Efforts to get the applicable Third Party to agree to all reasonable comments made by the JDC and Biogen Idec with respect to such Third Party Technology Agreements and the terms thereof. Prior to execution of any such Third Party Technology Agreement, AVEO shall present the agreement in substantially final form to the JDC for review and final approval. Unless Biogen Idec otherwise agrees, the JDC shall not provide final approval to any such Third Party Technology Agreement unless (A) the Third Party Technology that is subject to such Third Party Technology Agreement may be used by, sublicensed to, or the benefits made available to, Biogen Idec and its Affiliates and Sublicensees

in connection with the Development, Manufacture and Commercialization of Licensed Product pursuant to, and in accordance with, the terms of this Agreement, and (B) in the event that such Third Party Technology may not be used by and sublicensed to Biogen Idec and its Affiliates and Sublicensees in connection with the Development, Manufacture and Commercialization of Licensed Product under this Agreement, then such Third Party Technology is available for licensing, as a matter of course, separately from the licensor of such Third Party Technology with respect of both the AVEO Territory and the Licensed Territory on terms that, at the time of final JDC approval, would be substantially the same as the terms obtained by AVEO with respect to the AVEO Territory. Upon final review and approval by the JDC of any Third Party Technology Agreement in accordance with this Section 3.6, AVEO shall execute and deliver such Third Party Technology Agreement and such Third Party Technology Agreement shall be an AVEO In-License for purposes of this Agreement. AVEO shall provide Biogen Idec with an unredacted copy of such fully executed Third Party Technology Agreement. Notwithstanding anything in this Agreement to the contrary, in the event the JDC unanimously agrees that Biogen Idec shall enter into a Third Party Technology Agreement in accordance with the process outlined in this Section 3.6, then Biogen Idec shall execute and deliver such Third Party Technology Agreement and provide an unredacted copy of such fully executed Third Party Technology Agreement to AVEO which such Third Party Technology Agreement shall be a Biogen Idec In-License. The Know-how and Patent Rights underlying a Biogen Idec In-License shall be deemed to be Biogen Idec Collaboration Technology. As promptly as practicable after the execution of such Third Party Technology Agreement (unless already done prior to the execution of such Third Party Technology Agreement), the Development Plan shall be amended to include actions required related to any such Third Party Technology Agreement and the Third Party Technology that is subject thereto. Except as set forth in Section 3.6(b) below, unless and until the JDC provides final approval of a Third Party Technology Agreement as contemplated above in this Section 3.6(a), neither Party shall enter into such Third Party Technology Agreement. For the sake of clarity, the terms of this Section 3.6 shall not apply to AVEO In-licenses entered into prior to the Option Exercise Date.

(b) Failure to Agree. In the event that the JDC determines that a Third Party Technology Agreement should not be pursued or the representatives of either Party on the JDC will not agree, or do not agree in a timely manner, to the terms that the other Party or the representatives of the other Party on the JDC proposes or propose to accept, and no further discussions are authorized by the JDC or are ongoing by the JDC, either Party alone shall have the right to enter into an agreement with such Third Party on such terms as such Party and the Third Party shall agree in connection with rights to Develop, Manufacture and/or Commercialize a Licensed Product in each Party's respective territory. In addition, in the event that AVEO is required to negotiate and enter into any Third Party Technology Agreement pursuant to this Section 3.6 but AVEO does not do so, or is unable to do so, in a timely manner, then Biogen Idec shall have the right (but not the obligation) to negotiate and enter into such Third Party Technology Agreement. In the event AVEO enters into a Third Party Technology Agreement under this Section 3.6(b), (i) such agreement shall not be considered an AVEO In-License, (ii) the underlying Patent Rights shall not be considered AVEO Patent Rights or AVEO Collaboration Patent Rights, and (iii) the underlying Know-how shall not be considered AVEO Know-how or AVEO Collaboration Know-how. In the event Biogen Idec or any of its Affiliates enters into a Third Party Technology Agreement under this Section 3.6(b), (i) such agreement shall not be considered a Biogen Idec In-License, (ii) the underlying Patent Rights shall not be

considered Biogen Idec Collaboration Patent Rights, and (iii) the underlying Know-how shall not be considered Biogen Idec Collaboration Know-how. Notwithstanding anything express or implied in the foregoing provisions of this Section 3.6(b) to the contrary, (A) AVEO agrees that it and its Affiliates will not assert any rights acquired under any Third Party Technology Agreement entered into by AVEO under the terms of this Section 3.6(b) against Biogen Idec or any of its Affiliates or Sublicensees with respect to the Development, Manufacture or Commercialization of Licensed Product by Biogen Idec or any of its Affiliates or Sublicensees pursuant to, and in accordance with, the terms of this Agreement, and (B) Biogen Idec agrees that it and its Affiliates will not assert any rights acquired under any Third Party Technology Agreement entered into by Biogen Idec under the terms of this Section 3.6(b) against AVEO or any of its Affiliates or Sublicensees with respect to the Development, Manufacture or Commercialization of Licensed Product by AVEO or any of its Affiliates or Sublicensees pursuant to, and in accordance with, the terms of this Agreement; provided, however, that nothing in this sentence shall prevent or restrict, or be deemed a representation with respect to, the ability of a Third Party licensor to fully assert its rights against a Party, and notwithstanding anything express or implied in the foregoing provisions of this sentence to the contrary, the provisions of clause (A) of this sentence shall not apply with respect to any Licensed Product if Biogen Idec is not required to pay royalties to AVEO pursuant to Section 8.5 hereof on Net Sales by Biogen Idec and its Affiliates and Sublicensees of such Licensed Product in the Licensed Territory, and the provisions of clause (B) of this sentence shall not apply with respect to any Licensed Product if the license rights granted by AVEO to Biogen Idec and its Affiliates pursuant to, and in accordance with, Section 3.1 hereof are not applicable to such Licensed Product for any reason or if AVEO is not required to pay royalties to Biogen Idec pursuant to Section 8.6 hereof on Net Sales by AVEO and its Affiliates and Sublicensees of such Licensed Product in the AVEO Territory. Each Party that enters into a Third Party Technology Agreement that is not considered an AVEO In-License or a Biogen Idec In-License, as the case may be, by virtue of the foregoing provisions of this Section 3.6(b) shall, at the request of the other Party made at any time during the License Term, agree to include any rights under such Third Party Technology Agreement that such Party Controls in the licenses granted to the other Party under Article III, as AVEO Technology or Biogen Idec Collaboration Technology, as the case may be, provided that the other Party makes payment to such Party of all amounts that the other Party would have been required to pay under this Agreement in connection with such Third Party Technology Agreement if such Third Party Technology Agreement had been considered an AVEO In-License or a Biogen Idec In-License, as the case may be, under this Agreement from and after the date that such Party entered into such Third Party Technology Agreement, in which case such Third Party Technology Agreement shall be considered an AVEO In-License or a Biogen Idec In-License, as the case may be.

3.7. Right of First Negotiation. In the event that AVEO proposes to license or sublicense or otherwise grant to a Third Party all or any portion of the rights of AVEO to Commercialize Licensed Product in a particular country of the AVEO Territory, other than solely for purposes of a relationship of the type described in Section 3.3(e), regardless of whether AVEO or a Third Party makes the initial proposal, then AVEO will promptly notify Biogen Idec in writing thereof. As soon as practicable, Biogen Idec will respond to AVEO in writing regarding its interest in entering into negotiations to obtain such rights and the Parties will promptly commence exclusive, good faith negotiations through and until the [**] following the date that AVEO gives such written notice to Biogen Idec. Upon commencement of such

negotiations, AVEO shall advise Biogen Idec of the factors that AVEO considers to be commercially material to its decision to grant Commercialization rights with respect to Licensed Product in such country of the AVEO Territory. If AVEO and Biogen Idec are unable to agree on material terms within [**] after receipt by Biogen Idec of AVEO's notice of its intent to transfer Commercialization rights, AVEO shall thereafter be free to negotiate and /or enter into an agreement with any Third Party on such terms as AVEO may decide in its sole discretion

3.8. No Inconsistent Third Party Agreements; Amendments. During the Agreement Term, neither Party nor any of its Affiliates shall enter into any in-license of Third Party intellectual property pursuant to which such Party or any of its Affiliates grants to such Third Party rights under or to AVEO Technology or Biogen Idec Collaboration Technology, as the case may be, that would contravene or be inconsistent or in conflict with the rights of the other Party under this Agreement. During the Agreement Term, neither Party nor any of its Affiliates shall amend, modify or terminate any in-license of Third Party intellectual property (including, without limitation, any such in-license that is in effect as of the Effective Date) without the prior written consent of the other Party (which may be granted or withheld by such other Party in its absolute discretion) if such amendment, modification or termination would materially adversely affect any of the rights that such other Party or any of its Affiliates would have under this Agreement if such amendment, modification or termination were not effected.

3.9. M&A Events. In the event of an M&A Event, as defined below, to which AVEO is a party, (i) the Patent Rights owned or otherwise Controlled by the Third Party acquiror or any of its Affiliates immediately prior to the effectiveness of the M&A Event will be specifically excluded from the definition of AVEO Patent Rights and AVEO Collaboration Patent Rights, (ii) the Know-how owned or otherwise Controlled by the Third Party acquiror or any of its Affiliates prior to the effective date of the M&A Event will be specifically excluded from the definition of AVEO Know-how, (iii) in no event shall any agreement that such Third Party acquiror or any of its Affiliates is a party prior to the effective date of the M&A Event be considered an AVEO In-License, (iv) any product owned or otherwise Controlled by the Third Party acquiror or any of its Affiliates immediately prior to the effectiveness of the M&A Event shall be specifically excluded from the definition of Licensed Product, and (v) the restrictive covenants set forth in Section 3.4 shall not apply to any ERBB3 Antibody that is not a Licensed Product by reason of the foregoing clause (iv) (it being understood and agreed that the provisions of this clause (v) shall not limit Biogen Idec's rights under Section 13.1 or Section 14.5(e)). In the event of any M&A Event to which Biogen Idec is a party, the Patent Rights owned or Controlled by the Third Party acquiror or any of its Affiliates immediately prior to the effectiveness of the M&A Event and the Patent Rights covering Know-how developed or acquired after the effective date of the M&A Event (other than Biogen Idec Collaboration Patent Rights) and any ERBB3 Antibody that is not a Licensed Product by reason of the foregoing clause (iv) shall not be subject to the covenant not to sue granted to AVEO under Section 3.2(b) or Section 3.6(b). For purposes of this Agreement, an M&A Event with respect to a Party shall mean any of the following: (a) the sale or disposition of all or substantially all of the assets of such Party or its direct or indirect parent corporation to a Third Party, (b) the acquisition by a Third Party which constitutes one person, as such term is used in Section 13(d) and 14(d) of the Securities Exchange Act of 1934, as amended (the "Exchange Act"), together with any such person's "affiliates" or "associates", as such terms are defined in the Exchange Act, other than an employee benefit plan (or related trust) sponsored or maintained by such Party or any of its Affiliates, of more than 50% of the

outstanding shares of voting capital stock of such Party or its direct or indirect parent corporation, or (c) the merger or consolidation of such Party or its direct or indirect parent corporation with or into another corporation, other than, in the case of this clause (c), an acquisition or a merger or consolidation of a Party or its direct or indirect parent corporation in which holders of shares of the voting capital stock of the Party or its direct or indirect parent corporation, as the case may be, immediately prior to the acquisition, merger or consolidation will have at least fifty percent (50%) of the ownership of voting capital stock of the acquiring Third Party or the surviving corporation in such merger or consolidation, as the case may be, immediately after the merger or consolidation.

ARTICLE IV.
GOVERNANCE DURING LICENSE TERM

4.1. Joint Development Committee Formation. As soon as reasonably practicable after the Option Exercise Date, and in any event not later than thirty (30) days after the Option Exercise Date, the Parties shall establish a joint development committee (the "JDC"). The JDC shall consist of three (3) representatives designated by each Party, or such other number as the Parties may from time to time mutually agree. Each Party shall appoint its initial representatives on the JDC at the time of formation, but may, from time to time, substitute one or more of its representatives, in its sole discretion, effective upon notice to the other Party of such change. Each Party shall have at least one JDC representative who is a senior employee (vice president level or above) and shall designate him/her upon designation to the JDC as its senior representative (such representative, such Party's "Senior Representative"). All JDC representatives shall have appropriate expertise and ongoing familiarity with Development of biopharmaceutical products. Additional representatives or consultants may from time to time, by mutual consent of the Parties, be invited to attend JDC meetings, provided that such representatives and consultants are subject to written obligations that are no less stringent than the confidentiality obligations and restrictions on use set forth in Article X. Each Party shall bear its own expenses relating to attendance at JDC meetings by its representatives.

4.2. Chairperson. The chairperson of the JDC (the "JDC Chairperson") shall be a representative of AVEO. The JDC Chairperson's responsibilities shall include (i) scheduling meetings as described in Section 4.3, or more frequently if the JDC determines it necessary; (ii) setting agendas for meetings with solicited input from other members; and (iii) confirming and delivering minutes to the JDC for review and final approval.

4.3. Meetings. The first JDC meeting shall be held within sixty (60) days after the Option Exercise Date, and the JDC shall meet in accordance with a schedule established by mutual agreement of the Parties, but, unless the Parties otherwise agree, the JDC shall meet no less frequently than once each Calendar Quarter, with the location for such meetings alternating between AVEO and Biogen Idec facilities in Massachusetts (or such other locations as determined by the JDC). Alternatively, the JDC may meet by means of teleconference, videoconference or other similar communications equipment, but at least one (1) meeting per Calendar Year shall be conducted in person.

4.4. JDC Responsibilities. The JDC shall have the following responsibilities with respect to the Development of Licensed Product during the License Term:

(i) reviewing and approving (A) the Development Plan, (B) each annual update to the Development Plan, (C) any other modifications to the Development Plan, in each case within thirty (30) days after each submission thereof to the JDC (or sooner as circumstances warrant), and (D) guidelines for conduct of Territory-Specific Clinical Trials and Post-Approval Clinical Studies;

(ii) monitoring and overseeing Development of Licensed Product in the Field in the Territory, and monitoring the Parties' respective commitments relating to shared Development Costs;

(iii) reviewing updates from AVEO regarding the Development of the Licensed Product in the Territory, and updates from Biogen Idec regarding the conduct of Territory-Specific Clinical Trials and Post Approval Clinical Studies, including, in each case a review of (a) the status of such Development efforts; (b) the results of pre-clinical and clinical studies of Licensed Product in the Field completed since the last update; (c) the design of proposed pre-clinical and clinical studies, and (d) the content of proposed regulatory filings related to Licensed Product in the Field in the Territory;

(iv) regularly assessing the progress of conduct of the Development Plan against the timelines and budgets contained therein, and reviewing relevant data, and considering issues of priority; and

(v) coordinate on issues related to Manufacture of Licensed Product for the Field in the Territory, subject to Article VII.

For purposes of clarity, it is expected that with respect to the sharing of information regarding the Licensed Product, each Party will, through the JDC and through regular communication between each Party's designated Collaboration Manager, keep the other Party informed at a detailed level about all activities related to the Development and Manufacture of the Licensed Product in the Field under this Agreement, and will provide all information requested by the other Party related to the Development and Manufacture of the Licensed Product in the Field.

The JDC shall not have the authority to modify the terms of this Agreement.

4.5. Appointment of Subcommittees, Project Teams and Collaboration Managers. The JDC shall be empowered to create such subcommittees of itself and project teams as it may deem appropriate or necessary. Each such subcommittee and project team shall report to the JDC, which shall have authority to approve or reject recommendations or actions proposed thereby subject to the terms of this Agreement. Each Party shall also designate a collaboration manager (each a "Collaboration Manager"), who shall be responsible for day-to-day coordination between the Parties and will serve to facilitate communication between the Parties with respect to Development, Manufacture and Commercialization of Licensed Product under this Agreement. Each Party may change its designated Collaboration Manager from time to time upon written notice to the other Party.

4.6. Meeting Materials and Minutes.

(a) Meeting Materials. Each Party will provide the members of the JDC with copies, which may be in electronic format, of all materials it intends to present at a JDC meeting. The JDC may also request at any time specific data or information related to Development activities or any other data to which the JDC is entitled under this Agreement or that a written report be prepared in advance of any meeting summarizing certain material data and information arising out of the conduct of the Development of Licensed Product or any other data to which the JDC is entitled under this Agreement and the Party or appropriate committee to whom such request is made shall promptly provide to the other Party or the JDC such report, data or information.

(b) Minutes. A secretary shall be appointed for each meeting and shall prepare minutes of the meeting, which such minutes shall be subject to approval by the JDC.

4.7. Decisions.

(a) Day-to-Day Management. The Parties agree that (i) decisions with respect to the day-to-day management of Development of Licensed Product in the Field in the Territory (other than the conduct of Territory-Specific Clinical Trials and Post-Approval Clinical Studies in the Licensed Territory) shall not be within the purview of the JDC, but instead shall be the sole responsibility of AVEO, and (ii) decisions with respect to the day-to-day management of Territory-Specific Clinical Trials and Post-Approval Clinical Studies in the Licensed Territory shall not be within the purview of the JDC, but instead shall be the sole responsibility of Biogen Idec, in each case provided such decisions are consistent with the Development Plan, and, subject, in each case to the restrictions contained in Section 4.8(a) and 4.8(b).

(b) JDC Decisions. During the License Term, decisions within the purview of the JDC shall be made by the JDC by consensus, with the representatives of each Party collectively having one vote on behalf of such Party. For each meeting of the JDC, at least two (2) representatives of each Party shall constitute a quorum. Action on any matter may be taken at a meeting, by teleconference, videoconference or by written agreement.

4.8. Deadlocks. The JDC shall attempt to resolve any and all disputes relating to Development of Licensed Product during the License Term by consensus. If the JDC is unable to reach a consensus with respect to a dispute within its purview related to Development of Licensed Product then the dispute shall be submitted to the Senior Representatives for review. If the Senior Representatives cannot reach an agreement regarding such dispute within thirty (30) days after submission to them for resolution, then, if the dispute is one over which the JDC has authority pursuant to this Agreement: (i) Biogen Idec shall have final-decision-making authority with respect to decisions related to Territory-Specific Clinical Trials and Post-Approval Clinical Trials required or reasonably useful in connection with Regulatory Approval or Commercialization of Licensed Product in the Licensed Territory, and (ii) AVEO shall have the final decision-making authority with respect to all other decisions related to Development, subject in each case to paragraphs (a) and (b) of this Section 4.8. Notwithstanding anything in this Agreement to the contrary, any decision within the purview of the JDC for which one of the

Parties has exercised its final decision-making authority, as set forth in this Agreement, shall be considered a decision or approval of the JDC.

(a) Limitations on Decision-Making Authority. Neither Party may exercise its final decision-making authority during the License Term: (i) to require the other Party to perform any Development activities for which it is not responsible under this Agreement or, subject to Section 5.2, to amend the Development Plan in such a way that it no longer meets the Development Plan Guidelines set forth in Exhibit B (the "Development Plan Guidelines"); (ii) to resolve any dispute as to what level of effort constitutes Commercially Reasonable Efforts; (iii) to decide to conduct, sponsor, fund or otherwise support a clinical study, including a Territory-Specific Clinical Trial or a Post-Approval Clinical Study that would materially and adversely affect the Development or Commercialization of the Licensed Product in the other Party's Territory; (iv) to decide to pursue or not to pursue the negotiation and execution of a Third Party Technology Agreement subject to, and in accordance with, Section 3.6 hereof; (v) to require a Party to take any action that would, or fail to take any action where the failure to take such action would, violate any applicable Law, rule or regulation or infringe the intellectual property rights of Third Parties; (vi) to expand or narrow the responsibilities of the JDC; (vii) to increase or change the budget for Development Costs; (viii) to establish guidelines for the conduct by Biogen Idec of any of the Development activities contemplated under Section 5.1(b) hereof or (ix) to amend this Agreement. For the avoidance of doubt, subject to Section 5.2, any decision by the JDC with respect to any of the items referred to in the foregoing clauses (i)-(viii) of this Section 4.8(a) must be unanimous and, in the event of any disagreement or deadlock at the JDC with respect to any of such items, neither Party may exercise its final decision-making authority with respect to such matter during the License Term.

(b) Other Disputes. With respect to all disputes between the Parties during the License Term related to Development or Manufacture of Licensed Product under this Agreement that are not subject to either Party's final decision-making authority as set forth in Section 4.7 or this Section 4.8, the dispute resolution provisions of Article XV shall apply.

ARTICLE V.
DEVELOPMENT DURING LICENSE TERM

5.1. Development.

(a) General. Except as set forth in paragraph (b), AVEO shall be solely responsible for Development of Licensed Product in the Field for both the Licensed Territory and the AVEO Territory during the License Term, and shall use Commercially Reasonable Efforts during the License Term to Develop Licensed Product in the Field for both the Licensed Territory and the AVEO Territory. Each Party shall use Commercially Reasonable Efforts to conduct the Development activities contemplated under the Development Plan approved by the JDC, as amended from time-to-time in accordance with Section 5.2, in accordance with the terms of such Development Plan.

(b) Territory Specific. Biogen Idec shall be solely responsible for conducting Territory-Specific Clinical Trials and Post-Approval Clinical Studies of Licensed Product in the Field where the data or other Know-how generated will have applicability only to the Licensed

Territory and, except with respect to safety data, will only be used in filings for Regulatory Approval in the Licensed Territory, and shall use Commercially Reasonable Efforts to conduct such Development activities during the License Term in accordance with guidelines for such activities established by the JDC.

5.2. Development Plan.

(a) The "Initial Development Plan" shall hereafter mean the Delivered Initial Development Plan which shall be the Development Plan unless and until amended or updated by the JDC.

(b) The JDC shall review the Development Plan not less frequently than annually and shall develop detailed and specific Development Plan updates, which shall update or include an overall Development multi-year budget for specified activities and an annual Development budget for Development of Licensed Product for the upcoming Calendar Year. The JDC's review shall continue until the completion of Licensed Product Development activities in both the Licensed Territory and the AVEO Territory. Either Party may also develop and submit to the JDC from time to time other proposed substantive amendments to the Development Plan, including, without limitation, any proposed substantive amendments to the Development Plan for purpose of Developing new Licensed Products in any indication or indications or new indications for Licensed Products already in Development or Commercialization. The JDC shall review such proposed amendments and may approve such proposed amendments or any other proposed amendments that the JDC may consider from time to time in its discretion and, upon such approval by the JDC, the Development Plan shall be amended accordingly; provided, that in all cases any such amendments are in accordance with the Development Plan Guidelines. For the sake of clarity, (x) if the JDC cannot agree on an amendment to a Development Plan, the dispute resolution mechanism set forth in Section 4.8 shall apply, and (y) if the JDC cannot agree on an upcoming Calendar Year's budget for Development Costs under any Development Plan, the budget for the upcoming Calendar Year shall be identical in amount to the amount budgeted for the relevant activities included in the last-approved multi-year budget showing the relevant activities.

