AVEO PHARMACEUTICALS INC
Form 424B5
April 04, 2019
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Filed pursuant to Rule 424(b)(5)
Registration No. 333-221837

Prospectus Supplement

(To Prospectus dated December 15, 2017)

AVEO PHARMACEUTICALS, INC.

21,739,131 Shares of Common Stock

Warrants to Purchase up to 21,739,131 Shares of Common Stock

AVEO Pharmaceuticals, Inc. is offering 21,739,131 shares of common stock and warrants to purchase up to 21,739,131 shares of common stock. We are also offering the shares of common stock issuable from time to time upon exercise of the warrants being offered by this prospectus supplement.

The shares of common stock and warrants will be sold in fixed combinations, with each share of common stock that we sell in this offering being accompanied by a warrant to purchase one share of common stock. The public offering price per share of common stock and the accompanying warrant is $1.15. Each warrant will have an exercise price of $1.25 per share of common stock, will be immediately exercisable from and after the date of issuance and expire on the second anniversary of such date. The shares of common stock and warrants are immediately separable and will be issued separately, but can only be purchased together in this offering.

Our common stock is listed on The Nasdaq Capital Market under the symbol AVEO. There is no established trading market for any of the warrants, and we do not expect a market to develop. We do not intend to apply for a listing for any of the warrants on any securities exchange or other nationally recognized trading system. Without an active trading market, the liquidity of the warrants will be limited.

The last reported sale price for our common stock on April 3, 2019, was $1.31 per share.

This investment involves risk. See Risk Factors beginning on page S-17 and in filings with the U.S. Securities and Exchange Commission that are incorporated by reference in this prospectus supplement.

	Per Share and Accompanying Warrant	Total
Public offering price	$ 1.15	$ 25,000,000.65
Underwriting discounts and commissions[(1)]	$ 0.0805	$ 1,750,000.05
Proceeds, before expenses, to AVEO Pharmaceuticals, Inc.	$ 1.0695	$ 23,250,000.60

(1) See Underwriting beginning on page S-36 for additional information regarding total underwriter compensation, including expenses for which we have agreed to reimburse the underwriter.

Delivery of the shares of common stock and the warrants to investors is expected on or about April 8, 2019. We have granted the underwriter an option for a period of 30 days to purchase up to 3,260,869 additional shares of common stock and/or to purchase warrants to purchase an aggregate of up to 3,260,869 shares of our common stock, in any combinations thereof, from us at the public offering price per share of common stock of $1.14 or the public offering price per warrant of $0.01, as applicable, less the underwriting discounts and commissions.

Neither the U.S. Securities and Exchange Commission nor any state securities commission has approved or disapproved of these securities or determined if this prospectus supplement or the accompanying prospectus is truthful or complete. Any representation to the contrary is a criminal offense.

H.C. Wainwright & Co.

The date of this prospectus supplement is April 3, 2019

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ABOUT THIS PROSPECTUS SUPPLEMENT

This document is in two parts. The first