5.3. Records and Information. Each Party will maintain scientific records related to its Development efforts with respect to Licensed Product in the Field, in sufficient detail and in a good scientific manner appropriate for patent and regulatory purposes, and which will fully and properly reflect all work done and results achieved in the performance of the Development activities with respect to the Licensed Product in the Field under this Agreement. During the License Term, each Party will have the right, during normal business hours and upon reasonable notice, at its own expense, to inspect and copy (or request the other Party to copy) all records of the other Party maintained in connection with the work done and results achieved in the performance of Development activities performed under this Agreement, but solely to the extent to which such records relate to Development of Licensed Product in the Field. All such records, and the information disclosed therein, as well as all disclosures made pursuant to Section 5.4, will be maintained in confidence by the Party receiving the information in accordance with Article X and will only be used for purposes permitted under Article X.

5.4. Development Costs.

(a) Cost Sharing. The Parties shall share Development Costs during the License Term as follows: (i) all Development Costs incurred by or on behalf of AVEO, Biogen Idec and their respective Affiliates with respect to Development of Licensed Product in the Field, other than those Development Costs specified in clauses (ii) and (iii) and other than Pre-Option Exercise Phase 3 Manufacturing Costs (which are covered by Section 5.4(b) below), will be shared equally by the Parties; (ii) all Development Costs incurred by or on behalf of AVEO or its Affiliates with respect to Territory-Specific Clinical Trials or Post-Approval Clinical Studies in the AVEO Territory where the data or other Know-how generated (other than safety data) will not be used in filings to support Regulatory Approval in the Licensed Territory, shall be borne one hundred percent (100%) by AVEO; and (iii) all Development Costs incurred by Biogen Idec or its Affiliates with respect to Territory-Specific Clinical Trials or Post-Approval Clinical Studies in the Licensed Territory where the data or other Know-how generated (other than safety data) will not be used in filings to support Regulatory Approval in the AVEO Territory, shall be borne one hundred percent (100%) by Biogen Idec. The Parties shall discuss and attempt to mutually determine in good faith how specific Development Costs are allocated in accordance with the foregoing sentence.

(b) Pre-Option Exercise Phase 3 Manufacturing Costs. [**] of Pre-Option Exercise Phase 3 Manufacturing Costs shall be reimbursed by Biogen Idec to AVEO as an additional payment upon delivery of the Option Exercise Fee.

5.5. Development Cost Reimbursement.

(a) Cost Reimbursement. No later than [**] prior to the end of each Calendar Quarter during the License Term, AVEO shall provide Biogen Idec with a non-binding, good-faith estimate of the Development Costs expected to be incurred by AVEO and its Affiliates during such Calendar Quarter. Within [**] after the end of each Calendar Quarter during the License Term, AVEO shall provide Biogen Idec with a reasonably detailed statement of the Development Costs actually incurred by AVEO and its Affiliates in the Calendar Quarter just ended (a "Quarterly Cost Notice"). Within [**] of Biogen Idec's receipt of a Quarterly Cost Notice, Biogen Idec shall pay to AVEO an amount equal to [**] of the total Development Costs shown for such Calendar Quarter on the Quarterly Cost Notice, except that if any such Development Costs are to be borne one hundred percent (100%) by Biogen Idec under Section 5.4 then such costs shall be identified separately in the Quarterly Cost Notice, and Biogen Idec shall pay AVEO one hundred percent (100%) of such Development Costs (the "Cost Payment"). Such statement shall include, but not be limited to, the number of individuals doing the work, the amount of time spent on the work, the nature of the work and supporting documentation for disbursements, including, to the extent requested by Biogen Idec, copies of invoices received from Third Parties. Notwithstanding anything in this Agreement to the contrary, except as set forth in paragraph (b), the total actual Development Costs incurred by AVEO or any of its Affiliates for a Calendar Year shall not exceed [**] of the budgeted Development Costs for such Calendar Year, as shown on the then current version of the Development Plan, or if no budget has been approved for such Calendar Year, on the last approved multi-year budget showing the relevant activities, except to the extent the JDC unanimously approves the increase over [**] of the budgeted Development Costs. Decisions of the JDC with respect to Development Cost

overruns shall be made in accordance with Section 4.7 and 4.8. Biogen Idec shall pay invoices received from AVEO under this paragraph within [**] of receipt.

(b) Product Liability Costs. Notwithstanding anything in this Agreement to the contrary, Biogen Idec will reimburse AVEO for its share of the Development Costs specified in clause (iv) of Section 1.34 whether or not such costs are consistent with the Development Plan or budget, provided that if any settlement amounts are to be included in Development Costs, both Parties must approve such settlement in advance.

5.6. Other Expenses. Except as expressly set forth in this Agreement, each of Biogen Idec and AVEO shall be solely responsible for its own out-of-pocket costs and disbursements incurred, and for providing the necessary facilities, supplies, personnel and other resources necessary, in the performance of its obligations under this Agreement.

5.7. Regulatory. Except as may be otherwise specified by the JDC and except with respect to Territory-Specific Clinical Trials or Post-Approval Clinical Studies conducted by or on behalf of Biogen Idec or any of its Affiliates or Sublicensees, AVEO (or its Affiliates or Sublicensees) shall be responsible for, and shall be the holder of, all INDs (including IND submissions) for Licensed Product in the Field in both the AVEO Territory and the Licensed Territory and for all Regulatory Approvals (including BLA submissions) for Licensed Product in the Field in the AVEO Territory. Except as may be otherwise specified by the JDC, after the Option Exercise Date, Biogen Idec (or its Affiliates or Sublicensees) shall be responsible for, and shall be the holder of, all INDs (including IND submissions) with respect to Territory-Specific Clinical Trials or Post-Approval Clinical Studies conducted by or on behalf of Biogen Idec or any of its Affiliates or Sublicensees, and all Regulatory Approvals (including BLA submissions) for the Licensed Product in the Field in the Licensed Territory. Following the Option Exercise Date, Biogen Idec, after an agreed-upon time (such time to be determined by the JDC), Biogen Idec shall assume responsibility for the INDs for the Licensed Territory. The Party responsible for a submission shall (i) oversee, monitor and coordinate all regulatory actions, communications and filings with each Regulatory Authority related to such submission, (ii) be responsible for interfacing, corresponding and meeting with each Regulatory Authority related to such submission, and (iii) be responsible for maintaining all regulatory filings; provided, that, the other Party shall have a right to have one or more of its employees attend, as an observer, any meetings with Regulatory Authorities for which the other Party is responsible under this Section 5.7, and to participate in major planning meetings occurring before or after any such meeting with Regulatory Authorities, and shall be provided in advance with the materials prepared for any such meeting. Notwithstanding anything in this Agreement to the contrary, each Party shall have the right to review and comment on any regulatory submission related to Licensed Product in the Field made by the other Party under this paragraph, through the JDC, and such other Party shall consider in good faith the comments made by the commenting Party. In addition, each Party shall provide the other Party, in a timely manner, with written notice and copies of: (a) all IND submissions with respect to Licensed Product; (b) all filings and submissions for Regulatory Approval regarding the Licensed Product; and (c) all Regulatory Approvals obtained or denied, with respect to Licensed Product, in each case within the Field. Except as set forth in Section 5.11 and 5.12, and subject to Section 5.13, each Party shall have access to all data contained or referenced in any regulatory submissions or applications for Regulatory Approvals with respect to Licensed Product made by the other Party, in each case as

may be reasonably necessary to enable the Party accessing such data to exercise its rights, and fulfill its obligations, under this Agreement to Develop, Manufacture and Commercialize Licensed Product. Each Party shall provide appropriate notification of such data access right of the other Party to the appropriate Regulatory Authorities. In addition, except as set forth in Section 5.11 and 5.12, and subject to Section 5.13, each Party shall have the right to cross-reference and make any other use of the other Party's INDs for Licensed Product that it would have if it were the owner, including without limitation access to all data contained or referenced in such INDs, in each case as may be reasonably necessary to enable such Party exercising such right of cross-reference to exercise its rights, and fulfill its obligations, under this Agreement to Develop, Manufacture and Commercialize Licensed Product. Notwithstanding anything in this Agreement to the contrary, the provisions of this Section 5.7 shall not apply to regulatory submissions or Regulatory Approvals for New Licensed Product or New Indication Existing Licensed Product that a Party Develops pursuant to, and in accordance with, Section 5.11 or Section 5.12, which such regulatory submissions and Regulatory Approvals shall be the sole responsibility of and solely owned by such Party.

5.8. Adverse Event and Complaint Reporting Procedures.

(a) Each Party will maintain a record of any and all complaints it or its Affiliates or Sublicensees receives with respect to Licensed Product in connection with Development or Commercialization of Licensed Product during the License Term. Each Party will notify the other Party in reasonable detail of any complaint received by it or its Affiliates or Sublicensees with respect to Licensed Product within sufficient time to allow the other Party and its Affiliates or Sublicensees to comply with any and all regulatory and other requirements imposed upon them in any jurisdiction in which Licensed Product is tested in clinical studies, including Post-Approval Studies, or being marketed or sold.

(b) AVEO will maintain a global safety database for Licensed Product. The cost of implementing and maintaining the global safety database shall be included as Development Costs, and shared equally by the Parties. Biogen Idec will have access to all data in the global safety database, subject to reasonable procedures to be mutually agreed upon by the Parties and set forth in the Drug Safety Information Exchange Agreement, as defined below. Biogen Idec will provide AVEO with all adverse event information and safety data relating to Licensed Product in its control through access to the global safety database. Biogen Idec will ensure that each of its Affiliates and Sublicensees will report to Biogen Idec or directly to AVEO the details around any adverse events and serious adverse events relating to Licensed Product in its control within the time periods for such reporting as specified in the Drug Safety Information Exchange Agreement. The holder of the relevant IND shall be responsible for submitting adverse event reports with respect to Licensed Product in the Field to applicable Regulatory Authorities; provided that, upon Regulatory Approval, Biogen Idec shall be responsible for submitting all required adverse event reports with respect to Licensed Product to the applicable Regulatory Authorities in the Licensed Territory. Biogen Idec's costs associated with submitting adverse event reports in the Licensed Territory shall be borne by Biogen Idec. Upon Regulatory Approval, AVEO shall be responsible for submitting all other required adverse event reports with respect to the Licensed Product to the applicable Regulatory Authorities in the AVEO Territory. AVEO's costs associated with submitting adverse event reports in the Licensed Territory as the IND holder during Development, to the extent applicable, shall be treated as a

Development Costs to be borne by the Parties as specified in Section 5.4. AVEO's costs associated with submitting adverse event reports with respect to the Licensed Product to the applicable Regulatory Authorities in the AVEO Territory shall be borne by AVEO.

(c) At such time as is deemed appropriate by the JDC, the Parties will develop and agree in writing on a Drug Safety Information Exchange Agreement that will include safety data exchange procedures governing the coordination of collection, investigation, reporting, and exchange of information concerning any adverse experiences, and any product quality and product complaints involving adverse experiences, related to the Licensed Product, sufficient to enable each Party to comply with its legal and regulatory obligations and consistent with the terms of this Agreement.

5.9. Recalls, Market Withdrawals or Corrective Actions. If any Regulatory Authority issues or requests a recall or takes a similar action in connection with Licensed Product, or if either Party determines that an event, incident or circumstance has occurred that may result in the need for a recall or market withdrawal, the Party notified of such recall or similar action, or the Party that desires such recall, withdrawal or similar action, shall within twenty-four (24) hours, advise the other Party thereof by telephone or facsimile. Biogen Idec, in consultation with AVEO (except in the case of a government mandated recall, when Biogen Idec may, if there is not sufficient time, act without such consultation, but shall notify AVEO as soon as possible), shall decide whether to conduct a recall or product withdrawal of Licensed Product in the Licensed Territory and the manner in which any such recall or withdrawal shall be conducted. AVEO, in consultation with Biogen Idec (except in the case of a government mandated recall, when AVEO may, if there is not sufficient time, act without such advance consultation, but shall notify Biogen Idec as soon as possible) shall decide whether to conduct a recall or product withdrawal of Licensed Product in the AVEO Territory and the manner in which any such recall or withdrawal shall be conducted. Each Party shall make available to the other Party, upon request, all pertinent records in its control that may reasonably be needed by the requesting Party in effecting a recall or withdrawal of Licensed Product.

5.10. Medical Inquiries. Upon Regulatory Approval, Biogen Idec, at its sole cost, shall handle all medical questions or inquiries from members of the medical profession in the Licensed Territory regarding Licensed Product in the Field. AVEO shall handle all medical questions or inquiries from members of the medical profession regarding the Licensed Product in the Field in the Licensed Territory prior to Regulatory Approval in the Licensed Territory. The costs of such activities shall be treated as Development Costs to be borne by the Parties as specified in Section 5.4. AVEO, at its sole cost, shall handle all medical questions or inquiries from members of the medical profession in the AVEO Territory regarding Licensed Product in the Field.

5.11. Opt-out Rights for New Products.

(a) Opt-out Process. In the event that either Party proposes an amendment, modification or update of the Development Plan for purposes of Developing a new Licensed Product for an existing or a new indication (a "New Licensed Product"), and the other Party's representatives on the JDC do not approve or consent to such amendment, modification or update, then, notwithstanding anything express or implied elsewhere in this Agreement to the

contrary, the Party that proposed the New Licensed Product (the "Funding Party") may, by written notice to the other Party given within [**] of the JDC's vote, elect to trigger the provisions of this Section 5.11 with respect to such New Licensed Product, in which case the provisions of this Section 5.11 shall become applicable to such New Licensed Product on the date such written notice is given (in each case, the "Section 5.11 Opt-out Effective Date"). From and after the Section 5.11 Opt-out Effective Date with respect to a New Licensed Product, and subject to the provisions of Section 5.11(b), (i) the Funding Party may proceed with Development and Manufacturing of such New Licensed Product in the AVEO Territory and/or the Licensed Territory at its sole cost, and such Development and Manufacturing activities with respect to such New Licensed Product shall be the responsibility and within the control of such Funding Party, (ii) the Funding Party may Develop or Manufacture such New Licensed Product through Affiliates and Sublicensees and may grant to Affiliates and Sublicensees the right to Develop or Manufacture such New Licensed Product, subject to all of the provisions of Article III, (iii) neither the non-Funding Party nor any of its Affiliates or Sublicensees shall have any rights in or to the clinical data generated after the Section 5.11 Opt-out Effective Date by the Funding Party or any of its Affiliates or Sublicensees with respect to such New Licensed Product, (iv) neither the Funding Party nor any of its Affiliates or Sublicensees may Commercialize such New Licensed Product in the non-Funding Party's Territory and (v) neither the non-Funding Party nor any of its Affiliates or Sublicensees may Commercialize such New Licensed Product in the non-Funding Party's Territory.

(b) Effect of Opt-out. For purposes of clarity the following provisions will apply with respect to any New Licensed Product from and after the Section 5.11 Opt-out Effective Date:

(i) Responsibility and control over the Development of such New Licensed Product shall be entirely in the control of the Funding Party and the JDC shall have no decision-making authority with respect to such Development, provided that the Funding Party shall keep the JDC reasonably informed of the plan for Development of the New Licensed Product, the progress of Development activities, and, subject to the other terms of this Section 5.11, the results of such Development efforts;

(ii) Neither Party shall have any obligation under Article V hereof with respect to such New Licensed Product;

(iii) Any and all clinical data related to such New Licensed Product that is generated by the Funding Party or any of its Affiliates or Sublicensees from and after the Section 5.11 Opt-out Effective Date shall be specifically excluded from the definition of AVEO Collaboration Know-how and AVEO Know-how, in the event AVEO is the Funding Party or from the definition of Biogen Idec Collaboration Know-how in the event Biogen Idec is the Funding Party;

(iv) Neither the non-Funding Party nor any of its Affiliates or Sublicensees shall have the right to access any data related to such New Licensed Product generated solely by or on behalf of the Funding Party or any of its Affiliates or Sublicensees from and after the Section 5.11 Opt-out Effective Date, including to the extent contained in any INDs, BLAs or other submissions related to such New Licensed

Product, or to include any such data, in any regulatory filings or submissions in such Party's Territory or to cross-reference or otherwise make use of or use such data, except for any adverse event data required by Law to be disclosed by the non-Funding Party or any of its Affiliates or Sublicensees;

(v) If the Funding Party is not at such time responsible for Manufacturing under Article VII, the Funding Party shall be entitled to Manufacture such New Licensed Product for its needs, and shall have the right to deal directly with any Third Party contract manufacturer of the other Party to arrange for such Third Party contract manufacturer to Manufacture and supply such New Licensed Product to such Party and its Affiliates and Sublicensees for the purposes contemplated in this Section 5.11;

(vi) The provisions of Section 8.4 shall not be applicable with respect to such New Licensed Product; and

(vii) The provisions of Article VIII (other than Section 8.4) and Article IX shall continue to be applicable with respect to such New Licensed Product.

5.12. Opt-out Rights for New Indications.

(a) Opt-out Process. In the event that either Party proposes an amendment, modification or update of the Development Plan for purposes of Developing an existing Licensed Product in a new indication (a "New Indication Existing Licensed Product") and such new indication is commercially viable in the AVEO Territory and EU (a "Commercially Viable Indication"), and the other Party's representatives on the JDC do not approve or consent to such amendment, modification or update, then, notwithstanding anything express or implied elsewhere in this Agreement to the contrary, the Party that proposed such new indication (the "New Indication Funding Party") may, by written notice to the other Party, given within [**] of the JDC's vote, elect to trigger the provisions of this Section 5.12 with respect to such New Indication Existing Licensed Product, in which case the provisions of this Section 5.12 shall become applicable to such New Indication Existing Licensed Product on the date such written notice is given (in each case, the "Section 5.12 Opt-out Effective Date"). From and after the Section 5.12 Opt-out Effective Date with respect to a New Indication Existing Licensed Product, and subject to the provisions of Section 5.12(b) and Section 5.13 below, (i) the New Indication Funding Party may proceed with Development and Manufacturing of such New Indication Existing Licensed Product in the AVEO Territory and/or the Licensed Territory at its sole cost, and such Development and Manufacturing activities with respect to such New Indication Existing Licensed Product shall be the responsibility and within the control of the New Indication Funding Party, (ii) the New Indication Funding Party may Develop or Manufacture such New Indication Existing Licensed Product through Affiliates and Sublicensees and may grant to Affiliates and Sublicensees the right to Develop or Manufacture such New Indication Existing Licensed Product, subject to all of the provisions of Article III, (iii) the non-New Indication Funding Party and its Affiliates and Sublicensees shall not have any rights in or to the clinical data generated after the Section 5.12 Opt-out Effective Date by the New Indication Funding Party or any of its Affiliates or Sublicensees with respect to such New Indication Existing Licensed Product, other than safety data; (iv) neither the New Indication Funding Party

nor any of its Affiliates or Sublicensees may Commercialize such New Indication Existing Licensed Product in the other Party's Territory; and (v) neither the non-New Indication Funding Party nor any of its Affiliates or Sublicensees may Commercialize such New Indication Existing Licensed Product in the non-New Indication Funding Party's Territory.

(b) Effect of Opt-out. For purposes of clarity, and subject to Section 5.13 below, the following provisions will apply with respect to any New Indication Existing Licensed Product from and after the Section 5.12 Opt-out Effective Date:

(i) Responsibility and control over the Development of such New Indication Existing Licensed Product shall be entirely in the control of the New Indication Funding Party and the JDC shall have no decision-making authority with respect to such Development, provided that the New Indication Funding Party shall keep the JDC reasonably informed of the plan for Development of the New Indication Existing Licensed Product, the progress of Development activities, and, subject to the other terms of this Section 5.12, the results of such Development efforts;

(ii) Neither Party shall have any obligation under Article V hereof with respect to such New Indication Existing Licensed Product except under Sections 5.8 and 5.9;

(iii) Any and all clinical data related to such New Indication Existing Licensed Product that is generated by the New Indication Funding Party or any of its Affiliates or Sublicensees from and after the Section 5.12 Opt-out Effective Date shall be specifically excluded from the definition of AVEO Collaboration Know-how or AVEO Know-how, in the event AVEO is the New Indication Funding Party, and from the definition of Biogen Idec Collaboration Know-how in the event Biogen Idec is the New Indication Funding Party, subject, in each case, to Section 5.8;

(iv) Neither the non-New Indication Funding Party nor any of its Affiliates or Sublicensees shall have the right to access any data related to such New Indication Existing Licensed Product generated solely by or on behalf of the New Indication Funding Party or any of its Affiliates or Sublicensees from and after the Section 5.12 Opt-out Effective Date, including to the extent contained in any INDs, BLAs or other submissions related to such New Indication Existing Licensed Product, or to include any such data, in any regulatory filings or submissions in such Party's Territory or to cross-reference or otherwise make use of or use such data;

(v) If the New Indication Funding Party is not, at such time, responsible for Manufacturing the applicable Licensed Product under Article VII, at the request of the New Indication Funding Party, the other Party shall Manufacture and supply, or cause to be Manufactured and supplied, the reasonable requirements of the New Indication Funding Party and its Affiliates and Sublicensees for such New Indication Existing Licensed Product pursuant to, and in accordance with, the provisions of Article VII;

(vi) The provisions of Section 8.4 shall not be applicable with respect to such New Indication Existing Licensed Product; and

(vii) The provisions of Article VIII (other than Section 8.4) and Article IX shall continue to be applicable with respect to such New Indication Existing Licensed Product.

5.13. Opt-in.

(a) Opt-in. Following a Section 5.12 Opt-out Effective Date with respect to a New Indication Existing Licensed Product, in the event that (i) the New Indication Funding Party receives Regulatory Approval to Commercialize such New Indication Existing Licensed Product in such Commercially Viable Indication in the New Indication Funding Party's Territory (such new indication being hereinafter referred to as the "Opt-in Indication"), and (ii) the pivotal trial(s) with respect to such New Indication Existing Licensed Product for which Regulatory Approval was received were initially designed to support Regulatory Approval in both the AVEO Territory and the Licensed Territory (and the Regulatory Approval was received from the FDA (in the case that AVEO was the New Indication Funding Party) or either (A) EMEA or (B) the applicable Regulatory Authority in any one of Germany, France, Spain, Italy or the United Kingdom (in the case that Biogen Idec was the New Indication Funding Party)), then the New Indication Funding Party shall give written notice (in each case, the "Opt-in Notice") to the other Party that the New Indication Funding Party has received a Regulatory Approval to Commercialize such New Indication Existing Licensed Product in such Opt-in Indication in the New Indication Funding Party's Territory under this Agreement, in which case the provisions of this Section 5.13 shall become applicable to such New Indication Existing Licensed Product with respect to such Opt-in Indication (in each case, an "Opt-in New Indication Existing Licensed Product") on the date such written notice is given (in each case, the "Opt-in Notice Date"). From and after the Opt-in Notice Date with respect to an Opt-in New Indication Existing Licensed Product, and subject to the provisions of Section 5.13(b), the non-New Indication Funding Party (the "Opt-in Party") shall be required to make a cash payment to the New Indication Funding Party, within [**] of the Opt-in Notice Date, equal to one hundred percent (100%) of the aggregate Development Costs incurred by the New Indication Funding Party from and after the Section 5.12 Opt-out Effective Date to the date of the Regulatory Approval that was the subject of the Opt-in Notice to the extent such Development Costs are specific to such Opt-in New Indication Existing Licensed Product and would have been shared equally under Section 5.4 if the Opt-in Party had not opted out under Section 5.12 (the "Opt-in Payment"). "Development Costs" for purposes of this paragraph shall mean the category of costs set forth in Section 1.34, but without the requirement that such costs be set forth in a Development Plan approved by the JDC, and provided such Development Costs shall be subject to the auditing provisions of Section 8.16(b) to the same extent as applicable to Development Costs incurred by AVEO under this Agreement. Commencing upon the date of full payment of the Opt-in Payment(the "Opt-in Effective Date"), the Opt-in Party and its Affiliates and Sublicensees shall have rights in or to the clinical data generated after the Section 5.12 Opt-out Effective Date by the New Indication Funding Party or any of its Affiliates or Sublicensees with respect to such Opt-in New Indication Existing Licensed Product for purposes of seeking and obtaining Regulatory Approval of such Opt-in New Indication Existing Licensed Product in the Opt-in Party's Territory under this Agreement, and for all purposes of this Agreement shall be treated as though the Opt-in Party

had not triggered its rights under Section 5.12(a) hereof in the first place with respect to such Opt-in New Indication Existing Licensed Product in such Opt-in Indication.

(b) Effect of Opt-in. For purposes of clarity the following provisions will apply with respect to any Opt-in New Indication Existing Licensed Product from and after the Opt-in Effective Date:

(i) Responsibility and control over the Development and Regulatory Approval of such Opt-in New Indication Existing Licensed Product in the Opt-in Party's Territory under this Agreement shall be entirely in the control of the Opt-in Party and the JDC shall have no decision-making authority with respect to such Development and Regulatory Approval, provided that the Opt-in Party shall keep the JDC reasonably informed of the plan for Development and Regulatory Approval of the Opt-in New Indication Existing Licensed Product, the progress of Development activities, and, subject to the other terms of this Section 5.13, the results of such Development efforts;

(ii) Neither Party shall have any obligation under Article V hereof with respect to such Opt-in New Indication Existing Licensed Product other than under Section 5.8 and 5.9;

(iii) If Biogen Idec is the Opt-in Party, any and all clinical data related to such Opt-in New Indication Existing Licensed Product that was generated by AVEO or any of its Affiliates or Sublicensees from and after the Section 5.12 Opt-out Effective Date with respect to such Opt-in New Indication Existing Licensed Product shall be specifically included in the definition of AVEO Collaboration Know-how or AVEO Know-how;

(iv) If AVEO is the Opt-in Party, any and all clinical data related to such Opt-in New Indication Existing Licensed Product that was generated by Biogen Idec or any of its Affiliates or Sublicensees from and after the Section 5.12 Opt-out Effective Date with respect to such Opt-in New Indication Existing Licensed Product shall be specifically included in the definition of Biogen Idec Collaboration Know-how;

(v) The Opt-in Party and its Affiliates and Sublicensees shall have the right to access any data related to such Opt-in New Indication Existing Licensed Product generated by or on behalf of the other Party or any of its Affiliates or Sublicensees from and after the Section 5.12 Opt-out Effective Date with respect to such Opt-in New Indication Existing License Product, including to the extent contained in any INDs, BLAs or other submissions related to such Opt-in New Indication Existing Licensed Product, or to include any such data, in any regulatory filings or submissions in the Opt-in Party's Territory or to cross-reference or otherwise make use of or use such data;

(vi) At the request of the Opt-in Party if the other Party is at such time responsible for Manufacturing under Article VII, such other Party shall Manufacture and supply, or cause to be Manufactured and supplied, the reasonable requirements of the Opt-in Party and its Affiliates and Sublicensees for such Opt-in New Indication Existing Licensed Product pursuant to, and in accordance with, the provisions of Article VII;

(vii) If Biogen Idec is the Opt-in Party, the provisions of Section 8.4 shall be applicable with respect to such Opt-in New Indication Existing Licensed Product; and

(viii) The provisions of Article VIII and Article IX shall continue to be applicable with respect to such Opt-in New Indication Existing Licensed Product.

ARTICLE VI.
COMMERCIALIZATION DURING LICENSE TERM

6.1. General. Biogen Idec shall be solely responsible for all Commercialization activities relating to the Licensed Product in the Field in the Licensed Territory during the License Term, and shall use Commercially Reasonable Efforts to Commercialize Licensed Products in those countries in the Licensed Territory in which Regulatory Approval has been obtained, including by providing appropriate incentives consistent with its normal business practices to Sales Representatives involved in the Commercialization of the Licensed Product in the Licensed Territory. AVEO shall be solely responsible for all Commercialization activities relating to the Licensed Product in the Field in the AVEO Territory and shall use Commercially Reasonable Efforts to Commercialize Licensed Products in those countries in the AVEO Territory in which Regulatory Approval has been obtained, including by providing appropriate incentives consistent with its normal business practices to Sales Representatives involved in the Commercialization of the Licensed Product in the AVEO Territory.

6.2. Joint Commercialization Team.

(a) Formation. Commencing with the initiation of the first Phase 3 Clinical Study of the Licensed Product in the Territory, the Parties shall establish a joint commercialization team ("JCT") to serve as a forum to discuss Commercialization of the Licensed Product in the Field in the Parties' respective Territory. The JCT shall consist of three (3) representatives designated by each Party, or such other number as the Parties may from time to time mutually agree. Each Party shall appoint its initial representatives on the JCT at the time of formation, but may, from time to time, substitute one or more of its representatives, in its sole discretion, effective upon notice to the other Party of such change. Each Party shall have at least one JCT representative who is a senior employee (vice president level or above), and all JCT representatives shall have appropriate expertise and ongoing familiarity with Commercialization of biopharmaceutical products. Additional representatives or consultants may from time to time, by mutual consent of the Parties, be invited to attend JCT meetings, provided such representatives and consultants are subject to written obligations that are no less stringent than the confidentiality obligations and restrictions on use set forth in Article X. Each Party shall bear its own expenses relating to attendance at JCT meetings by its representatives.

(b) Chairperson. The chairperson of the JCT (the "JCT Chairperson") shall alternate at one-year intervals between a representative of AVEO and a representative of Biogen Idec, with the initial JCT Chairperson being a representative of AVEO. The JCT Chairperson's responsibilities shall include (i) scheduling meetings at such frequency as described in paragraph (c) or as the JCT otherwise determines is necessary; (ii) setting agendas for meetings with

solicited input from other members; and (iii) confirming and delivering minutes to the JCT for review and final approval.

(c) Meetings. The JCT shall meet in accordance with a schedule established by mutual agreement of the Parties, but, unless the Parties otherwise agree, the JCT shall meet no less frequently than once each Calendar Year, with the location for such meetings alternating between AVEO and Biogen Idec facilities in Massachusetts (or such other locations as are determined by the JCT). Alternatively, the JCT may meet by means of teleconference, videoconference or other similar communications equipment.

(d) Responsibilities. The responsibilities of the JCT include:

(i) discussing global branding and positioning and publications strategy of Licensed Product in the Territory;

(ii) receiving updates from each Party regarding the Commercialization of the Licensed Product in the Territory;

(iii) coordinating with the JDC regarding Development matters as necessary or appropriate with respect to Commercialization of Licensed Product in the Territory; and

(iv) to the extent consistent with Article VII, coordinating Manufacturing activities related to the Commercialization of the Licensed Product in the Territory.

(e) Decision-Making. Notwithstanding anything in this Agreement to the contrary the JCT shall have no decision-making authority. Biogen Idec shall have sole decision-making authority with respect to Commercialization of Licensed Product in the Field in the Licensed Territory, and AVEO shall have sole decision-making authority with respect to Commercialization of Licensed Product in the Field in the AVEO Territory.

6.3. Commercialization Costs. The costs of Commercialization activities in the Licensed Territory shall be borne one hundred percent (100%) by Biogen Idec. The costs of Commercialization activities in the AVEO Territory shall be borne one hundred percent (100%) by AVEO.

6.4. Advertising and Promotional Materials. Biogen Idec will be responsible for the creation, preparation, production, reproduction and filing with the applicable Regulatory Authorities, of relevant written sales, promotion and advertising materials relating to the Licensed Product ("Promotional Materials") for use in the Licensed Territory, and AVEO will responsible for the creation, preparation, production, reproduction and filing with the applicable Regulatory Authorities, of all Promotional Materials in the AVEO Territory. All such Promotional Materials will be compliant with all applicable Laws. Subject to any limitations imposed by applicable Law, all such Promotional Materials and all documentary information and oral presentations (where practicable) regarding the marketing and promotion of the Licensed Product in the Field in the Licensed Territory shall acknowledge the Parties' license arrangement with respect to the Licensed Product. Copies of all Promotional Materials used in the Licensed

Territory will be archived by Biogen Idec in accordance with applicable Law. Copies of all Promotional Materials used in the AVEO Territory will be archived by AVEO in accordance with applicable Law. Upon AVEO's reasonable request, copies of the core Promotional Materials used by Biogen Idec in the Licensed Territory shall be translated into English (where applicable) and provided to AVEO. Upon Biogen Idec's reasonable request, copies of core Promotional Materials for Licensed Product used by AVEO or any of its Affiliates or Sublicensees in the Field in the AVEO Territory shall be provided in English to Biogen Idec.

6.5. Sales and Distribution. Biogen Idec shall be responsible for booking sales and shall warehouse and distribute the Licensed Product in the Licensed Territory. AVEO shall be responsible for booking sales and shall warehouse and distribute Licensed Product in the AVEO Territory. If Biogen Idec or any of its Affiliates or Sublicensees receive any orders for Licensed Product in the Field for the AVEO Territory, they shall refer such orders to AVEO. If AVEO or any of its Affiliates or Sublicensees receive any orders for Licensed Product in the Field in the Licensed Territory, they shall refer such orders to Biogen Idec.

6.6. Reporting. Commencing upon the first Regulatory Approval of Licensed Product in the Field in the applicable Territory, each Party shall prepare and deliver to the JCT, by no later than each March 31 (for the period ending December 31 of the prior Calendar Year), a written report summarizing such Party's Commercialization activities for the Licensed Product in the Field performed to date (or updating such report for activities performed since the last such report submitted hereunder, as applicable).

6.7. Other Responsibilities. Without intending to limit in any way Biogen Idec's overall responsibility for Commercialization of Licensed Product in the Field in the Licensed Territory during the License Term and AVEO's responsibility for Commercialization of Licensed Product in the AVEO Territory during the License Term, the Parties agree that Biogen Idec shall be solely responsible for the following functions in the Licensed Territory and AVEO shall be solely responsible for the following functions in the AVEO Territory during the License Term:

(i) handling all returns of the Licensed Product; and

(ii) handling all aspects of Licensed Product order processing, invoicing and collection, distribution, inventory and receivables.

6.8. Export Monitoring. Biogen Idec and its Affiliates and Sublicensees will use Commercially Reasonable Efforts to monitor and prevent exports of the Licensed Product from the Licensed Territory to the AVEO Territory, using methods commonly used in the industry for such purpose, and shall promptly inform AVEO of any such exports of the Licensed Product from the Licensed Territory to the AVEO Territory, and the actions taken to prevent such exports. Biogen Idec agrees to take any actions reasonably requested in writing by AVEO that are consistent with applicable Law and regulation to prevent exports of the Licensed Product from the Licensed Territory to the AVEO Territory. Biogen Idec shall ensure that it has in effect provisions with those of its Affiliates or Sublicensees who are Commercializing Licensed Products in the Licensed Territory that require such Affiliates and Sublicensees to use efforts consistent with those required of Biogen Idec in this Section 6.8. AVEO and its Affiliates and

Sublicensees will use Commercially Reasonable Efforts to monitor and prevent exports of the Licensed Product from the AVEO Territory to the Licensed Territory, using methods commonly used in the industry for such purpose, and shall promptly inform Biogen Idec of any such exports of the Licensed Product from the AVEO Territory to the Licensed Territory, and the actions taken to prevent such exports. AVEO agrees to take any actions reasonably requested in writing by Biogen Idec that are consistent with applicable Law and regulation to prevent exports of the Licensed Product from the AVEO Territory to the Licensed Territory. AVEO shall ensure that it has in effect provisions with those of its Affiliates or Sublicensees who are Commercializing Licensed Products in the AVEO Territory that require such Affiliates and Sublicensees to use efforts consistent with those required of AVEO in this Section 6.8.

ARTICLE VII.
MANUFACTURE

7.1. Development Supply. Subject to the provisions set forth below in this Section 7.1 and Sections 7.3, 7.5 and 7.6 hereof, AVEO, itself or through an Affiliate or Third Party contractor, shall have the sole right to, and shall be solely responsible for, the Manufacture of supplies of Licensed Product required for all Development of Licensed Product by AVEO, Biogen Idec and their respective Affiliates and Sublicensees in the AVEO Territory and the Licensed Territory pursuant to this Agreement. AVEO shall use Commercially Reasonable Efforts to meet its Manufacturing obligations under this Section 7.1. Subject to the provisions set forth below in Sections 7.3, 7.5 and 7.6 hereof, at the written request of Biogen Idec, which request may be made at any time and from time to time after the Option Exercise Date and shall in any event be made by Biogen Idec with sufficient advance notice to be commercially reasonable (or with such other period of advance notice as the Parties may otherwise agree), AVEO, itself or through an Affiliate or Third Party contractor, shall use Commercially Reasonable Efforts to Manufacture and supply Licensed Product to Biogen Idec and its Affiliates and Sublicensees in sufficient quantities to satisfy their respective reasonable requirements for use thereof in Development activities of Licensed Product pursuant to this Agreement.

7.2. Commercial Supply. Subject to the provisions set forth below in this Section 7.2 and Sections 7.4, 7.5, 7.6 and 7.7 hereof, AVEO, itself or through an Affiliate, shall have the sole right to, and shall be solely responsible for, the Manufacture of supplies of Licensed Product required for all Commercialization of Licensed Product by AVEO, Biogen Idec and their respective Affiliates and Sublicensees in the AVEO Territory and the Licensed Territory pursuant to this Agreement. AVEO shall use Commercially Reasonable Efforts to meet its Manufacturing obligations under this Section 7.2. In the event that AVEO elects not to exercise its right under this Section 7.2 to Manufacture itself or through an Affiliate and determines to Manufacture supplies of Licensed Product through a Third Party contractor, AVEO shall provide prompt written notice to Biogen Idec of its determination (which notice shall be given not later than [**] prior to the target date of commencement of the first Phase 3 Clinical Trial with respect to any Licensed Product (or with such other period of advance notice as the Parties may otherwise agree) (a "Contract Manufacturer Notice"). Subject to the provisions set forth below in 7.4, 7.5, 7.6 and 7.7 hereof, at the written request of Biogen Idec, which request may be made at any time and from time to time commencing upon the initiation of the first Phase 3 Clinical Trial with respect to any Licensed Product (or with such other period of advance notice as the Parties may otherwise agree), AVEO, itself or through an Affiliate or Third Party contractor,

shall use Commercially Reasonable Efforts to Manufacture and supply Licensed Product to Biogen Idec and its Affiliates and Sublicensees in sufficient quantities to satisfy their respective reasonable requirements for use thereof in Commercialization of such Licensed Product in the Field in the Licensed Territory.

7.3. Manufacturing Costs for Development. The Cost of Goods Sold of Licensed Product Manufactured pursuant to Section 7.1 hereof shall be included as Development Costs and shall be borne by the Parties as set forth in Section 5.4 hereof. Except as set forth in the preceding sentence and except for Pre-Option Exercise Phase 3 Manufacturing Costs, Biogen Idec and its Affiliates and Sublicensees shall otherwise have no responsibility or obligation to pay or reimburse AVEO for quantities of Licensed Product Manufactured by or on behalf of AVEO pursuant to Section 7.1 hereof.

7.4. Transfer Price for Commercial Supply. The purchase price payable by Biogen Idec and its Affiliates and Sublicensees for quantities of Licensed Product Manufactured and supplied by or on behalf of AVEO pursuant to Section 7.2 hereof shall be equal to the Cost of Goods Sold applicable to such quantities of Licensed Product.

7.5. Biogen Idec Right to Become Sole Phase 3 and Commercial Supplier. Notwithstanding the provisions of Section 7.1 or 7.2 above and subject to the provisions of this Section 7.5 and Sections 5.11, 7.6 and 7.7, Biogen Idec shall have the option to become the sole manufacturer and supplier of all quantities of any Licensed Product required for all Phase 3 Clinical Trials with respect to any Licensed Product and Commercialization of such Licensed Product by AVEO, Biogen Idec and their respective Affiliates and Sublicensees in the AVEO Territory and the Licensed Territory pursuant to this Agreement. Biogen Idec may exercise such option with respect to any Licensed Product by (i) giving written notice of exercise to AVEO no later than [**] after receipt by Biogen Idec of the Contract Manufacturer Notice and (ii) executing a Supply Agreement with AVEO in accordance with Section 7.7, including the timelines set forth in such Section, in which case Biogen Idec shall become the sole manufacturer and supplier of such Licensed Product required for Phase 3 Clinical Trials and commercial quantities of such Licensed Product, provided, that, unless AVEO agrees otherwise, Biogen Idec may not exercise its option to become the sole manufacturer if, (i) at the time Biogen Idec gives such written notice of exercise, AVEO is utilizing or planning to utilize a Third Party contract manufacturer as the commercial manufacturer and supplier of such Licensed Product and (ii) the per unit price of such Licensed Product quoted by Biogen Idec is higher than [**] of the lowest quote submitted by any Third Party contract manufacturer that, at the time of submitting such quote, has capacity in an FDA-approved manufacturing facility adequate for the manufacture of such Licensed Product. In the event that, pursuant to the foregoing provisions of this Section 7.5, Biogen Idec becomes the sole commercial manufacturer and supplier of any Licensed Product, then the provisions of Sections 7.1, 7.2, 7.3 and 7.4 shall thereafter apply to Biogen Idec with respect to such Licensed Product to the same extent that they previously applied to AVEO and the rights of Biogen Idec in Sections 7.1, 7.2, 7.3 and 7.4 shall thereafter apply to AVEO with respect to such Licensed Product to the same extent they previously applied to Biogen Idec. Notwithstanding anything in this Agreement, unless the Supply Agreement otherwise specifies, in the event Biogen Idec becomes the Party responsible for Manufacturing any Licensed Product pursuant to the terms of this Section 7.5 during the Option Exercise Period, but elects not the exercise the Option, Biogen Idec shall have the right to terminate its

supply obligation under this Section effective eighteen (18) months following written notice of such termination, given after such election, having been provided to AVEO, or such lesser amount of time as AVEO may specify in writing to Biogen Idec. In such event, Biogen Idec shall engage in a technology transfer process, at Biogen Idec's cost, for the purpose of enabling AVEO or a Third Party contract manufacturer designated by AVEO to Manufacture Licensed Product by or on behalf of AVEO and its Affiliates and Sublicensees.

7.6. Back-Up Supply Rights. In the event that, at any time during the period in which either Party has an obligation to Manufacture and supply Licensed Product pursuant to Section 7.1 or Section 7.2 hereof, such Party (the "Non-performing Manufacturing Party") is unable to Manufacture and supply sufficient quantities of such Licensed Product pursuant to Section 7.1 and/or Section 7.2, as the case may be, to meet the requirements therefor of the other Party and its Affiliates and Sublicensees as indicated in any good faith forecasts to be provided pursuant to the Supply Agreement or Section 7.1 and/or Section 7.2, as the case may be, then such other Party shall have the right (but not the obligation) to Manufacture or have Manufactured such Licensed Product and thereafter to satisfy all of the requirements of such other Party and its Affiliates and Sublicensees for quantities of such Licensed Product, except if and to the extent otherwise provided in the Supply Agreement. Such other Party may exercise its rights under this Section 7.6 with respect to any Licensed Product by giving thirty (30) days prior written notice to the Non-performing Manufacturing Party. Upon receipt by the Non-performing Manufacturing Party of written notice from the other Party to the effect that such other Party is exercising its rights under this Section 7.6, the Non-performing Manufacturing Party shall provide reasonable assistance, at its sole cost and expense, to enable such other Party to Manufacture or have Manufactured and supplied such Licensed Product. Such assistance shall include, without limitation, (i) engaging in any technology transfer process required in order to enable such other Party or any Third Party contract manufacturer engaged by such other Party to Manufacture such Licensed Product and/or (ii) introducing such other Party to any Third Party contract manufacturers utilized by the Non-performing Manufacturing Party and working with such other Party and such Third Party contract manufacturers and taking such actions as may be reasonably required in order to enable such other Party to obtain supply of such Licensed Product from such Third Party contract manufacturers. The Parties hereby acknowledge and agree that the Supply Agreement may provide for back-up supply rights that are different than those set forth in this Section 7.6 and to the extent of any conflict between any provisions of the Supply Agreement with respect to back-up supply rights and the provisions of this Section 7.6, the provisions of the Supply Agreement with respect to back-up supply rights shall control.

7.7. Supply Agreement. Prior to the initiation of the first Phase 3 Clinical Trial with respect to any Licensed Product, the Parties shall negotiate in good faith and enter into a supply agreement pursuant to which AVEO, itself or through an Affiliate or Third Party contractor, will Manufacture and supply to Biogen Idec and its Affiliates and Sublicensees such Licensed Product as required under Section 7.1 or 7.2 hereof, unless the Parties, as contemplated under Section 7.5 hereof, shall have agreed that Biogen Idec will be the manufacturer of such Licensed Product, in which case (i) such supply agreement must be entered into at least [**] prior to commencement of the first Phase 3 Clinical Trial, and (ii) such supply agreement will provide that Biogen Idec, itself or through an Affiliate or Third Party contractor, will Manufacture and supply to AVEO and its Affiliates and Sublicensees such Licensed Product as required under Sections 7.1, 7.2 and 7.5 hereof. Such supply agreement shall include the applicable terms set

forth in Sections 7.1, 7.2, 7.4 and 7.6 and shall contain such other provisions as the Parties mutually agree upon that are customary for supply agreements of this type. Pending the execution and delivery of such supply agreement, each of the Parties shall perform their respective obligations under this Article VII in accordance with its terms. Any supply agreement that is entered into by the Parties pursuant to this Section 7.7 is referred to in this Agreement as the "Supply Agreement."

ARTICLE VIII.
FINANCIAL PROVISIONS

8.1. Initial Fee. Within five (5) Business Days after the Effective Date, Biogen Idec shall pay to AVEO a non-creditable, non-refundable up-front option fee of five million U.S. dollars ($5,000,000).

8.2. Equity Purchase. Concurrent with the execution of this Agreement, Biogen Idec shall purchase thirty million U.S. dollars ($30,000,000) of AVEO's Series E Convertible Preferred Stock, $.001 par value per share, at a purchase price of $4.00 per share, pursuant to, and in accordance with the terms of, the form of Stock Purchase Agreement attached to this Agreement as Exhibit C.

8.3. Payments by Biogen Idec During Option Exercise Period. Subject to the terms and conditions of this Agreement, Biogen Idec shall pay AVEO a milestone payment (each, a "Pre-Exercise Milestone Payment") upon occurrence of each of the following events (each, a "Pre-Exercise Milestone"), on a one-time basis, in the particular amounts specified below, no later than [**] after written notice from AVEO of the occurrence of the applicable Pre-Exercise Milestone (which notice shall be accompanied by supporting documentation and information as is reasonably necessary and appropriate to demonstrate completion of the applicable Pre-Exercise Milestone:

(a) Panel Identification. Upon Panel Identification, Biogen Idec shall pay to AVEO five million U.S. dollars ($5,000,000). "Panel Identification" shall mean the first identification and in vitro and biochemical characterization of a panel of erbB3-specific murine antibodies.

(b) [**]. Upon [**], Biogen Idec shall pay to AVEO [**] U.S. dollars ($[**]). "[**]" shall mean [**] under this Agreement.

(c) [**]. Upon [**], Biogen Idec shall pay to AVEO [**] U.S. dollars ($[**]). "[**]" shall mean [**].

(d) Option Exercise Fee. In the event Biogen Idec elects to exercise the Option, it shall pay to AVEO a non-creditable, non-refundable option exercise fee of five million U.S. dollars ($5,000,000) (the "Option Exercise Fee") on or before the end of the Option Exercise Period.

(e) One Payment. Each of the Pre-Exercise Milestone Payments shall be payable only once during the Agreement Term (and for the avoidance of doubt, shall not be

payable on a Licensed Product-by-Licensed Product basis) irrespective of how many times any of the events specified herein may occur.

8.4. Milestones Payments by Biogen Idec After Exercise of Option. Subject to the terms and conditions of this Agreement, and only following exercise (if any) of the Option, Biogen Idec shall pay AVEO a milestone payment (each, an "Event Milestone Payment") upon occurrence of each of the following events (each, an "Event Milestone"), on a Licensed Product-by-Licensed Product basis, in the particular amounts specified below, no later than [**] after the occurrence of the Event Milestone:

Event Milestone	Event Milestone Payment
Receipt of the first Regulatory Approval of a Licensed Product from the EMEA	$25,000,000
[**]	$[**]

Each Event Milestone Payments shall be payable only once per Licensed Product, upon the first occurrence of the applicable Event Milestone with respect to such Licensed Product, regardless of the number of indications for which [**] is ultimately achieved.

8.5. Royalty Payments by Biogen Idec. Subject to the provisions of Section 8.8 and subject also to the adjustment, if any, to be made under Section 8.9(d), following exercise (if any) of the Option, Biogen Idec shall pay to AVEO royalties on Net Sales of Licensed Product in the Field by Biogen Idec and its Affiliates and Sublicensees in the Licensed Territory, as follows:

Net Sales Per Licensed Product	Royalty Percentage
On that portion of annual Net Sales Per Licensed Product less than or equal to $[**]	[**]%
On that portion of annual Net Sales Per Licensed Product greater than $[**] but less than or equal to $[**]	[**]%
On that portion of annual Net Sales Per Licensed Product greater than $[**]	[**]%

8.6. Royalty Payments by AVEO. Subject to the provisions of Section 8.8 and subject also to the adjustment, if any, to be made under Section 8.9(d), following exercise (if any) of the Option, AVEO shall pay to Biogen Idec royalties on Net Sales by AVEO and its Affiliates and Sublicensees of Licensed Product in the Field in the AVEO Territory, as follows:

Net Sales Per Licensed Product	Royalty Percentages
On that portion of annual Net Sales Per Licensed Product less than or equal to $[**]	[**]%

On that portion of annual Net Sales Per Licensed Product greater than $[**] but less than or equal to $[**]	[**]%
On that portion of annual Net Sales Per Licensed Product greater than $[**]	[**]%

8.7. Restriction on Bundling. If a Party or its Affiliates or Sublicensees sell Licensed Product to a Third Party who also purchases other products or services from such Party or its Affiliates, such Party shall not, and shall require its Affiliates and Sublicensees not to, (i) bundle or include any Licensed Product as part of any incentive programs, chargebacks, disease management programs or similar programs based on multiple product offerings or (ii) discount or price the Licensed Product, in the case of either of the foregoing clauses (i) or (ii), such that the applicable rebate, discount, other form of reimbursement for, or the price of, the Licensed Product in such arrangement is inconsistent with the rebate, discount, or other form of reimbursement for, or price of, the Licensed Product when sold separately to such Person from any such other products or services sold to such Person.

8.8. Royalty Term. On a country-by-country and Licensed Product-by-Licensed Product basis, royalties shall be payable under Section 8.5 or 8.6, as the case may be, during the period commencing on the first sale of such Licensed Product in the Field in such country for any purpose and ending upon the later of (a) the date of expiration, unenforceability or invalidation of the last Valid Claim of AVEO Patent Rights or Collaboration Patent Rights Covering Licensed Product in such country, or (b) expiration of Data Exclusivity in such country (the "Royalty Term"). The royalties payable with respect to Net Sales of a Licensed Product shall be reduced, on a country-by-country and Licensed Product-by-Licensed Product basis, to [**] of the amounts otherwise payable pursuant to Section 8.5 or 8.6, as the case may be, during any portion of the Royalty Term when there is no Valid Claim of an AVEO Patent Right or Collaboration Patent Right Covering such Licensed Product in such country. Upon expiration of the Royalty Term applicable to a Party in a particular country with respect to a particular Licensed Product, the license granted to such Party under Article III with respect to such Licensed Product shall convert to a fully paid-up, non-royalty-bearing license in the applicable country.

8.9. Third Party Licenses.

(a) Existing Third Party Licenses. As of the Effective Date, there are no AVEO In-Licenses except as set forth in Exhibit D, and there are no Biogen Idec In-Licenses.

(b) For Licensed Territory. Subject to Section 8.9(d), Biogen Idec shall bear [**] of any royalties, upfront fees, milestones and other payments under AVEO In-Licenses or Biogen Idec In-Licenses to the extent reasonably allocable to the Commercialization (or Development and Manufacturing in support of Commercialization) of a Licensed Product in the Field in the Licensed Territory. Any such amounts shall be paid by Biogen Idec or paid by AVEO and reimbursed by Biogen Idec; provided that if such amounts are paid by AVEO, AVEO shall invoice Biogen Idec for the amounts identified on a Calendar Quarter basis, and Biogen Idec shall pay such invoices within thirty (30) days after receipt of AVEO's invoice.

(c) For AVEO Territory. Subject to Section 8.9(d), AVEO shall bear [**] of any royalties, upfront fees, milestones and other payments under AVEO In-Licenses and Biogen

Idec In-Licenses to the extent reasonably allocable to the Commercialization (or Development and Manufacturing in support of Commercialization) of a Licensed Product in the Field in the AVEO Territory. Any such amounts shall be paid by AVEO or Biogen Idec and reimbursed by AVEO; provided that if such amounts are paid by Biogen Idec, Biogen Idec shall invoice AVEO for the amounts identified on a Calendar Quarter basis, and AVEO shall pay such invoices within thirty (30) days after receipt of Biogen Idec's invoice.

(d) Reduction. Royalties payable by Biogen Idec to AVEO pursuant to Section 8.5 shall be reduced by an amount equal to [**] of all royalties, upfront fees, milestones and other payments under (i) the AVEO In-Licenses, (ii) the Biogen Idec In-Licenses and (iii) any other Third Party Technology Agreement pursuant to which Biogen Idec or any of its Affiliates or Sublicensees acquired Know-how or Patent Rights that are necessary for the Development, Manufacture or Commercialization of Licensed Product in the Licensed Territory, in each case to the extent actually paid by Biogen Idec or any of its Affiliates; provided that in no event shall the royalty payable to AVEO under Section 8.5 be reduced to less than [**] of the full royalty determined at the rates set forth in Section 8.5. Royalties payable by AVEO to Biogen Idec pursuant to Section 8.6 shall be reduced by an amount equal to [**] of all royalties, upfront fees, milestones and other payments under (i) the AVEO In-Licenses, (ii) the Biogen Idec In-Licenses and (iii) any other Third Party Technology Agreement pursuant to which AVEO or any of its Affiliates or Sublicensees acquired Know-how or Patent Rights that are necessary for the Development, Manufacture or Commercialization of Licensed Product in the AVEO Territory, in each case to the extent actually paid by AVEO or any of its Affiliates; provided that in no event shall the royalty payable to Biogen Idec under Section 8.6 be reduced to less than [**] of the full royalty determined at the rates set forth in Section 8.6. Amounts not otherwise used by a Party to reduce royalties as a result of the limitations set forth in this Section 8.9(d) in a period incurred may be used to reduce royalties in future periods until fully utilized.

(e) Disagreements. In the event that a Party disagrees with the other Party's assessment of the necessity of a Third Party Technology Agreement that is not a Biogen Idec In-license or AVEO In-license, the objecting Party shall send written notice to such effect to the other Party, and the Parties shall appoint a mutually agreed upon independent Third Party intellectual property lawyer with expertise in the patenting of biologics, and appropriate professional credentials in the relevant jurisdiction, to determine the question of the necessity of the relevant Patent Right, taking into account such Third Party's assessment of the validity and enforceability of such Patent Right in addition to an infringement assessment. The determination of the Third Party expert engaged under the preceding sentence shall be binding on the Parties solely for purposes of applying the offsets under this Section 8.9. The costs of any Third Party expert engaged under this paragraph shall be paid by the Party against whose position the Third Party's determination is made.

(f) Exclusions. Notwithstanding anything express or implied in this Section 8.9 to the contrary, the provisions of this Section 8.9 shall not apply to any royalties, license fees or other fees paid by either Party or any of its Affiliates to Third Parties in respect of the Manufacture of Licensed Product and included in Cost of Goods Sold.

8.10. Payments; Reports. Within [**] after the end of each Calendar Quarter for which royalties are payable by one Party to the other Party under either Section 8.5 or Section 8.6, the

Party that owes the royalty (the "Royalty-paying Party") shall submit to the other Party a report, on a country-by-country basis, providing in reasonable detail an accounting of all Net Sales by the Royalty-paying Party and its Affiliates and Sublicensees in the Licensed Territory with respect to Net Sales by Biogen Idec and its Affiliates and Sublicensees and with respect to the AVEO Territory with respect to Net Sales by AVEO and its Affiliates and Sublicensees (including, in each case, an accounting of all unit sales of the Licensed Product and a calculation of the deductions from gross invoice price to Net Sales in accordance with Section 1.63) made during such Calendar Quarter and the calculation of the applicable royalties under Section 8.5 or 8.6, as the case may be. The Royalty-paying Party shall, at the time the Royalty-paying Party submits the report, pay to the other Party all amounts due to such other Party under Section 8.5 or 8.6, as the case may be, as indicated in the applicable report.

8.11. Taxes. The Royalty-paying Party will make all payments to the other Party under this Agreement without deduction or withholding except to the extent that any such deduction or withholding is required by applicable Law to be made on account of Taxes (as that term is defined below). Any Tax required to be withheld under applicable Law on amounts payable under this Agreement will promptly be paid by Royalty-paying Party on behalf of the other Party to the appropriate governmental authority, and the Royalty-paying Party will furnish the other Party with proof of payment of such Tax. Any such Tax required to be withheld will be an expense of and borne by the Party receiving the payment. The Royalty-paying Party will give notice of its intention to begin withholding any such Tax in advance and cooperate to use reasonable and legal efforts to reduce such Tax on payments made to the other Party hereunder. Upon the written request of the Royalty-paying Party, the other Party shall instruct the Royalty-paying Party as to the applicable withholding rate and related regulations for any country (or all countries) within the applicable Territory. The Royalty-paying Party shall be entitled to rely upon the other Party's withholding instructions without verification thereof, and shall withhold in accordance therewith and shall remit payment to the appropriate governmental authority in accordance with this Section 8.11. The Parties will cooperate with respect to all documentation required by any relevant government taxing authority or reasonably requested by either Party to secure a reduction in the rate of applicable withholding Taxes. Solely for purposes of this Section 8.11, "Tax" or "Taxes" means any present or future taxes, levies, imposts, duties, charges, assessments or fees of any nature (including interest, penalties and additions thereto) that are imposed by a Government Authority.

8.12. United States Dollars. All dollar ($) amounts specified in this Agreement are United States dollar amounts.

8.13. Currency Conversion. All payments to be made by either Party to the other Party shall be made in U.S. Dollars, to a bank account designated by the Party to be paid. In the case of sales outside the United States, royalty payments shall be converted to U.S. Dollars in accordance with the following: the rate of currency conversion shall be calculated using the month-end spot rates as published by The Wall Street Journal, Eastern Edition.

8.14. Blocked Payments. If, by reason of applicable laws or regulations in any country, it becomes impossible or illegal for a Party or any of its Affiliates or Sublicensees to transfer, or have transferred on its behalf, royalties or other payments to the other Party, the Royalty-paying Party shall promptly notify the other Party of the conditions preventing such transfer and such

royalties or other payments shall be deposited in local currency in the relevant country to the credit of the Party to whom the royalty is owed in a recognized banking institution designated by such Party or, if none is designated by such Party within a period of thirty (30) days, in a recognized banking institution selected by the other Party or its Affiliates or Sublicensees, as the case may be, and identified in a notice given to the Party on whose account the funds are deposited.

8.15. Late Payments. The paying Party shall pay interest to the receiving Party on the aggregate amount of any payments that are not paid on or before the date such payments are due under this Agreement at a simple rate per annum equal to the lesser of [**] percent ([**]%) per month or the highest rate permitted by applicable law, calculated on the number of days such payments are paid after the date such payments are due.

8.16. Records and Audits.

(a) Royalties. Each Party shall keep complete and accurate records of the underlying revenue and expense data relating to the calculations of Net Sales and payments required by Sections 8.5, 8.6 and 8.9. Each Party (the "Auditing Party") shall have the right, [**] at its own expense, to have an nationally recognized, independent, certified public accounting firm, selected by it and reasonably acceptable to the other Party, review any such records of the other Party and its Affiliates and Sublicensees (the "Audited Party") in the location(s) where such records are maintained by the audited Party upon reasonable notice (which shall be no less than [**] prior notice) and during regular business hours and under obligations of strict confidence, for the sole purpose of verifying the basis and accuracy of payments made under Sections 8.5, 8.6 and 8.9 within the [**] period preceding the date of the request for review. The Audited Party shall receive a copy of each such report concurrently with receipt by the Auditing Party. Should such inspection lead to the discovery of a discrepancy to the Auditing Party's detriment, the Audited Party shall pay within [**] after its receipt from the accounting firm of the certificate any undisputed amount of the discrepancy. The Auditing Party shall pay the full cost of the review unless the underpayment of royalties is greater than five percent (5%) of the amount due for the entire period being examined, in which case the Audited Party shall pay the reasonable cost charged by such accounting firm for such review. Any overpayment of royalties by the Audited Party revealed by an examination shall be paid back by the Auditing Party to the Audited Party within [**].

(b) Development Costs. AVEO shall keep complete and accurate records of Development Costs. Biogen Idec shall have the right, [**] at its own expense, to have an independent, certified public accounting firm, selected by Biogen Idec and reasonably acceptable to AVEO, review any such records of AVEO in the location(s) where such records are maintained by AVEO upon reasonable notice (which shall be no less than [**] prior notice) and during regular business hours and under obligations of strict confidence, for the sole purpose of verifying the basis and accuracy of its reimbursements made for Development Costs under Sections 5.4 within the [**] period preceding the date of the request for review. AVEO shall receive a copy of each such report concurrently with receipt by Biogen Idec. Should such inspection lead to the discovery of a discrepancy to Biogen Idec's detriment, AVEO shall pay within [**] after its receipt from the accounting firm of the certificate any undisputed amount of the discrepancy. Biogen Idec shall pay the full cost of the review unless there has been an

overpayment of Development Costs by Biogen Idec for the period being examined in an amount greater than five percent (5%) of the amount due for the entire period being examined, in which case AVEO shall pay the reasonable cost charged by such accounting firm for such review. Any underpayment of Development Costs by Biogen Idec revealed by an examination shall be paid by Biogen Idec within [**].

ARTICLE IX.
INTELLECTUAL PROPERTY OWNERSHIP, PROTECTION AND RELATED MATTERS

9.1. Inventorship. Inventorship for patentable inventions conceived or reduced to practice during the course of the performance of activities pursuant to this Agreement shall be determined in accordance with United States patent laws for determining inventorship.

9.2. Ownership. Subject to the licenses and rights granted to Biogen Idec under this Agreement, AVEO shall own the entire right, title and interest in and to all inventions and discoveries (and Patent Rights claiming patentable inventions therein) first made or discovered solely by employees or consultants of AVEO or acquired solely by AVEO in the course of Development, Manufacture or Commercialization of Licensed Product. Subject to the licenses and rights granted to AVEO under this Agreement, Biogen Idec shall own the entire right, title and interest in and to all inventions and discoveries (and Patent Rights claiming patentable inventions therein) first made or discovered solely by employees or consultants of Biogen Idec or acquired solely by Biogen Idec in the course of Development, Manufacture or Commercialization of Licensed Product. The Parties shall jointly own any inventions and discoveries (and Patent Rights claiming patentable inventions therein) first made or discovered jointly in the course of Development, Manufacture or Commercialization of Licensed Product.

9.3. Prosecution and Maintenance of Patent Rights.

(a) AVEO Technology. AVEO shall have the sole right to, at AVEO's discretion, file, conduct prosecution, and maintain (including the defense of any interference or opposition proceedings), all Patent Rights comprising AVEO Technology (other than Joint Collaboration IP), in AVEO's name. AVEO shall provide to Biogen Idec copies of all prosecution filings related to AVEO Patent Rights and AVEO Collaboration Patent Rights comprising claims Covering Licensed Product sent to or received from patent offices in the Licensed Territory, unless otherwise directed by Biogen Idec, and, with respect to patent applications having information not previously filed that is intended to be submitted to patent offices in the Licensed Territory, shall use reasonable efforts to provide Biogen Idec with a draft of each such filing reasonably in advance of submission, provide Biogen Idec an opportunity to provide comments on and make request of AVEO concerning such filings and shall consider in good faith any comments regarding such draft application that Biogen Idec may timely provide. In addition, AVEO shall provide to Biogen Idec such other information related to prosecution of the AVEO Patent Rights and AVEO Collaboration Patent Rights in the Licensed Territory as Biogen Idec may from time to time reasonably request to allow Biogen Idec to track prosecution and maintenance of such Patent Rights. In the event AVEO decides not to file a patent application on AVEO Know-how or AVEO Collaboration Know-how specific to Licensed Product in a country of the Licensed Territory, or decides to abandon prosecution of any claim of

an AVEO Patent Right or AVEO Collaboration Patent Right comprising claims Covering Licensed Product in a country of the Licensed Territory or decides to not otherwise maintain or extend any AVEO Patent Rights or AVEO Collaboration Patent Right comprising claims Covering Licensed Product in a country of the Licensed Territory, AVEO shall give Biogen Idec written notice sufficiently in advance of any loss of rights to allow Biogen Idec to file, prosecute, maintain or extend, as the case may be, such AVEO Patent Rights or AVEO Collaboration Patent Rights, in AVEO's name, in such country.

(b) Biogen Idec Collaboration Technology. Biogen Idec shall have the sole right, at Biogen Idec's discretion, to file, conduct prosecution, and maintain (including the defense of any interference or opposition proceedings), all Patent Rights comprising Biogen Idec Collaboration Technology (other than Joint Collaboration IP), in Biogen Idec's name. In the event Biogen Idec decides not to file a patent application on Biogen Idec Collaboration Know-how in a country of the Territory specific to Licensed Product, or decides to abandon prosecution of any claim of Biogen Idec Collaboration Patent Right in a country of the Territory comprising claims Covering Licensed Product or decides to not otherwise maintain or extend any Biogen Idec Collaboration Patent Right comprising claims Covering Licensed Product in a country of the Territory, Biogen Idec shall give AVEO written notice sufficiently in advance of any loss of rights to allow AVEO optionally to file, prosecute, maintain or extend, as the case may be, such Biogen Idec Collaboration Patent Rights, in Biogen Idec's name, in such country.

(c) Joint Collaboration IP.

(i) AVEO shall have the first right, at AVEO's discretion, to file, conduct prosecution, and maintain (including the defense of any interference or opposition proceedings), all Patent Rights included in Joint Collaboration IP, in the names of both AVEO and Biogen Idec. Biogen Idec shall use Commercially Reasonable Efforts to make available to AVEO or its authorized attorneys, agents or representatives, such of its employees as AVEO in its reasonable judgment deems necessary in order to assist it in obtaining patent protection for such Joint Collaboration IP. Each Party shall sign, or use Commercially Reasonable Efforts to have signed, all legal documents necessary to file and prosecute patent applications or to obtain or maintain patents in respect of such Joint Collaboration IP, at its own cost.

(ii) If AVEO elects not to seek or continue to seek or maintain patent protection on any Joint Collaboration IP in the Licensed Territory, Biogen Idec shall have the right, at Biogen Idec's discretion, to seek, prosecute and maintain in any country in the Licensed Territory patent protection on such Joint Collaboration IP in the names of both AVEO and Biogen Idec. AVEO shall use Commercially Reasonable Efforts to make available to Biogen Idec its authorized attorneys, agents or representatives, such of AVEO's employees as are reasonably necessary to assist Biogen Idec in obtaining and maintaining the patent protection described under this Section 9.3(c)(ii). AVEO shall sign or use Commercially Reasonable Efforts to have signed all legal documents necessary to file and prosecute such patent applications or to obtain or maintain such patents.

(iii) With respect to Patent Rights included in the Joint Collaboration IP, the Party filing, prosecuting and maintaining such Patent Rights shall provide the other Party, within ten (10) Business Days after submitting or receiving such filings or correspondence, with copies of all filings and correspondence submitted to and received from patent offices in the Licensed Territory and, with respect to substantive filings and correspondence to be submitted to patent offices in the Licensed Territory, shall use reasonable efforts to provide the other Party with drafts of such filings and correspondence reasonably in advance of submission and shall consider in good faith any comments regarding such filings and correspondence that the other Party may timely provide.

9.4. Patent Term Extensions. The Parties shall cooperate, if necessary and appropriate, with each other in gaining patent term extension (including those extensions available under U.S. Drug Price Competition and Patent Term Restoration Act of 1984, the Supplementary Certificate of Protection of Member States of the EU and other similar measures in any other country) wherever applicable to Patent Rights Controlled by either Party that Cover the Licensed Product in the Territory. The Parties shall, if necessary and appropriate, use reasonable efforts to agree upon a joint strategy relating to patent term extensions, but, in the absence of mutual agreement with respect to any extension issue, the patent or the claims of the patent shall be selected on the basis of the scope, enforceability and remaining term of the patent in the relevant country or region. All filings for such extensions shall be made by the Party owning such patent or, in the case of Patent Rights included in the Joint Collaboration IP, by the Party responsible for filing, prosecuting and maintaining such Patent Rights in accordance with this Section 9.4.

9.5. Patent Expenses. The patent filing, prosecution and maintenance expenses incurred after the Option Exercise Date under Section 9.3 with respect to AVEO Patent Rights, AVEO Collaboration Patent Rights, Biogen Idec Collaboration Patent Rights and Joint Collaboration Patent Rights, in each case with claims covering Licensed Product in the Licensed Territory shall be borne by Biogen Idec. The patent filing, prosecution and maintenance expenses incurred under Section 9.3 with respect to AVEO Patent Rights, AVEO Collaboration Patent Rights, Biogen Idec Collaboration Patent Rights and Joint Collaboration Patent Rights in each case with claims covering Licensed Product in the AVEO Territory shall be borne by AVEO. In all other cases, the patent filing, prosecution and maintenance expenses incurred during the Agreement Term with respect to Patent Rights comprised of AVEO Technology and Biogen Idec Collaboration Technology ("Patent Expenses") shall be borne by the Party responsible for filing, prosecuting and maintaining such Patent Rights under this Section 9.5.

9.6. Third Party Infringement.

(a) Notices. Each Party shall promptly report in writing to the other Party any (i) known or suspected infringement of any AVEO Technology or Biogen Idec Collaboration Technology, including any Joint Collaboration IP or (ii) unauthorized use or misappropriation of any Confidential Information or Know-how of a Party by a Third Party of which it becomes aware, in each case only to the extent relevant to the Licensed Product or the Development, Manufacture or Commercialization of the Licensed Product and involving a competing product

("Competitive Infringement") in the Territory, and shall provide the other Party with all available evidence supporting such infringement, or unauthorized use or misappropriation.

(b) Rights to Enforce.

(i) AVEO's First Right. Subject to the provisions of any Third Party agreement under which AVEO's rights in AVEO Technology are granted and subject to paragraph (ii), AVEO shall have the sole and exclusive right to initiate an infringement or other appropriate suit anywhere in the world against any Third Party who at any time has infringed, or is suspected of infringing, any Patent Rights, or of using without proper authorization any Know-how comprising AVEO Technology or Joint Collaboration IP for which AVEO has prosecution responsibility under Section 9.3.

(ii) Biogen Idec's First Right. Subject to the provisions of any Third Party agreement under which Biogen Idec's rights in Biogen Idec Collaboration Technology are granted, Biogen Idec shall have the sole and exclusive right to initiate an infringement or other appropriate suit anywhere in the world against any Third Party who at any time has infringed, or is suspected of infringing, any Patent Rights, or of using without proper authorization any Know-how, comprising Biogen Idec Collaboration Technology or Joint Collaboration IP for which Biogen Idec has prosecution responsibility under Section 9.3.

(iii) Requests to Initiate Enforcement Action. AVEO will consider in good faith any request from Biogen Idec to initiate an infringement or other appropriate suit in the Licensed Territory against any Third Party with respect to a Competitive Infringement of AVEO Technology or Joint Collaboration I.P. for which AVEO has prosecution responsibilities under Section 9.3; provided, however, that AVEO shall not be required to initiate any such suit. If, however, AVEO elects not to initiate such suit, or otherwise does not commence suit within one-hundred eighty (180) days of Biogen Idec's request made under the preceding sentence, Biogen Idec shall have the right to initiate such suit and to join AVEO as a party. Biogen Idec will consider in good faith any request from AVEO to initiate an infringement or other appropriate suit against any Third Party with respect to a Competitive Infringement in the AVEO Territory of a Biogen Idec Collaboration Patent Right or any Joint Collaboration I.P. for which Biogen Idec has prosecution responsibilities under Section 9.3; provided, however, that Biogen Idec shall not be required to initiate any such suit. If, however, Biogen Idec elects not to initiate such suit, or otherwise does not commence suit within one-hundred eighty (180) days of AVEO's request made under the preceding sentence, AVEO shall have the right to initiate such suit and to join Biogen Idec as a party. For the sake of clarity, in no event shall Biogen Idec have the right to enforce in the AVEO Territory any AVEO Patent Rights, AVEO Collaboration Patent Rights or Joint Collaboration IP for which Biogen Idec has prosecution responsibilities under Section 9.3, and in no event shall AVEO have the right to enforce in the Licensed Territory Biogen Idec Collaboration Patent Rights or Joint Collaboration IP for which AVEO has prosecution responsibilities under Section 9.3.

(c) Procedures; Expenses and Recoveries. The Party having the right to initiate any infringement suit under Section 9.6(b) above shall have the sole and exclusive right to select counsel for any such suit and shall pay all expenses of the suit, including attorneys' fees and court costs and reimbursement of the other Party's reasonable out-of-pocket expense in rendering assistance requested by the initiating Party; provided that with respect to any such suit, the Parties may mutually agree to jointly bear such costs and expenses, in which case the allocation of recoveries described below may be adjusted as mutually agreed by the Parties. If required under applicable law in order for the initiating Party to initiate or maintain such suit, or if either Party is unable to initiate or prosecute such suit solely in its own name or it is otherwise advisable to obtain an effective legal remedy, in each case, the other Party shall join as a party to the suit and will execute and cause its Affiliates to execute all documents necessary for the initiating Party to initiate litigation to prosecute and maintain such action. In addition, at the initiating Party's request, the other Party shall provide reasonable assistance to the initiating Party in connection with an infringement suit at no charge to the initiating Party except for reimbursement by the initiating Party of reasonable out-of-pocket expenses incurred in rendering such assistance. The non-initiating Party shall have the right to participate and be represented in any such suit by its own counsel at its own expense. If the Parties obtain from a Third Party, in connection with such suit, any damages, license fees, royalties or other compensation (including any amount received in settlement of such litigation) in respect of a Competitive Infringement, such amounts shall be allocated, subject to any adjustment to such allocation agreed by the Parties in connection with an agreement to jointly bear the costs and expenses of the infringement action as described above, as follows:

(i) first, to reimburse each Party for all expenses of the suit incurred by such Party, including attorneys' fees and disbursements, court costs and other litigation expenses;

(ii) second, [**] percent ([**]%) of the balance to be paid to (x) AVEO, in respect of a Competitive Infringement in the AVEO Territory, and (y) Biogen Idec, in respect of a Competitive Infringement in the Licensed Territory, as the case may be; and

(iii) third, the remainder to be paid to the Party that did not receive the balance under clause (ii).

9.7. Third Party Infringement Claims. If a Party becomes aware of any claim that the Development, Manufacture or Commercialization of the Licensed Product in the Field infringes the Patent Rights of any Third Party in the Licensed Territory, such Party shall promptly notify the other Party. In any such instance, the Parties shall cooperate and shall mutually agree upon an appropriate course of action which may include settlement of such claim. Each Party shall have an equal right to participate in any settlement discussions that are held with such Third Parties.

9.8. Patent Marking. Each Party agrees to comply with the patent marking statutes in each country in which the Licensed Product is sold by such Party or its Affiliates or Sublicensees.

9.9. Trademarks.

(a) Corporate Names and Logos. Each Party and its Affiliates shall retain all right, title and interest in and to its and their respective corporate names and logos.

(b) Creation and Registration of Trademarks. AVEO or its Affiliates or Sublicensees will create and register product trademarks for use with Licensed Product throughout the AVEO Territory, and Biogen Idec or its Affiliates or Sublicensees will create and register product trademarks for use with Licensed Product throughout the Licensed Territory (collectively, the "Product Trademarks"). Each Party (or its Affiliates or Sublicensees, as appropriate) shall own all rights to its Product Trademarks, and all goodwill associated therewith, throughout the world, and to any Internet domain names incorporating the applicable Product Trademarks or any variation or part of such Product Trademarks used as its URL address or any part of such address.

(c) License to Trademarks. AVEO shall grant to Biogen Idec and its Affiliates and Sublicensees an exclusive license to use AVEO's Product Trademarks to Commercialize the Licensed Product in the Field in the Licensed Territory, and Biogen Idec shall grant to AVEO and its Affiliates and Sublicensees an exclusive license to use Biogen Idec's Product Trademarks to Commercialize the Licensed Product in the Field in the AVEO Territory. If a Party uses the Product Trademark of the other Party with respect to Licensed Product, as permitted under this Agreement, such Party agrees that the quality of the Licensed Product and the Commercialization thereof shall be consistent with the quality standards applied by the owner of the Product Trademark thereto. In addition, the Party using the Product Trademark of the other Party under this Section 9.9 shall comply strictly with the trademark style and usage standards of the Party that owns the Product Trademark as communicated to such Party from time to time with respect to the Product Trademarks. The Party using the Product Trademark of the other Party, shall, at the request and expense of the Party that owns the Product Trademark, from time to time, submit to the Party that owns the Product Trademark for approval a reasonable number of production samples of the Licensed Product and related packaging materials. If the Party that owns the Product Trademark reasonably objects to the quality of the Licensed Product or the usage of the Product Trademarks in connection with any sample, it shall give written notice of such objection to the other Party within sixty (60) days after receipt of the relevant sample, specifying the way in which such usage of the Product Trademarks fails to meet the style, usage or quality standards for the Licensed Product set forth in the second and third sentences of this Section 9.9(c), and such Party shall immediately cease sale and distribution of the Licensed Product using such Product Trademark. If the Party using such Product Trademark wishes to continue to distribute and sell the Licensed Product, it must remedy the failure and submit further samples to the Party that owns the Product Trademark for approval.

(d) Maintenance and Costs. If a Product Trademark owned by AVEO or any of its Affiliates or Sublicensees is used by Biogen Idec or any of its Affiliates or Sublicensees to promote and sell the Licensed Product in the Licensed Territory, then AVEO will use Commercially Reasonable Efforts to establish, maintain and enforce such Product Trademarks in the applicable countries of the Licensed Territory. Biogen Idec shall be responsible for [**] of the costs of such efforts in the Licensed Territory and Biogen Idec shall reimburse AVEO for all such costs incurred by AVEO within [**] after receiving any invoice from AVEO for such costs.

If a Product Trademark owned by Biogen Idec or any of its Affiliates or Sublicensees is used by AVEO or any of its Affiliates or Sublicensees to promote and sell the Licensed Product in the AVEO Territory, then Biogen Idec will use Commercially Reasonable Efforts to establish, maintain and enforce such Product Trademarks in the applicable countries in the AVEO Territory. AVEO shall be responsible for [**] of the costs of such efforts in the AVEO Territory and AVEO shall reimburse Biogen Idec for all such costs incurred by Biogen Idec within [**] after receiving any invoice from AVEO for such costs.

(e) Infringement of Trademarks. If either Party becomes aware of any infringement of any Product Trademark by a Third Party in the Licensed Territory, such Party shall promptly notify the other Party and the Parties shall consult with each other and jointly determine the best way to prevent such infringement, including by the institution of legal proceedings against such Third Party.

ARTICLE X.
CONFIDENTIALITY

10.1. Confidential Information. During the Agreement Term and for a period of ten (10) years after any termination or expiration hereof, each Party agrees to keep in confidence and not to disclose to any Third Party, or use for any purpose, except pursuant to, and in order to carry out, the terms and objectives of this Agreement, any Confidential Information of the other Party. The terms of this Agreement shall be considered Confidential Information of both Parties hereunder. The restrictions on the disclosure and use of Confidential Information set forth in the first sentence of this Section 10.1 shall not apply to any Confidential Information that:

(i) was known by the receiving Party prior to disclosure by the disclosing Party hereunder (as evidenced by the receiving Party's written records or other competent evidence);

(ii) is or becomes part of the public domain through no fault of the receiving Party;

(iii) is disclosed to the receiving Party by a Third Party having a legal right to make such disclosure without violating any confidentiality or non-use obligation that such Third Party has to the disclosing Party and provided such third party is not disclosing such information on behalf of the disclosing Party; or

(iv) is independently developed by personnel of the receiving Party who did not have access to the relevant Confidential Information of the other Party (as evidenced by the receiving Party's written records or other competent evidence).

In addition, if either Party is required to disclose Confidential Information of the other Party by regulation, law or legal process, including by the rules or regulations of the United States Securities and Exchange Commission, or similar regulatory agency in a country other than the United States, or of any stock exchange or Nasdaq, such Party shall provide prior written notice and a copy of such intended disclosure to such other Party if possible under the circumstances to enable such other Party to seek a protective order or other appropriate remedy concerning any such disclosure, shall consider in good faith the other Party's comments and reasonably

cooperate (at the expense of the Party seeking to restrict such disclosure) to obtain any such order or other remedy, and shall disclose only such Confidential Information of such other Party as is legally required to be disclosed. In addition, either Party may disclose to bona fide potential investors or lenders, potential acquirors/acquirees, existing or potential collaborators or licensees or to such Party's consultants and advisors, the existence and terms of this Agreement to the extent necessary in connection with a proposed equity or debt financing of such Party, or a proposed acquisition or business combination, so long as such recipients are bound in writing to maintain the confidentiality of such information in accordance with the terms of this Agreement

10.2. Permitted Disclosures. Each Party agrees that it and its Affiliates shall provide or permit access to Confidential Information received from the other Party and such Party's Affiliates and representatives only to the receiving Party's employees, consultants, advisors and permitted subcontractors, Sublicensees and sub-distributors, and to the employees, consultants, advisors and permitted subcontractors, Sublicensees and sub-distributors of the receiving Party's Affiliates, who in such Party's reasonable judgment have a need to know such Confidential Information to assist the receiving Party with the activities contemplated by this Agreement and who are subject to obligations of confidentiality and non-use with respect to such Confidential Information similar to the obligations of confidentiality and non-use of the receiving Party pursuant to Section 10.1; provided that AVEO and Biogen Idec shall each remain responsible for any failure by its Affiliates, and its and its Affiliates' respective employees, consultants, advisors and permitted subcontractors, Sublicensees and sub-distributors, to treat such Confidential Information as required under Section 10.1 (as if such Affiliates, employees, consultants, advisors and permitted subcontractors, Sublicensees and sub-distributors were Parties directly bound to the requirements of Section 10.1). Each Party may also disclose Confidential Information of the other Party to Regulatory Authorities, but solely in connection with the activities contemplated by this Agreement.

10.3. Publicity. Upon the execution of this Agreement, AVEO shall be entitled to issue a mutually agreed press release regarding the subject matter of this Agreement in the form attached as Exhibit E (the "Initial Release"). After such Initial Release, neither Party shall issue a press release or public announcement relating to this Agreement without the prior written approval of the other Party, which approval shall not be unreasonably withheld or delayed, except that (i) a Party may issue such a press release or public announcement if the contents of such press release or public announcement have been previously been made public pursuant to the Initial Release or otherwise, other than through a breach of this Agreement by the issuing Party, (ii) a Party may issue such a press release or public announcement if required by applicable Law, including by the rules or regulations of the United States Securities and Exchange Commission (SEC) or similar regulatory agency in a country other than the United States or of any stock exchange or Nasdaq, (iii) either Party may, to the extent required by applicable Law, disclose in SEC filings or filings with a similar regulatory agency in a country other than the United States or with any stock exchange or Nasdaq, the terms of this Agreement, including by filing a copy of this Agreement, or the amounts paid to or received from the other Party under this Agreement, and (iv) AVEO may issue such a press release or public announcement regarding Development of Licensed Product (without use of Biogen Idec's or any of its Affiliates name), subject in each case to the next sentence. In the event of disclosures under clause (ii) or (iii) of the foregoing sentence, and during the License Term, under clause (iv), the Party planning to make such disclosure shall first notify the other Party of such planned

press release or public announcement at least three Business Days in advance of issuing such press release or making such public announcement (or, with respect to press releases and public announcements made pursuant to the foregoing clause (ii) or (iii), with as much advance notice as possible under the circumstances if it is not possible to provide notice at least three Business Days in advance) for the sole purpose of allowing the other Party to review the proposed press release or public announcement for the inclusion of its Confidential Information or the use of its name; provided that the Party subject to the requirement shall include in such press release or public announcement made pursuant to the foregoing clause (ii) or (iii) only such information relating to the Licensed Product or this Agreement as is required by such applicable Law.

10.4. Publications.

(a) Option Exercise Period. During the Option Exercise Period, AVEO shall be free to publish the results of Development carried out on the Licensed Product.

(b) License Term. During the License Term, subject to the restrictions provided below, the JDC shall determine the publication strategy for the Territory. In the event, either Party, consistent with the publication strategy adopted by the JDC, proposes to publish or present the results of Development carried out on the Licensed Product, such publication or presentation shall be subject to the prior review by the other Party for patentability and protection of such other Party's Confidential Information. Each Party shall provide to the other Party the opportunity to review any proposed abstracts, manuscripts or summaries of presentations that cover the results of Development of the Licensed Product during the License Term. Each Party shall designate a person or persons who shall be responsible for reviewing such publications. Such designated person shall respond in writing promptly and in no event later than thirty (30) days after receipt of the proposed material with either approval of the proposed material or a specific statement of concern, based upon either the need to seek patent protection or concern regarding competitive disadvantage arising from the proposal. In the event of concern, the submitting Party agrees not to submit such publication or to make such presentation that contains such information until the other Party is given a reasonable period of time (not to exceed sixty (60) days) to seek patent protection for any material in such publication or presentation that it believes is patentable or to resolve any other issues, and the submitting Party shall remove from such proposed publication any Confidential Information of the other Party as requested by such other Party. With respect to any proposed abstracts, manuscripts or summaries of presentations by investigators or other Third Parties, including Affiliates or Sublicensees, such materials shall be subject to review under this Section 10.4 to the extent that the contracting Party has the right to do so, provided that each Party agrees to use Commercially Reasonable Efforts to include in any agreement with investigators and other Third Parties a right for both Parties to review publications and presentations consistent with the terms of this Section 10.4.

ARTICLE XI.
REPRESENTATIONS AND WARRANTIES; CERTAIN COVENANTS

11.1. Representations of Authority. AVEO and Biogen Idec each represents and warrants to the other Party that, as of the Effective Date, it has full right, power and authority to enter into this Agreement and to perform its respective obligations under this Agreement and that

it has the right to grant to the other the licenses and sublicenses granted pursuant to this Agreement.

11.2. Consents. AVEO and Biogen Idec each represents and warrants to the other Party that, except for any Regulatory Approvals, pricing or reimbursement approvals, manufacturing approvals or similar approvals necessary for the Development, Manufacture or Commercialization of Licensed Product, all necessary consents, approvals and authorizations of all government authorities and other persons required to be obtained by it as of the Effective Date in connection with the execution, delivery and performance of this Agreement have been obtained by the Effective Date.

11.3. No Conflict. AVEO and Biogen Idec each represents and warrants to the other Party that, notwithstanding anything to the contrary in this Agreement, the execution and delivery of this Agreement by such Party, the performance of such Party's obligations hereunder and the licenses and sublicenses to be granted by such Party pursuant to this Agreement (a) do not conflict with or violate any requirement of applicable Laws existing as of the Effective Date and applicable to such Party and (b) do not conflict with, violate, breach or constitute a default under any contractual obligations of such Party or any of its Affiliates existing as of the Effective Date.

11.4. Compliance with Laws. Each Party shall comply with all Laws applicable to the Development, Manufacture and Commercialization of Licensed Product, including applicable Drug Regulation Laws.

11.5. Enforceability. AVEO and Biogen Idec each represents and warrants to the other Party that, as of the Effective Date, this Agreement is a legal and valid obligation binding upon it and is enforceable against it in accordance with its terms.

11.6. Additional Representations and Warranties of AVEO. AVEO represents and warrants to Biogen Idec that, as of the Effective Date:

(a) Patent Rights. Exhibit A sets forth a complete and accurate list of AVEO Patent Rights owned by AVEO in the (i) Licensed Territory and (ii) the AVEO Territory that Cover AVEO Know-how necessary for the Development, Manufacture or Commercialization of Licensed Product as contemplated on the Effective Date. AVEO owns all right, title and interest in and to the AVEO Patent Rights listed on Exhibit A.

(b) No Conflict. AVEO has not granted, and will not grant during the term of this Agreement, rights to any Third Party under the AVEO Technology that conflict with the rights granted to Biogen Idec hereunder. AVEO has not granted rights to any Third Party under the AVEO Technology to Develop, Manufacture or Commercialize Licensed Product in the Field in the AVEO Territory or the Licensed Territory.

(c) U.S. Government Funding. Neither AVEO nor any of its Affiliates is or has been a party to any agreement with the U.S. federal government or an agency thereof pursuant to which the U.S. federal government or such agency provided funding for the Development of Licensed Product.

(d) No Infringement. To the knowledge of AVEO, except as otherwise disclosed to Biogen Idec, the use or practice of AVEO Technology and the Development, Manufacture and Commercialization of Licensed Product in the manner contemplated under this Agreement will not infringe any Patent Rights or result in the misappropriation or misuse of Know-How of any Third Party. No claim of infringement of the Patent Rights of any Third Party has been made, nor to AVEO's knowledge threatened, against AVEO or any of its Affiliates with respect to the Development, Manufacture or Commercialization of Licensed Product, and there are no other claims, judgments or settlements against or owed by AVEO or any of its Affiliates or to which AVEO or any of its Affiliates is a party or, to AVEO's knowledge, pending or threatened claims or litigation, in either case relating to the AVEO Technology or Licensed Product. To AVEO's knowledge, (i) no claim of infringement of the Patent Rights of any Third Party has been made, nor threatened, against any of AVEO's Sublicensees with respect to the Development, Manufacture or Commercialization of Licensed Product and (ii) there are no other claims, judgments or settlements against or owed by any of AVEO's Sublicensees, nor any pending or threatened claims or litigation, in either case relating to the AVEO Technology or Licensed Product.

(e) Available Information. AVEO has made available to Biogen Idec all material information in AVEO's possession or Control relating to Licensed Product that is material to an assessment of the feasibility of the Development, Manufacture and Commercialization of Licensed Product as conducted by or on behalf of AVEO to date.

(f) Compliance with Law. To AVEO's knowledge, all of the studies, tests and pre-clinical and clinical trials of Licensed Product conducted prior to, or being conducted as of, the Effective Date by or on behalf of AVEO have been and are being conducted in all material respects in accordance with applicable laws, rules and regulations.

(g) In-licenses. Except as set forth in Exhibit D, there are no agreements between AVEO or any of its Affiliates, on the one hand, and any Third Party, on the other hand, pursuant to which AVEO has (i) in-licensed any Patent Rights or Know-how owned or Controlled by such Third Party to the extent that such Patent Rights or Know-how are included in AVEO Technology, or (ii) agreed to make any payments (including royalties) to any Third Party or agreed to undertake or observe any restrictions or obligations with respect to the Development, Manufacture or Commercialization of Licensed Product.

11.7. No Warranties. EXCEPT AS OTHERWISE EXPRESSLY SET FORTH HEREIN, NEITHER PARTY MAKES ANY REPRESENTATION OR EXTENDS ANY WARRANTIES OF ANY KIND, EITHER EXPRESS OR IMPLIED, TO THE OTHER PARTY, AND EACH PARTY HEREBY DISCLAIMS ALL IMPLIED WARRANTIES OF MERCHANTABILITY, FITNESS FOR A PARTICULAR PURPOSE AND NONINFRINGEMENT WITH RESPECT TO LICENSED PRODUCT. EACH PARTY HEREBY DISCLAIMS ANY REPRESENTATION OR WARRANTY THAT THE DEVELOPMENT, MANUFACTURE AND COMMERCIALIZATION OF THE LICENSED PRODUCT PURSUANT TO THIS AGREEMENT WILL BE SUCCESSFUL OR THAT ANY PARTICULAR SALES LEVEL WITH RESPECT TO LICENSED PRODUCT WILL BE ACHIEVED.

11.8. No Debarment. Neither Party nor any of its Affiliates has been debarred or is subject to debarment and neither Party nor any of its Affiliates will use in any capacity, in connection with the Development, Manufacture or Commercialization of the Licensed Product, any Person who has been debarred pursuant to Section 306 of the United States Federal Food, Drug, and Cosmetic Act, or who is the subject of a conviction described in such section. Each Party agrees to inform the other Party in writing immediately if it or any Person who is performing services hereunder is debarred or is the subject of a conviction described in Section 306, or if any action, suit, claim, investigation or legal or administrative proceeding is pending or, to the best of such Party's knowledge, is threatened, relating to the debarment or conviction of such Party or any Person used in any capacity by such Party or any of its Affiliates in connection with the Development, Manufacture or Commercialization of the Licensed Product.

11.9. Additional Representation of Biogen Idec. Biogen Idec represents and warrants to AVEO that, as of the Effective Date, Biogen Idec is an indirect wholly-owned subsidiary of Biogen Idec Inc., a corporation organized and existing under the laws of the State of Delaware.

ARTICLE XII.
INDEMNIFICATION

12.1. Indemnification by Biogen Idec. Biogen Idec shall indemnify, hold harmless, and defend AVEO, its Affiliates, and their respective directors, officers, employees and agents (the "AVEO Indemnitees") from and against any and all Losses incurred or suffered by the AVEO Indemnitees in connection with any third party claim arising out of or resulting from, directly or indirectly, (i) any breach of, or inaccuracy in, any representation or warranty made by Biogen Idec in this Agreement, or any breach or violation of any covenant or agreement of Biogen Idec in or pursuant to this Agreement, (ii) the negligence or willful misconduct by or of Biogen Idec, its Affiliates and their respective Sublicensees, or their respective directors, officers, employees and agents in the performance of Biogen Idec's obligations under this Agreement, (iii) the Commercialization or use of Licensed Product in the Licensed Territory or any other activities of Biogen Idec or any of its Affiliates or Sublicensees in the Licensed Territory or (iv) AVEO's observance of, or reliance upon, Biogen Idec's withholding instructions provided pursuant to Section 8.11 of this Agreement. Biogen Idec shall have no obligation to indemnify the AVEO Indemnitees to the extent that the Losses arise out of or result from, directly or indirectly, (a) any breach of, or inaccuracy in, any representation or warranty made by AVEO in this Agreement, (b) any breach or violation of any covenant or agreement of AVEO in or pursuant to this Agreement, (c) the negligence or willful misconduct by or of any of the AVEO Indemnitees or any of AVEO's Sublicensees, distributors or contractors or any of their respective employees or agents, (d) any manufacturing defect in any Licensed Product supplied to Biogen Idec or its Affiliates, Sublicensees, distributors or contractors by or on behalf of AVEO as defined in and subject to the terms of the Supply Agreement, (e) actual or alleged infringement or misappropriation by Biogen Idec or any of its Affiliates, Sublicensees, distributors or contractors of the Patent Rights or Know-how of any Third Party to the extent arising from the use or practice of AVEO Technology or Joint Collaboration IP pursuant to, and in accordance with, the provisions of this Agreement or (f) any Loss arising from or related to the Commercialization or use of Licensed Product in the AVEO Territory.

12.2. Indemnification by AVEO. AVEO shall indemnify, hold harmless, and defend Biogen Idec, its Affiliates and their respective directors, officers, employees and agents (the "Biogen Idec Indemnitees") from and against any and all Losses incurred or suffered by the Biogen Idec Indemnitees arising out of or resulting from, directly or indirectly, (i) any breach of, or inaccuracy in, any representation or warranty made by AVEO in this Agreement, or any breach or violation of any covenant or agreement of AVEO in or pursuant to this Agreement, (ii) the negligence or willful misconduct by or of AVEO, its Affiliates and their respective Sublicensees, or their respective directors, officers, employees and agents in the performance of AVEO's obligations under this Agreement, or (iii) the Commercialization or use of Licensed Product in the AVEO Territory or any other activities of AVEO or any of its Affiliates or Sublicensees in the AVEO Territory, or (iv) Biogen Idec's observance of, or reliance upon, AVEO's withholding instructions provided pursuant to Section 8.11 of this Agreement. AVEO shall have no obligation to indemnify the Biogen Idec Indemnitees to the extent that the Losses arise out of or result from, directly or indirectly, (a) any breach of, or inaccuracy in, any representation or warranty made by Biogen Idec in this Agreement, (b) any breach or violation of any covenant or agreement of Biogen Idec in or pursuant to this Agreement, (c) the negligence or willful misconduct by or of any of the Biogen Idec Indemnitees, or any of Biogen Idec's Sublicensees, distributors or contractors or any of their respective employees or agents, (d) any manufacturing defect in any Licensed Product supplied to AVEO or any of its Affiliates, Sublicensees, distributors or contractors by or on behalf of Biogen Idec as defined in and subject to the terms of the Supply Agreement, (e) actual or alleged infringement or misappropriation by AVEO or any of its Affiliates, Sublicensees, distributors or contractors of the Patent Rights or Know-how of any Third Party to the extent arising from the use or practice of Biogen Idec Collaboration Technology or Joint Collaboration IP pursuant to, and in accordance with, the provisions of this Agreement or (f) any Loss arising from or related to the Commercialization or use of Licensed Product in the Biogen Idec Territory.

12.3. Indemnification Procedure. In the event of any such claim against any Biogen Idec Indemnitee or AVEO Indemnitee (individually, an "Indemnitee"), the Indemnitee shall promptly notify the other Party in writing of the claim and the indemnifying Party shall manage and control, at its sole expense, the defense of the claim and its settlement. The Indemnitee shall cooperate with the indemnifying Party and may, at its option and expense, be represented in any such action or proceeding. The indemnifying Party shall not be liable for any settlements, litigation costs or expenses incurred by any Indemnitee without the indemnifying Party's written authorization. Notwithstanding the foregoing, if the indemnifying Party believes that any of the exceptions to its obligation of indemnification of the Indemnitees set forth in this Article XII may apply, the indemnifying Party shall promptly notify the Indemnitees, and the Indemnitees shall then have the right to be represented in any such action or proceeding by separate counsel at their expense; provided that the indemnifying Party shall be responsible for payment of such expenses if the Indemnitees are ultimately determined to be entitled to indemnification from the indemnifying Party.

12.4. Limitation of Liability. NEITHER PARTY HERETO WILL BE LIABLE FOR SPECIAL, INCIDENTAL, CONSEQUENTIAL OR PUNITIVE DAMAGES ARISING OUT OF THIS AGREEMENT OR THE EXERCISE OF ITS RIGHTS HEREUNDER, INCLUDING LOST PROFITS ARISING FROM OR RELATING TO ANY BREACH OF THIS AGREEMENT, REGARDLESS OF ANY NOTICE OF SUCH DAMAGES, EXCEPT AS A

RESULT OF A PARTY'S WILLFUL MISCONDUCT OR WILLFUL BREACH OF THE CONFIDENTIALITY AND NON-USE OBLIGATIONS IN ARTICLE X. NOTHING IN THIS SECTION 12.4 IS INTENDED TO LIMIT OR RESTRICT THE INDEMNIFICATION RIGHTS OR OBLIGATIONS OF EITHER PARTY.

12.5. Insurance. Each Party shall maintain insurance during the License Term and for a period of at least [**] after the last commercial sale of a Licensed Product in the Field in the Territory under this Agreement, or, if Development of Licensed Products ceases prior to Regulatory Approval, [**] after termination of such Development, with a reputable, solvent insurer in an amount appropriate for its business and products of the type that are the subject of this Agreement, and for its obligations under this Agreement. Specifically, each Party shall maintain product and clinical trial liability insurance of at least [**] per occurrence on a worldwide basis. Notwithstanding the foregoing, either Party may satisfy its obligations under this Section 12.5 through a program of self-insurance, provided such Party has assets and earnings sufficient to cover the potential indemnified Losses. Each Party will further ensure compliance with all foreign local clinical trial liability insurance requirements that may apply with respect to Licensed Product(s). Upon request, each Party shall provide the other Party with evidence of the existence and maintenance of such insurance coverage.

ARTICLE XIII.
CONTROL ASSUMPTION OPTIONS

13.1. M&A Event Control Assumption Option. If, at any time during the Agreement Term, an M&A Event occurs involving AVEO (or any of its Affiliates) and a Person that, at the time of the consummation of such M&A Event, directly or indirectly (including by any Affiliate of such Person), is Developing or Commercializing a Directly Competitive Product in the AVEO Territory or the Licensed Territory within the Field or, at any time after such consummation of the M&A Event, develops or acquires a Directly Competitive Product (such Person being hereinafter referred to as a "Competing Acquiror") and such Competing Acquiror has not, within six (6) months of either consummation of the M&A Event in the event the Directly Competitive Product is being Developed or Commercialized as of such consummation date or otherwise within six (6) months of the date of first development or acquisition of such Directly Competitive Product (the "Divestiture Period") divested the Directly Competitive Product, terminated Development and Commercialization of such Directly Competitive Product or assigned this Agreement pursuant to Section 16.5 to a Third Party that is not itself Developing or Commercializing a Directly Competitive Product, then Biogen Idec may exercise, in the manner set forth further below in this Section 13.1, its right to trigger the provisions of this Section 13.1 (the "M&A Control Assumption Option"), whereupon (A) Biogen Idec shall assume the rights, responsibilities and obligations of AVEO under Articles IV and V of this Agreement with AVEO assuming the rights, responsibilities and obligations of Biogen Idec under such provisions, provided that notwithstanding anything to the contrary contained in Section 4.8(b), in the event the M&A Control Assumption Option is triggered, Biogen Idec will have final decision-making authority to increase or change the budget for Development Costs, and (B) Biogen Idec shall have the right (but not the obligation) to assume any or all of the rights, responsibilities and obligations of AVEO under Article VII and/or Article IX by giving AVEO at least 30 days prior written notice at any time and from time to time after the exercise of the M&A Control Assumption Option, which written notice shall specify the rights, responsibilities and obligations

of AVEO under Article VII and/or IX being assumed by Biogen Idec. In the event that Biogen Idec exercises the M&A Control Assumption Option prior to the Option Exercise Date, (i) the provisions of Article II shall terminate (except to the extent otherwise provided in clause (iii) below), (ii) the exercise of the M&A Control Assumption Option shall be deemed, for all purposes of this Agreement, to be the exercise of the Option by Biogen Idec, (iii) Biogen Idec shall be responsible for preparing and delivering to AVEO the Delivered Initial Development Plan and, if at the time of delivery of such plan, AVEO has not previously delivered the Data Package to Biogen Idec, such plan shall set forth Biogen Idec's Development efforts in connection with the Proof of Concept Study, and, if at the time of the delivery of such plan, AVEO has previously delivered the Data Package to Biogen Idec, such plan shall meet the criteria therefor set forth in clauses (ii) and (iii) of Section 2.9 and (iv) if the Delivered Initial Development Plan provides for the conduct of the Proof of Concept Study in accordance with the provisions of the foregoing clause (iii), AVEO shall be obligated to pay and reimburse Biogen Idec for all costs and expenses incurred by Biogen Idec in connection with the Development and Manufacture of Licensed Product through the completion of the Proof of Concept Study for a single indication, and upon completion of the Proof of Concept Study Biogen Idec shall reimburse AVEO for [**] of the Pre-Phase 3 Manufacturing Costs. For purposes of this Section 13.1, (x) any reference in the definition of "Proof of Concept Study" to the Proof of Concept Development Plan shall be deemed to be a reference to the Delivered Initial Development Plan provided pursuant to this Section 13.1, and (y) any reference in the definition of "Pre-Phase 3 Manufacturing Costs" to the Option Exercise Date shall be deemed to be a reference to the date of the completion of the Proof of Concept Study. In addition, upon exercise of the M&A Control Assumption Option, the royalties payable by Biogen Idec under Section 8.5 shall be reduced by [**]. The M&A Control Assumption Option shall be exercised by providing written notice to AVEO no later than [**] after the date that AVEO and/or the Competing Acquiror sends written notice to Biogen Idec stating that the Divestiture Period has expired and that Biogen Idec may exercise its rights under this Section 13.1. In addition to the foregoing obligations, in the event Biogen Idec exercise its M&A Control Assumption Option under this paragraph, it shall thereafter provide to AVEO copies of filings, submissions and correspondence with respect to AVEO Technology under Section 9.3(a) in the AVEO Territory and consider AVEO's comments to the same extent as AVEO provides such information and considers Biogen Idec's comments with respect to AVEO Technology under Section 9.3(a) prior to the exercise of the M&A Control Assumption Option.

13.2. Termination Right. The provisions of Section 13.1 shall not be deemed to limit Biogen Idec's right under Section 14.5 with respect to consummation of an M&A Event involving AVEO or any of its Affiliates and a Competing Acquiror.

13.3. Insolvency Control Assumption Option. Without limiting any legal or equitable remedies that Biogen Idec may have, including under this Article XIII, if, at any time during the Agreement Term, an Insolvency Event involving AVEO occurs, then Biogen Idec may exercise, in the manner set forth further below in this Section 13.3, its right to trigger the provisions of this Section 13.3 (the "Insolvency Control Assumption Option"), whereupon (A) Biogen Idec shall assume the rights, responsibilities and obligations of AVEO under Articles IV and V of this Agreement with AVEO assuming the rights, responsibilities and obligations of Biogen Idec under such provisions, provided that notwithstanding anything to the contrary contained in Section 4.8(b), in the event the Insolvency Control Assumption Option is triggered, Biogen Idec

will have final decision-making authority to increase or change the budget for Development Costs, and (B) Biogen Idec shall have the right (but not the obligation) to assume any or all of the rights, responsibilities and obligations of AVEO under Article VII and/or Article IX by giving AVEO at least 30 days prior written notice at any time and from time to time after the exercise of the Insolvency Control Assumption Option, which written notice shall specify the rights, responsibilities and obligations of AVEO under Article VII and/or IX being assumed by Biogen Idec. In the event that Biogen Idec exercises the Insolvency Control Assumption Option prior to the Option Exercise Date, (i) the provisions of Article II shall terminate (except to the extent otherwise provided in clause (iv) below), (ii) the exercise of the Insolvency Control Assumption Option shall be deemed, for all purposes of this Agreement, to be the exercise of the Option by Biogen Idec, (iii) the royalties payable by Biogen Idec under Section 8.5 shall be reduced by [**], (iv) Biogen Idec shall be responsible for preparing and delivering to AVEO the Delivered Initial Development Plan and, if at the time of delivery of such plan, AVEO has not previously delivered the Data Package to Biogen Idec, such plan shall set forth Biogen Idec's Development efforts in connection with the Proof of Concept Study, and, if at the time of the delivery of such plan, AVEO has previously delivered the Data Package to Biogen Idec, such plan shall meet the criteria therefor set forth in clauses (ii) and (iii) of Section 2.9 and (v) if the Delivered Initial Development Plan provides for the conduct of the Proof of Concept Study in accordance with the provisions of the foregoing clause (iv), AVEO shall be obligated to pay and reimburse Biogen Idec for all costs and expenses incurred by Biogen Idec in connection with the Development and Manufacture of Licensed Product through the completion of the Proof of Concept Study for a single indication, and upon completion of the Proof of Concept Study Biogen Idec shall reimburse AVEO for [**] of the Pre-Phase 3 Manufacturing Costs. For purposes of this Section 13.3, (x) any reference in the definition of "Proof of Concept Study" to the Proof of Concept Development Plan shall be deemed to be a reference to the Delivered Initial Development Plan provided pursuant to this Section 13.3, and (y) any reference in the definition of "Pre-Phase 3 Manufacturing Costs" to the Option Exercise Date shall be deemed to be a reference to the date of the completion of the Proof of Concept Study. The Insolvency Control Assumption Option shall be exercised by providing written notice to AVEO no later than [**] after the Insolvency Event with respect to AVEO. In addition to the foregoing obligations, in the event Biogen Idec exercise its Insolvency Control Assumption Option under this paragraph, it shall thereafter provide to AVEO copies of filings, submissions and correspondence with respect to AVEO Technology under Section 9.3(a) in the AVEO Territory and consider AVEO's comments to the same extent as AVEO provides such information and considers Biogen Idec's comments with respect to AVEO Technology under Section 9.3(a) prior to the exercise of the Insolvency Control Assumption Option. For purposes of this Agreement, the term "Insolvency Event" means that AVEO (i) commits an act of bankruptcy, is declared bankrupt, voluntarily files or has filed against it a petition for bankruptcy or reorganization unless such petition is dismissed within sixty (60) days of filing or such petition is for a reorganization under Chapter 11 of the Bankruptcy Code (as defined below) or any relevant foreign equivalent thereof and AVEO is not in default at the time of the filing of such petition or at any time during such reorganization of any of its obligations under this Agreement, (ii) enters into a procedure of winding up or dissolution, or (iii) should a trustee or receiver be appointed for its business assets or operations. All rights and licenses granted under or pursuant to this Agreement are, and shall otherwise be deemed to be, for the purposes of Section 365(n) of Title 11, U.S. Code ("Bankruptcy Code") license rights to "intellectual property" as defined under Section 101(60) of

the Bankruptcy Code. The Parties agree that any Party, as a licensee hereunder, shall retain and may fully exercise all of its rights and elections under the Bankruptcy Code or any relevant foreign equivalent thereof.

ARTICLE XIV.
TERM; TERMINATION AND REMEDIES FOR BREACH

14.1. Term. This Agreement shall become effective as of the Effective Date, and, in the event Biogen Idec does not exercise the Option by the end of the Option Exercise Period, shall terminate at the end of the Option Exercise Period, unless earlier terminated in accordance with this Article XIV. In the event Biogen Idec exercises the Option in accordance with Article II (or is deemed to have exercised the Option pursuant to Sections 13.1, 13.3 or 14.5(b)), this Agreement shall continue in full force until the later of (a) the last to expire Royalty Term and (b) such time as any Development activities that were pending before the expiration of the last to expire Royalty Term are no longer being conducted by either Party under this Agreement.

14.2. Termination for Convenience. Biogen Idec shall have the right to terminate this Agreement with respect to any Licensed Product at any time upon at least three months (3) months' prior written notice to AVEO.

14.3. Remedies for Breach.

(a) Breach in Respect of Monetary Obligation. In the event that a Party is in material breach of this Agreement with respect to one of its financial obligations hereunder and has not cured such material breach within [**] after written notice describing the nature of such material breach is provided to the breaching Party, the non-breaching Party shall have the immediate right to elect its remedies for material breach set forth in Section 14.5.

(b) Breach in Respect of Non-Monetary Obligation. In the event a Party (the "Notifying Party") is concerned that there has been or may be a failure by the other Party (the "Notified Party") to meet one or more of its non-financial obligations under this Agreement and such failure constitutes, or could reasonably be expected to give rise to, a material breach of this Agreement, the Notifying Party shall send written notice to the Notified Party specifying in detail the nature of the concern and specifically referencing this Section 14.3(b) (a "Section 14.3 Notice"). Within [**] of delivery of such Section 14.3 Notice, the Parties shall meet to discuss the circumstances surrounding the perceived failure, the impediments that are impacting performance, the actions that the Parties believe are reasonably necessary to address such failure, and each Party's view of the plan and timeline within which such failure could reasonably be remedied. If not originally provided with the Section 14.3 Notice, within [**] after the meeting held under the preceding sentence, the Notifying Party shall provide the Notified Party with a written plan that is prepared with a good faith intent to allow the Notified Party an adequate amount of time to address the perceived performance issues as determined in the reasonable discretion of the Notifying Party, and which shall include specific activities to be performed and the timeline for performance of such activities (the "Cure Plan"). Within [**] of receipt, the Notified Party shall provide written notice to the Notifying Party of its election to implement or not implement the Cure Plan. In the event the Notified Party either (A) fails to respond within such [**] period, (B) elects not to implement the Cure Plan within [**] of receipt of such Cure

Plan, or (C) elects to implement the Cure Plan, and thereafter fails to meet any milestone included in the Cure Plan, following written notice thereof by the Notifying Plan, and a one-time [**] opportunity to cure such milestone failure, then the Notifying Party shall have the right to elect its remedies for material breach as set forth in Section 14.5; provided that (i) the failure giving rise to the Section 14.3 Notice constitutes a material breach of this Agreement by the Notified Party and (ii) such material breach has not otherwise been cured on or prior to the [**] following the delivery of the Section 14.3 Notice applicable to such material breach. In the event the Notified Party elects to implement the Cure Plan within [**] of receipt thereof, and is continuing to execute in full compliance with such Cure Plan (subject to the one-time cure period for the first failed milestone under such Cure Plan), the Notifying Party's right to elect its remedies for material breach as set forth in Section 14.5 shall be suspended until such time, if any, as the Notified Party fails to continue to execute in full compliance with the Cure Plan (*e.g.*, such suspension shall immediately terminate upon the second failure to meet a milestone). Notwithstanding anything in this Agreement to the contrary, a Party's decision whether or not to implement the Cure Plan shall not be deemed an admission or acknowledgement of breach nor will a failure to execute in accordance with the Cure Plan be considered a separate and independent breach of this Agreement.

14.4. Termination by Biogen Idec Upon Certain M&A Events. Without limiting any legal or equitable remedies that Biogen Idec may have, including under Section 13.1, in the event an M&A Event occurs involving AVEO (or any of its Affiliates) and a Person that, at the time of the consummation of such M&A Event, or at any time thereafter during the Agreement Term, directly or indirectly (including by any Affiliate), is Developing or Commercializing any Directly Competitive Product in the AVEO Territory or the Licensed Territory within the Field, then Biogen Idec shall have the right under this Section 14.4 to terminate this Agreement in its entirety by giving written notice of termination to AVEO and/or such Person. Such written notice of termination shall specify that it is being given by Biogen Idec pursuant to this Section 14.4 and must be given within [**] after the later of (i) the date of the consummation of the M&A Event and (ii) the date that AVEO and/or such Person sends written notice to Biogen Idec stating that the M&A Event has been consummated and that Biogen Idec may terminate this Agreement pursuant to this Section 14.4. Any termination of this Agreement pursuant to this Section 14.4 shall become effective on the date (the "Section 14.4 Termination Effective Date") that is the later of (i) the effective date of termination specified in such written notice of termination given by Biogen Idec pursuant to this Section 14.4 or (ii) the last [**] of the [**] following the date in which such written notice of termination is given by Biogen Idec pursuant to this Section 14.4, if on or prior to such Section 14.4 Termination Effective Date such Person has not divested such Directly Competitive Product, terminated Development and Commercialization of such Directly Competitive Product or assigned this Agreement pursuant to Section 16.5 to a Third Party that is not itself Developing or Commercializing a Directly Competitive Product.

14.5. Special Remedies for Breach.

(a) AVEO Remedy for Breach by Biogen Idec. Without limiting any other legal or equitable remedies that AVEO may have, in the event of any material breach of the Agreement by Biogen Idec that occurs during the Option Exercise Period, that has not been cured by Biogen Idec in accordance with the provisions of Section 14.3 and in respect of which

AVEO elects, in accordance with the provisions of Section 14.3, to pursue its remedies under this Section 14.5(a), the Option shall immediately terminate, and Biogen Idec shall have no further right to exercise the Option. Without limiting any other legal or equitable remedies that AVEO may have, in the event of any material breach of the Agreement by Biogen Idec that occurs during the License Term, that has not been cured by Biogen Idec in accordance with the provisions of Section 14.3 and in respect of which AVEO elects, in accordance with the provisions of Section 14.3, to pursue its remedies under this Section 14.5(a), this Agreement shall continue in full force and effect subject to the automatic modification thereof as follows:

(i) Biogen Idec shall no longer have the right under Section 5.11 or 5.12 to proceed with Development of New Licensed Products or a New Indication Existing Licensed Products in the event the JDC does not approve or consent to such Development;

(ii) The licenses and rights granted to Biogen Idec under Section 3.1 hereof shall immediately terminate with respect to the Licensed Product that was the subject of the applicable breach (each such Licensed Product being referred to as a "Breached Licensed Product");

(iii) The licenses and rights granted to AVEO pursuant to Section 3.2(a) shall continue with respect to the Breached Licensed Product and be converted automatically to worldwide licenses and rights with respect to the Breached Licensed Product such that AVEO and its Affiliates and Sublicensees shall have the right under such converted worldwide licenses and rights to Develop, Manufacture and Commercialize such Breached Licensed Product in the AVEO Territory and the Licensed Territory, and AVEO shall continue to have the right to grant sublicenses (subject to provisions similar to those set forth in Section 3.3 (other than subclauses (i), (ii) and (vi) of Section 3.3(b)) that are applicable to sublicenses of licenses granted by Biogen Idec to AVEO pursuant to Section 3.2(a) hereof);

(iv) Responsibility and control over the Development of the Breached Licensed Product shall rest solely with AVEO and the JDC shall have no decision-making authority with respect to such Breached Licensed Product and AVEO shall use Commercially Reasonable Efforts during the License Term to Develop the Breached Licensed Product in the Field for both the Licensed Territory and the AVEO Territory ;

(v) Responsibility and control over the Commercialization of the Breached Licensed Product in the AVEO Territory and the Licensed Territory shall rest solely with AVEO and AVEO shall use Commercially Reasonable Efforts to Commercialize such Breached Licensed Products in those countries in the AVEO Territory and the Licensed Territory in which Regulatory Approval has been obtained, including by providing appropriate incentives consistent with its normal business practices to Sales Representatives involved in the Commercialization of the Licensed Product in the AVEO Territory;

(vi) Neither Party shall have any further obligation under Article V or Article VI with respect to the Breached Licensed Product;

(vii) Biogen Idec's obligations under Article VIII with respect to the Breached Licensed Product shall terminate;

(viii) AVEO's obligations under Article VIII with respect to the Breached Licensed Product shall continue (including, without limitation, the obligation thereunder to make payment of royalties), provided that the royalties that AVEO is required to pay Biogen Idec under Article VIII with respect to the Breached Licensed Product shall be increased by [**] if AVEO exercises its rights under this Section 14.5(a) with respect to the Breached Licensed Product prior to Regulatory Approval thereof in the Licensed Territory and shall be increased by [**] if AVEO exercises its rights under this Section 14.5(a) with respect to the Breached Licensed Product after Regulatory Approval thereof in the Licensed Territory;

(ix) AVEO shall make payment to Biogen Idec of royalties on Net Sales of the Breached Licensed Product in the Licensed Territory by AVEO and its Affiliates and Sublicensees (the terms of Article VIII and the foregoing clause (viii) shall apply to AVEO's obligation to pay royalties under this clause (ix) to the same extent as they apply to AVEO's obligation to pay royalties on Net Sales of the Breached Licensed Product in the AVEO Territory by AVEO and its Affiliates and Sublicensees);

(x) AVEO shall have the right (but not the obligation) to assume any or all of the rights, responsibilities and obligations of Biogen Idec under Article IX with respect to the Breached Licensed Product by giving Biogen Idec at least [**] prior written notice at any time and from time to time after the exercise by AVEO of its special remedies under this Section 14.5(a), which written notice shall specify the rights, responsibilities and obligations of Biogen Idec under Article IX with respect to the Breached Licensed Product being assumed by AVEO;

(xi) Biogen Idec shall as promptly as practicable transfer to AVEO or AVEO's designee (A) possession and ownership of all governmental or regulatory correspondence, conversation logs, filings and approvals (including all Regulatory Approvals and pricing and reimbursement approvals) relating to the Development, Manufacture or Commercialization of the Breached Licensed Product in the Licensed Territory, (B) copies of all data, reports, records and materials, commercialization plans, marketing plans, Promotional Materials, and other sales and marketing related information in Biogen Idec's possession or Control to the extent that such data, reports, records, materials or other information relate to the Commercialization of the Breached Licensed Product in the Licensed Territory, including customer lists and customer contact information and all Safety Data and other adverse event data in Biogen Idec's possession or Control, and (C) all records and materials in Biogen Idec's possession or Control containing Confidential Information of AVEO with respect to the Breached Licensed Product;

(xii) If the Breached Licensed Product is being Commercialized by Biogen Idec in any country in the Licensed Territory, then, if requested by AVEO, Biogen Idec shall appoint AVEO as its exclusive distributor of the Breached Licensed Product in the Licensed Territory and grant AVEO the right to appoint sub-distributors,

until the earlier of (A) such time as all Regulatory Approvals in the Licensed Territory with respect to the Breached Licensed Product have been transferred to AVEO or its designee and (B) [**] after AVEO has exercised its special remedies under this Section 14.5(a) with respect to the Breached Licensed Product;

(xiii) If AVEO so requests, Biogen Idec shall transfer to AVEO any Third Party agreements to which Biogen Idec is a party relating to the Development, Manufacture or Commercialization of the Breached Licensed Product in the AVEO Territory or the Licensed Territory, subject to any required consents of such Third Party;

(xiv) The provisions of Section 12.1(clauses (iii) and (f) thereof) shall apply to both the AVEO Territory and the Licensed Territory with respect to such Breached Licensed Product;

(xv) The provisions of Section 13.1 shall not apply with respect to such Breached Licensed Product;

(xvi) The provisions of Section 3.7 shall not apply with respect to such Breached Licensed Product; and

(xvii) Each Party shall execute all documents and take all such further actions, including, where applicable, the prompt assignment by Biogen Idec of regulatory submissions and Third Party agreements, as may be reasonably requested by the other Party in order to give effect to the foregoing clauses (i) through (xvi) as soon as practicable and in order to enable AVEO to Develop, Manufacture and Commercialize the Breached Licensed Product in the AVEO Territory and the Licensed Territory.

(b) Biogen Idec Remedy for Breach by AVEO. Without limiting any other legal or equitable remedies that Biogen Idec may have, in the event of any material breach of the Agreement by AVEO that occurs during the Agreement Term, that has not been cured by AVEO in accordance with the provisions of Section 14.3 and in respect of which Biogen Idec elects, in accordance with the provisions of Section 14.3, to pursue its remedies under this Section 14.5(b), this Agreement shall continue in full force and effect subject to the automatic modification thereof as follows:

(i) AVEO shall no longer have the right under Section 5.11 or 5.12 to proceed with Development of New Licensed Products or New Indication Existing Licensed Products in the event the JDC does not approve or consent to such Development;

(ii) In the event that Biogen Idec pursues its remedies under this Section 14.5(b) prior to the Option Exercise Date, (i) the provisions of Article II shall terminate, (ii) the exercise by Biogen Idec of its rights and remedies under this Section 14.5(b) shall be deemed, for all purposes of this Agreement, to be the exercise of the Option by Biogen Idec and (iii) the provisions of Section 8.3 shall terminate and Biogen Idec shall have no obligation to make any of the payments contemplated thereunder;

(iii) The licenses and rights granted to AVEO under Section 3.2 shall immediately terminate with respect to the Breached Licensed Product;

(iv) The licenses and rights granted to Biogen Idec pursuant to Section 3.1 shall continue with respect to the Breached Licensed Product and be converted automatically to worldwide licenses and rights with respect to the Breached Licensed Product such that Biogen Idec and its Affiliates and Sublicensees shall have the right under such converted worldwide licenses and rights to Develop, Manufacture and Commercialize such Breached Licensed Product in the AVEO Territory and the Licensed Territory, and Biogen Idec shall continue to have the right to grant sublicenses (subject to provisions similar to those set forth in Section 3.3 that are applicable to sublicenses of licenses granted by AVEO to Biogen Idec pursuant to Section 3.1 hereof);

(v) Responsibility and control over the Development of the Breached Licensed Product shall rest solely with Biogen Idec and the JDC shall have no decision-making authority with respect to such Breached Licensed Product and Biogen Idec shall use Commercially Reasonable Efforts during the License Term to Develop the Breached Licensed Product in the Field for both the Licensed Territory and the AVEO Territory;

(vi) Responsibility and control over the Commercialization of the Breached Licensed Product in the AVEO Territory and the Licensed Territory shall rest solely with Biogen Idec and Biogen Idec shall use Commercially Reasonable Efforts to Commercialize such Breached Licensed Products in those countries in the AVEO Territory and the Licensed Territory in which Regulatory Approval has been obtained, including by providing appropriate incentives consistent with its normal business practices to Sales Representatives involved in the Commercialization of the Licensed Product in the Licensed Territory;

(vii) Neither Party shall have any further obligation under Article V or Article VI with respect to the Breached Licensed Product;

(viii) AVEO's obligations under Article VIII with respect to the Breached Licensed Product shall terminate;

(ix) Biogen Idec's obligations under Section 8.4 with respect to the Breached Licensed Product shall terminate;

(x) Biogen Idec's obligations under Section 8.5 and Sections 8.7-8.16 with respect to the Breached Licensed Product shall continue, provided that the royalties that Biogen Idec is required to pay AVEO under Article VIII with respect to the Breached Licensed Product shall be increased by [**] if Biogen Idec exercises its rights under this Section 14.5(b) with respect to the Breached Licensed Product prior to Regulatory Approval thereof in the AVEO Territory and shall be increased by [**] if Biogen Idec exercises its rights under this Section 14.5(b) with respect to the Breached Licensed Product after Regulatory Approval thereof in the AVEO Territory;

(xi) Biogen Idec shall make payment to AVEO of royalties on Net Sales of the Breached Licensed Product in the AVEO Territory by Biogen Idec and its

Affiliates and Sublicensees (the terms of Article VIII and the foregoing clause (x) shall apply to Biogen Idec's obligation to pay royalties under this clause (xi) to the same extent as they apply to Biogen Idec's obligation to pay royalties on Net Sales of the Breached Licensed Product in the Licensed Territory by Biogen Idec and its Affiliates and Sublicensees);

(xii) Biogen Idec shall have the right (but not the obligation) to assume any or all of the rights, responsibilities and obligations of AVEO under Article IX with respect to the Breached Licensed Product by giving AVEO at least [**] prior written notice at any time and from time to time after the exercise by Biogen Idec of its special remedies under this Section 14.5(b), which written notice shall specify the rights, responsibilities and obligations of AVEO under Article IX with respect to the Breached Licensed Product being assumed by Biogen Idec;

(xiii) AVEO shall as promptly as practicable transfer to Biogen Idec or Biogen Idec's designee (A) possession and ownership of all governmental or regulatory correspondence, conversation logs, filings and approvals (including all Regulatory Approvals and pricing and reimbursement approvals) relating to the Development, Manufacture or Commercialization of the Breached Licensed Product in the AVEO Territory, (B) copies of all data, reports, records and materials, commercialization plans, marketing plans, Promotional Materials, and other sales and marketing related information in AVEO's possession or Control to the extent that such data, reports, records, materials or other information relate to the Commercialization of the Breached Licensed Product in the AVEO Territory, including customer lists and customer contact information and all Safety Data and other adverse event data in AVEO's possession or Control, and (C) all records and materials in AVEO's possession or Control containing Confidential Information of Biogen Idec with respect to the Breached Licensed Product;

(xiv) If the Breached Licensed Product is being Commercialized by AVEO in any country in the AVEO Territory, then, if requested by Biogen Idec, AVEO shall appoint Biogen Idec as its exclusive distributor of the Breached Licensed Product in the AVEO Territory and grant Biogen Idec the right to appoint sub-distributors, until the earlier of (A) such time as all Regulatory Approvals in the AVEO Territory with respect to the Breached Licensed Product have been transferred to Biogen Idec or its designee and (B) [**] after Biogen Idec has exercised its special remedies under this Section 14.5(b) with respect to the Breached Licensed Product;

(xv) If Biogen Idec so requests, AVEO shall transfer to Biogen Idec any Third Party agreements to which AVEO is a party relating to the Development, Manufacture or Commercialization of the Breached Licensed Product in the AVEO Territory or the Licensed Territory, subject to any required consents of such Third Party;

(xvi) The provisions of Section 12.2 (clauses (iii) and (f) thereof) shall apply to both the AVEO Territory and the Licensed Territory with respect to such Breached Licensed Product; and

(xvii) Each Party shall execute all documents and take all such further actions, including, where applicable, the prompt assignment by AVEO of regulatory submissions and Third Party agreements, as may be reasonably requested by the other Party in order to give effect to the foregoing clauses (i) through (xvi) as soon as practicable and in order to enable Biogen Idec to Develop, Manufacture and Commercialize the Breached Licensed Product in the AVEO Territory and the Licensed Territory.

(c) Termination by Biogen Idec for Convenience. If Biogen Idec terminates this Agreement for convenience under Section 14.2 during the Option Exercise Period, the Option shall immediately terminate, and Biogen Idec shall have no further right to exercise the Option. If Biogen Idec terminates this Agreement for convenience under Section 14.2 with respect to any Licensed Product during the License Term, then (i) Biogen Idec shall continue to pay its share of all Development Costs for such Licensed Product for a period of [**] following the date of such termination, and, if longer, shall also continue to pay its share of the Development Costs for such Licensed Product related to any ongoing clinical trials included in the then current Development Plan until such trials are completed, (ii) the licenses and rights granted to AVEO pursuant to Section 3.2(a) with respect to such Licensed Product shall survive and be converted automatically to worldwide licenses and rights such that AVEO and its Affiliates and Sublicensees shall have the right under such converted worldwide licenses and rights to Develop, Manufacture and Commercialize such Licensed Product in the AVEO Territory and the Licensed Territory, and AVEO shall continue to have the right to grant sublicenses (subject to provisions similar to those set forth in Section 3.3), (iii) Biogen Idec's obligations under Article VIII shall terminate with respect to such Licensed Product, (iv) AVEO's obligations under Article VIII shall survive with respect to such Licensed Product (including, without limitation, the obligation thereunder to make payment of royalties); (v) AVEO shall make payment to Biogen Idec of royalties on Net Sales of such Licensed Product in the Licensed Territory by AVEO and its Affiliates and Sublicensees (the terms of Article VIII shall apply to AVEO's obligation to pay royalties under this clause (v) to the same extent as it applies to AVEO's obligation to pay royalties on Net Sales of Licensed Product in the AVEO Territory by AVEO and its Affiliates and Sublicensees), (vi) the rights and obligations of each Party under Article IX with respect to such Licensed Product shall survive with respect to any intellectual property rights that are subject to surviving licenses granted by, or for the benefit of, AVEO under this Agreement, (vii) Biogen Idec shall as promptly as practicable transfer to AVEO or AVEO's designee (A) possession and ownership of all governmental or regulatory correspondence, conversation logs, filings and approvals (including all Regulatory Approvals and pricing and reimbursement approvals) relating to the Development, Manufacture or Commercialization of such Licensed Product in the Licensed Territory, (B) copies of all data, reports, records and materials, commercialization plans, marketing plans, Promotional Materials, and other sales and marketing related information in Biogen Idec's possession or Control to the extent that such data, reports, records, materials or other information relate to the Commercialization of such Licensed Product in the Licensed Territory, including customer lists and customer contact information and all Safety Data and other adverse event data in Biogen Idec's possession or Control, and (C) all records and materials in Biogen Idec's possession or Control containing Confidential Information of AVEO with respect to such Licensed Product, (viii) if the effective date of termination is after the First Commercial Sale of such Licensed Product in any country in the Licensed Territory, then, if requested by AVEO, Biogen Idec shall

appoint AVEO as its exclusive distributor of such Licensed Product in the Licensed Territory and grant AVEO the right to appoint sub-distributors, until the earlier of (1) such time as all Regulatory Approvals in the Licensed Territory with respect to such Licensed Product have been transferred to AVEO or its designee and (2) [**] after the effective date of termination, (ix) if AVEO so requests, Biogen Idec shall transfer to AVEO any Third Party agreements relating to the Commercialization of such Licensed Product in the Licensed Territory to which Biogen Idec is a party, subject to any required consents of such Third Party, and (x) all rights and obligations of the Parties under this Agreement (except for those contemplated in this Section 14.5(c) and those contemplated below in Sections 14.7, 14.8, 14.9 and 14.10) shall terminate with respect to such Licensed Product. Each Party shall execute all documents and take all such further actions, including, where applicable, the prompt assignment by Biogen Idec of regulatory submissions and Third Party agreements, as may be reasonably requested by AVEO in order to give effect to the foregoing clauses (i) through (x) as soon as practicable and in order to enable AVEO to Develop, Manufacture and Commercialize such Licensed Product in the AVEO Territory and the Licensed Territory.

(d) Termination by Biogen Idec Upon Certain M&A Events. If Biogen Idec terminates this Agreement under Section 14.4 during the Agreement Term, then (i) Biogen Idec shall continue to pay its share of all Development Costs for a period of [**] following the date of such termination, (ii) the licenses and rights granted to Biogen Idec under Section 3.1 hereof shall survive; (iii) the license and rights granted to AVEO under Section 3.2 shall survive; (iv) the rights and obligations of the Parties under Article III shall survive (other than Section 3.6(a) and the first four sentences of Section 3.6(b), which shall not survive); (v) AVEO's obligations under Article VIII shall survive (including, without limitation, the obligation thereunder to make payment of royalties) provided that such royalty obligations shall be reduced by [**]; (vi) Biogen Idec's obligations under Article VIII shall survive (including, without limitation, the obligation thereunder to make payment of royalties), provided that such royalty obligations shall be reduced by [**]; (vii) the rights and obligations of each Party under Article IX shall survive with respect to any intellectual property rights that are subject to surviving licenses granted by, or for the benefit of, such Party under this Agreement; and (viii) all rights and obligations of the Parties under this Agreement except for those contemplated by this Section 14.5(d), those set forth in Section 5.8 and 5.9, those set forth in Section 5.4 as they related to Development Costs incurred in connection with Section 5.8, and those contemplated below in Sections 14.6, 14.7, 14.8 and 14.9) shall terminate. For purposes of clarification, if Biogen Idec terminates this Agreement under Section 14.4 during the Agreement Term, then (a) each Party and its Affiliates and Sublicensees shall have the right to engage in Development and Manufacture of Licensed Product in the AVEO Territory and the Licensed Territory, and the JDC shall have no decision-making authority or oversight with respect to the Development or Manufacturing activities of the Parties, (b) AVEO and its Affiliates and Sublicensees shall have the right to Commercialize Licensed Product in the AVEO Territory but not the Licensed Territory and (c) Biogen Idec and its Affiliates and Sublicensees shall have the right to Commercialize Licensed Product in the Licensed Territory but not the AVEO Territory.

14.6. Manufacturing. In the event that this Agreement terminates for any reason or that a Party exercises its special remedies under Section 14.5 as a result of the material breach of this Agreement by the other Party, and in the event that the Party that is not then responsible for Manufacturing under Article VII and/or the Supply Agreement retains rights to Develop and

Commercialize Licensed Product under this Agreement following such termination or the exercise by such Party of its special remedies under Section 14.5, (A) the obligations under such Article VII and/or the Supply Agreement of the Party that is then responsible for Manufacturing shall continue in effect for a period of at least [**] following such termination or the exercise by the other Party of its special remedies under Section 14.5, as the case may be, or such longer period as the Parties may mutually agree, and (B) the Party that is not responsible for Manufacturing (the "non-Manufacturing Party") shall have the right to require the Party responsible for Manufacturing (the "Manufacturing Party") to engage in a technology transfer process, at the Manufacturing Party's costs, in the event the cause of the termination is breach by the Manufacturing Party, or at Biogen Idec's cost for a termination under Section 14.2, otherwise at the cost of the non-Manufacturing Party, for purposes of enabling the non-Manufacturing Party or any of its Affiliates or Third Party contract manufacturers to Manufacture Licensed Product by or on behalf of the non-Manufacturing Party and its Affiliates and Sublicensees for purposes of enabling the non-Manufacturing Party to exercise its rights under this Agreement, and the non-Manufacturing Party shall have the right to deal directly with any Third Party contract manufacturer of the Manufacturing Party or any of its Affiliates to arrange for such Third Party contract manufacturer to Manufacture and supply Licensed Product to the non-Manufacturing Party and its Affiliates and Sublicensees for the purposes of enabling the non-Manufacturing Party to exercise its rights under this Agreement.

14.7. Accrued Obligations. Expiration or termination of this Agreement shall not relieve the Parties of any obligation accruing prior to such expiration or termination.

14.8. Treatment of Sublicensees. In the event the license granted to Biogen Idec under Section 3.1 terminates for any reason or in the event that the license granted to AVEO under Section 3.2(a) terminates for any reason, each Sublicensee at such time under any such license that terminates shall continue to have the rights and licenses set forth in their sublicense agreements; provided, that such Sublicensee agrees in writing that (i) the Party that is the licensor in connection with such terminated license is entitled to enforce all relevant provisions of the applicable sublicense agreement directly against such Sublicensee and (ii) the Party that is the licensor in connection with such terminated license shall not assume, and shall not be responsible to such Sublicensee for, any representations, warranties or obligations made to such Sublicensee by the Party that was the licensee in connection with such terminated license, other than to permit such Sublicensee to exercise any rights to Licensed Product that are sublicensed under such sublicense agreement.

14.9. Survival. Any expiration or termination of this Agreement shall be without prejudice to the rights of either Party against the other accrued or accruing under this Agreement prior to expiration or termination, including payment obligations arising prior to such expiration or termination. The provisions of Section 8.16, Articles X, XII, XIV, XV and XVI shall survive any expiration or termination of this Agreement and all other provisions contained in this Agreement that by their explicit terms survive expiration or termination of this Agreement, shall survive. In addition, in the event of an expiration of this Agreement in accordance with the provisions of Section 14.1, the licenses granted in Sections 3.1 and 3.2(a) shall survive as perpetual, fully paid-up, non-royalty-bearing licenses. Except as set forth in this Article XIV, upon expiration of this Agreement in accordance with the provisions of Section 14.1 all other rights and obligations of the Parties under this Agreement terminate.

ARTICLE XV.
DISPUTE RESOLUTION

15.1. Continuance of Rights and Obligations During Pendency of Dispute Resolution. If there are any disputes in connection with this Agreement, including termination of this Agreement under Article XIV, all rights and obligations of the Parties shall continue until such time as any dispute has be resolved in accordance with the provisions of this Article XV.

15.2. Referral of Unresolved Matters to Senior Representatives. In the event that the Parties are unable to resolve a dispute within thirty (30) days from the date such dispute is first brought to the other Party's attention, the matter shall be referred to the Senior Representatives of each Party to be resolved by negotiation in good faith as soon as is practicable but in no event later than thirty (30) days after referral. A resolution, if any, of an issue referred to the Senior Representatives set forth in a writing signed by both Parties shall be final and binding on the Parties.

15.3. Equitable Relief. Notwithstanding anything to the contrary, each of the Parties hereby acknowledges that a breach of their respective obligations under this Agreement may cause irreparable harm and that the remedy or remedies at law for any such breach may be inadequate. Each of the Parties hereby agrees that, in the event of any such breach, in addition to all other available remedies hereunder, the non-breaching Party shall have the right to seek equitable relief to enforce the provisions of this Agreement.

ARTICLE XVI.
MISCELLANEOUS

16.1. Governing Law and Jurisdiction. The validity, construction and performance of this Agreement will be governed by and construed in accordance with the substantive laws of the Commonwealth of Massachusetts excluding any conflicts or choice of law rule or principle that might otherwise refer construction or interpretation of this Agreement to the substantive law of another jurisdiction.

16.2. Force Majeure. Neither Party shall be held liable or responsible to the other Party nor be deemed to have defaulted under or breached this Agreement for failure or delay in fulfilling or performing any term, other than an obligation to make payments hereunder, when such failure or delay is caused by or results from fire, floods, embargoes, government regulations, prohibitions or interventions, war, acts of war (whether war be declared or not), insurrections, riots, civil commotions, acts of God or any other cause beyond the reasonable control of the affected Party to anticipate, prevent, avoid or mitigate (a "Force Majeure Event"); provided that (i) the affected Party provides prompt notice to the other Party of such failure or delay, (ii) the affected Party uses commercially reasonable efforts to mitigate the effects of the Force Majeure Event, and (iii) the affected Party immediately resumes performance upon cessation of the Force Majeure Event. Notwithstanding the foregoing, any failure or delay in fulfilling a term shall not be considered a result of a Force Majeure Event if it arises from a failure of Biogen Idec or AVEO to comply with applicable Laws.

16.3. Further Assurances. Each Party hereto agrees to perform such acts, execute such further instruments, documents or certificates, and provide such cooperation in proceedings and actions as may be reasonably requested by the other Party in order to carry out the intent and purpose of this Agreement, including the registration or recordation of the rights granted hereunder.

16.4. Notices. Any notice required or permitted to be given hereunder shall be in writing and shall be deemed to have been properly given if delivered in person by a internationally recognized overnight courier, or by facsimile (and promptly confirmed by an overnight courier delivery), to the addresses given below or such other addresses as may be designated in writing by the Parties from time to time during the Agreement Term. Any notice sent by internationally recognized overnight courier as aforesaid shall be deemed to have been given three (3) days after being sent.

In the case of AVEO:

AVEO Pharmaceuticals, Inc.
75 Sidney St.Cambridge, MA 02139
Facsimile: 617-995-4995
Attention: Chief Business Officer

With a copy to:

AVEO Pharmaceuticals, Inc.
75 Sidney St.Cambridge, MA 02139
Facsimile: 617-995-4995
Attention: Corporate Counsel

In the case of Biogen Idec:

Biogen Idec International GmbH
Landis+Gyr-Strasse 3
6300 Zug
Switzerland
Attention: VP, Chief International Counsel
Facsimile: +41-41-392-1718

With a copy (which shall not constitute notice) to:

Biogen Idec Inc.
14 Cambridge Center
Cambridge, MA 02142
Attention: General Counsel
Facsimile: 617-679-3112

With an additional copy (which shall not constitute notice) to:

Bingham McCutchen LLP
One Federal StreetBoston, MA 02110
Attention: Julio E. Vega
William S. Perkins
Facsimile: 617-951-8736

16.5. Assignment. This Agreement may not be assigned or otherwise transferred by either Party, without the written consent of the other Party, such consent not to be unreasonably withheld, conditioned or delayed; provided, however, that either Party may, without such consent, assign this Agreement, in whole or in part, (i) to any of its Affiliates (provided the assigning Party continues at all times to remain liable for all obligations of such Party under this Agreement without regard to such assignment) and (ii) either Party, without such consent, may assign its rights and delegate its duties under this Agreement, whether by contract or operation of law, to a Third Party successor or purchaser of all or substantially all of such Party's business and assets, whether in a merger, sale of stock, sale of assets or other similar transaction, provided that the Third Party successor or purchaser provides written notice to the other Party that such Third Party agrees to be bound by the terms of this Agreement. Any purported assignment in violation of this Section 16.5 shall be void. Any permitted assignee shall assume all obligations of its assignor under this Agreement. Without limiting the generality or applicability of any other provision of this Agreement that may be applicable, the rights of AVEO under this Section 16.5 shall be subject to the rights of Biogen Idec under Sections 13.1 and 14.5 hereof.

16.6. Affiliate Performance. Any obligation of either Party under or pursuant to this Agreement may be satisfied, met or fulfilled, in whole or in part, at such Party's sole and exclusive option, either by such Party directly or by any Affiliate of such Party that such Party causes to satisfy, meet or fulfill such obligation, in whole or in part.

16.7. Amendment. The Parties hereto may amend, modify or alter any of the provisions of this Agreement, but only by a written instrument duly executed by both Parties hereto.

16.8. Entire Agreement. This Agreement, along with all schedules and exhibits attached hereto, contains the entire understanding of the Parties with respect to the subject matter hereof and supersedes all prior agreements, whether written or oral. Each Party confirms that it is not relying on any representations, warranties or covenants of the other Party except as specifically set out in this Agreement.

16.9. No Benefit to Third Parties. The provisions of this Agreement are for the sole benefit of the Parties and their successors and permitted assigns, and they shall not be construed as conferring any rights in any other Persons.

16.10. Waiver. The failure of a Party to enforce at any time for any period any of the provisions hereof shall not be construed as a waiver of such provisions or of the rights of such Party thereafter to enforce each such provision.

16.11. No Implied Licenses. Except as expressly and specifically provided under this Agreement, the Parties agree that neither Party is granted any implied rights to or under any of the other Party's current or future patents, trade secrets, copyrights, moral rights, trade or service marks, trade dress, or any other intellectual property rights.

16.12. Relationship of the Parties. The Parties agree that their relationship established by this Agreement is that of independent contractors. Furthermore, the Parties agree that this Agreement does not, is not intended to, and shall not be construed to, establish a partnership or joint venture, and nor shall this Agreement create or establish an employment, agency or any other relationship. Except as may be specifically provided herein, neither Party shall have any right, power or authority, nor shall they represent themselves as having any authority to assume, create or incur any expense, liability or obligation, express or implied, on behalf of the other Party, or otherwise act as an agent for the other Party for any purpose.

16.13. Severability. If any provision of this Agreement is held unenforceable by a court or tribunal of competent jurisdiction in a final unappealable order because it is invalid or conflicts with any Law of any relevant jurisdiction, then such provision shall be inoperative in such jurisdiction and the remainder of this Agreement shall remain binding upon the Parties hereto.

16.14. Interpretation.

(a) General. Unless the context of this Agreement otherwise requires, (a) words of one gender include the other gender; and (b) words using the singular or plural number also include the plural or singular number, respectively. Whenever this Agreement refers to a number of days, unless otherwise specified, such number shall refer to calendar days.

(b) Other Definitional and Agreement References. References to any agreement, contract, statute, act, or regulation are to that agreement, contract, statute, act, or regulation as amended, modified or supplemented from time to time in accordance with the terms hereof and thereof.

(c) Capitalization. Any capitalized terms used in any Exhibit or Schedule but not otherwise defined therein, shall have the meaning as defined in this Agreement.

(d) Date References. References from or through any date mean, unless otherwise specified, from and including or through and including, respectively.

(e) Schedules and Exhibits. All Schedules and Exhibits annexed hereto or referred to herein are hereby incorporated in and made a part of this Agreement as if set forth in full herein.

(f) Person References. References to any Person include the successors and permitted assigns of that Person.

(g) References to Parts of this Agreement. References to Articles, Sections, Schedules, and Exhibits are to Articles, Sections, Schedules, and Exhibits of this Agreement unless otherwise specified.

(h) Other Definitional and Interpretative Provisions. The words “hereof”, “herein” and “hereunder” and words of like import used in this Agreement shall refer to this Agreement as a whole and not to any particular provision of this Agreement. Whenever the words “include”, “includes” or “including” are used in this Agreement, they shall be deemed to be followed by the words “without limitation”, whether or not they are in fact followed by those words or words of like import. The word “or” is used in the inclusive sense (and/or). Writing”, “written” and comparable terms refer to printing, typing and other means of reproducing words (including electronic media) in a visible form.

(i) Headings. The Article and Section headings contained in this Agreement are for reference purposes only and shall not affect in any way the meaning or interpretation of this Agreement.

(j) Expenses. Except as otherwise expressly provided in this Agreement, each Party shall pay the fees and expenses of its respective lawyers and other experts and all other expenses and costs incurred by such Party incidental to the negotiation, preparation, execution and delivery of this Agreement.

16.15. Counterparts. This Agreement may be executed in any number of counterparts (including by facsimile), each of which shall be deemed an original, but all of which together shall constitute one and the same document.

[Signature Page Follows]

IN WITNESS WHEREOF, AVEO and Biogen Idec have caused this Agreement to be duly executed by their authorized representatives under seal, in duplicate on the Effective Date.

AVEO PHARMACEUTICALS, INC.

By: /s/ Tuan Ha-Ngoc
Name: Tuan Ha-Ngoc
Title: President and Chief Executive Officer

BIOGEN IDEC INTERNATIONAL GMBH

By: /s/ Hans Peter Hasler
Name: Hans Peter Hasler
Title: Geschaftsführer

Certain identified information has been excluded from the exhibit because it is both (i) not material and (ii) is the type of information that the registrant treats as private or confidential. Double asterisks denote omissions.

Exhibit 10.28

Execution Version

Amendment No. 1 to

Option and License Agreement

This is Amendment No. 1 to the Option and License Agreement by and between AVEO Pharmaceuticals, Inc. ("AVEO") and Biogen Idec International GmbH ("Biogen Idec") dated as of March 18, 2009 (the "Agreement"). The effective date of this Amendment No. 1 is March 18, 2014 (the "Amendment Effective Date"). Capitalized terms used in this Amendment No. 1 shall have the meanings set forth in the Agreement, except as otherwise provided in this Amendment.

1. Background.

(a) WHEREAS, under the terms of the Agreement, AVEO and Biogen Idec agreed to collaborate on the development of ERBB3 Antibodies, with Biogen Idec holding an option to obtain exclusive rights in the Licensed Territory to develop, manufacture and commercialize Licensed Products,

(b) WHEREAS, pursuant to the Development Plan, AVEO commenced a Phase 1 Clinical Trial of an ERBB3 Antibody known as AV-203 ("AV-203"),

(c) WHEREAS, the Parties have agreed to the termination of the option and license rights of Biogen Idec under the Agreement and the payment by AVEO to Biogen Idec of royalties and a portion of certain milestone payments received by AVEO relating to a Licensed Product, including AV-203, and

(d) WHEREAS, on or about August 31, 2011, Biogen Idec assigned its rights and obligations under the Agreement to Biogen Idec MA Inc. ("BIMA"), an upstream Affiliate (*i.e.* indirect, 100% controlling parent) of Biogen Idec.

NOW THEREFORE, in consideration of the foregoing and the mutual covenants contained in this Amendment No. 1, AVEO and BIMA, intending to be legally bound, hereby agree to the amendments to the Agreement as reflected in Sections 2-7 of this Amendment No. 1.

2. Termination of Option; Other Terminated Provisions.

(a) As of the Amendment Effective Date, the Option granted by AVEO to Biogen Idec pursuant to Section 2.1 of the Agreement shall terminate and be of no further force and effect. As a result of the termination of the Option, the following provisions of the Agreement shall terminate as of the Amendment Effective Date and be of no further force or effect: Article II (Option Grant and Development During Option Period), Article III (License Grants), Article IV (Governance During License Term), Article V (Development During License Term), Article VI

(Commercialization During License Term), Article VII (Manufacture), Article IX (Intellectual Property Ownership, Protection and Related Matters), Article XIII (Control Assumption Options) and Article XIV (Term; Termination and Remedies for Breach).

(b) The Parties agree that the following provisions of the Agreement shall terminate as of the Amendment Effective Date and be of no further force or effect: Section 8.1 (Initial Fee), Section 8.2 (Equity Purchase), Section 8.3 (Payments bv Biogen Idec During Option Exercise Period), Section 8.4 (Milestone Payments by Biogen Idec After Exercise of Option), Section 8.5 (Royalty Payments by Biogen Idec), Section 8.6 (Royalty Payments by AVEO), Section 8.7 (Restrictions on Bundling), Section 8.8 (Royalty Term), Section 8.9 (Third Party Licenses), Section 8.16(b) (Records and Audits — Development Costs) Section 10.3 (Publicity), Section 10.4 (Publications), Section 12.1 (Indemnification by Biogen Idec) and Section 12.5 (Insurance).

3. Continuing Provisions. The Parties agree that the following provisions of the Agreement shall continue following the Amendment Effective Date and be of full force and effect (such provisions, the "Continuing Provisions"): Article I (Definitions), Section 8.10 (Payments; Reports), Section 8.11 (Taxes), Section 8.12 (United States Dollars), Section 8.13 (Currency Conversion), Section 8.14 (Blocked Payments), Section 8.15 (Late Payments) and Section 8.16(a) (Records and Audits - Royalties), Section 10.1 (Confidential Information), Section 10.2 (Permitted Disclosures), Article XI (Representations and Warranties), Section 12.2 (Indemnification by AVEO), Section 12.3 (Indemnification Procedure), Section 12.4 (Limitation of Liability), Article XV (Dispute Resolution) and Article XVI (Miscellaneous).

4. AVEO Obligations

(a) Diligence Obligation. AVEO shall in good faith use reasonable efforts to seek a collaboration partner for the purpose of funding further Development and Commercialization of Licensed Products. For purposes of clarity, the Parties understand that AVEO shall not be required by the Agreement or this Amendment No. 1, to further Develop or Commercialize a Licensed Product in the absence of a Third Party collaborator.

(b) Payment Obligations. AVEO shall pay the percentage of Milestone Payments (as defined below) and royalties set forth in subsection (c) and (d) below (the "AVEO Payment Obligations") to BIMA up to a cumulative payment amount of $50 million (the "Maximum Payment"). AVEO's obligations with respect to the AVEO Payment Obligations shall continue until such time as BIMA has received from AVEO the Maximum Payment, after which time no further amounts shall be owed by AVEO to BIMA under the Agreement or this Amendment No. 1. The Aveo Payment Obligations are in lieu of all other payment obligations of AVEO to Biogen Idec and/or BIMA under the Agreement, including payments under Section 8.6 of the Agreement.

(c) Milestone Payments. AVEO shall pay to BIMA [**] percent ([**]%) of all Milestone Payments received by AVEO after the second anniversary of the Amendment Effective Date. Such payments shall be made within [**] days after the end of any Calendar Quarter in which any such Milestone Payments are received by AVEO. As used in this Amendment No. 1, "Milestone Payments" means any and all payments by a Third Party to AVEO in connection with

the achievement by AVEO or such Third Party (or any Sublicensee) of development, regulatory or commercial milestones relating to a Licensed Product, including sales-based milestones. For clarity, any upfront payments, payments for supplies or reimbursement of expenses are not included in Milestone Payments.

(d) Royalties on Net Sales. AVEO shall pay to BIMA royalties on Net Sales by AVEO, its Affiliates or Sublicensees of Licensed Products equal to [**] percent ([**]%) of such Net Sales. Such royalties shall be paid to BIMA in accordance with Section 8.10 of the Agreement.

(e) Applicable Provisions. For the avoidance of doubt, the provisions of Section 8.10 (Payments; Reports), Section 8.11 (Taxes), Section 8.12 (United States Dollars), Section 8.13 (Currency Conversion), Section 8.14 (Blocked Payments), Section 8.15 (Late Payments) and Section 8.16(a) (Records and Audits - Royalties) shall be applicable to payments under subsections (c) and (d) above.

5. Biogen Idec Obligations. As of the Amendment Effective Date, Biogen Idec and BIMA shall have no further obligations to AVEO under the Agreement, except to the extent such obligations arise under the Continuing Provisions.

6. Confidential Information. Notwithstanding anything to the contrary in Article X, the Parties agree that, in furtherance of its obligations under Section 4(a) of this Amendment No. 1, AVEO shall be allowed to disclose Confidential Information, including the Agreement and this Amendment No. 1, to potential Third Party collaborators and Sublicensees of Licensed Products; provided that, such potential collaborators and Sublicensees are subject to obligations of confidentiality and non-use consistent with the obligations set forth in Section 10.1 of the Agreement and AVEO shall remain responsible for any failure of such collaborator or sublicensee to treat such Confidential Information as required under Section 10.1 of the Agreement.

7. Term. Notwithstanding the termination of Section 14.1 of the Agreement, the Agreement, as amended by this Amendment No. 1, shall remain in effect until the expiration of AVEO's payment obligations under Section 4 above upon payment of amounts equal to the Maximum Payment.

IN WITNESS WHEREOF, AVEO and BIMA have caused this Amendment No. 1 to be duly executed by their authorized representatives on the Amendment Effective Date.

AVEO PHARMACEUTICALS, INC.

By: /s/ Tuan Ha Ngoc
Name: Tuan Ha-Ngoc
Title: President and Chief Executive Officer

BIOGEN IDEC MA INC.

By: /s/ Lynne Sullivan

Name: Lynne Sullivan

Title: Director

EXHIBIT 21.1

SUBSIDIARIES OF THE REGISTRANT

Name	Jurisdiction of Organization	Percentage Ownership
AVEO Pharma Limited	United Kingdom	100%
AVEO Securities Corporation	Massachusetts	100%
AVEO Pharma (Ireland) Limited	Ireland	100%

EXHIBIT 23.1

Consent of Independent Registered Public Accounting Firm

We consent to the incorporation by reference in the following Registration Statements:

(1) Registration Statement (Form S-8 Nos. 333-221838, 333-189565, 333-175390, 333-165530 and 333-250276) of AVEO Pharmaceuticals, Inc., and

(2) Registration Statement (Form S-3 No. 333-212051, No. 333-221837, and No. 333-249982) of AVEO Pharmaceuticals, Inc.;

of our reports dated March 16, 2021, with respect to the consolidated financial statements of AVEO Pharmaceuticals, Inc. and the effectiveness of internal control over financial reporting of Aveo Pharmaceuticals, Inc. included in this Annual Report (Form 10-K) for the year ended December 31, 2020.

/s/ Ernst & Young LLP

Boston, Massachusetts
March 16, 2021

EXHIBIT 31.1

CERTIFICATION

I, Michael Bailey, certify that:

1. I have reviewed this Annual Report on Form 10-K of AVEO Pharmaceuticals, Inc.;

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

4. The registrant's other certifying officer and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:

   (a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

   (b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, 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;

   (c) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

   (d) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

5. The registrant's other certifying officer and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):

   (a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

   (b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: March 16, 2021

/s/ Michael Bailey
Michael Bailey
Chief Executive Officer (Principal Executive Officer)

EXHIBIT 31.2

CERTIFICATION

I, Erick Lucera, certify that:

1. I have reviewed this Annual Report on Form 10-K of AVEO Pharmaceuticals, Inc.;

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

4. The registrant's other certifying officer and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:

   (a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

   (b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, 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;

   (c) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

   (d) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

5. The registrant's other certifying officer and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):

   (a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

   (b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: March 16, 2021

/s/ Erick Lucera
Erick Lucera
Chief Financial Officer (Principal Financial Officer)

EXHIBIT 32.1

CERTIFICATION PURSUANT TO 18 U.S.C. SECTION 1350,

AS ADOPTED PURSUANT TO

SECTION 906 OF THE SARBANES-OXLEY ACT OF 2002

In connection with the Annual Report on Form 10-K of AVEO Pharmaceuticals, Inc. (the "Company") for the fiscal year ended December 31, 2020 as filed with the Securities and Exchange Commission on the date hereof (the "Report"), the undersigned, Michael Bailey, Chief Executive Officer of the Company, hereby certifies, pursuant to 18 U.S.C. Section 1350, that, to his knowledge on the date hereof:

(1) The Report fully complies with the requirements of Section 13(a) or 15(d) of the Securities Exchange Act of 1934; and

(2) The information contained in the Report fairly presents, in all material respects, the financial condition and results of operations of the Company.

Date: March 16, 2021

/s/ Michael Bailey
Michael Bailey
Chief Executive Officer (Principal Executive Officer)

EXHIBIT 32.2

CERTIFICATION PURSUANT TO 18 U.S.C. SECTION 1350,

AS ADOPTED PURSUANT TO

SECTION 906 OF THE SARBANES-OXLEY ACT OF 2002

In connection with the Annual Report on Form 10-K of AVEO Pharmaceuticals, Inc. (the "Company") for the fiscal year ended December 31, 2020 as filed with the Securities and Exchange Commission on the date hereof (the "Report"), the undersigned, Erick Lucera, Chief Financial Officer of the Company, hereby certifies, pursuant to 18 U.S.C. Section 1350, that, to his knowledge on the date hereof:

(1) The Report fully complies with the requirements of Section 13(a) or 15(d) of the Securities Exchange Act of 1934; and

(2) The information contained in the Report fairly presents, in all material respects, the financial condition and results of operations of the Company.

Date: March 16, 2021

/s/ Erick Lucera
Erick Lucera
Chief Financial Officer (Principal Financial Officer)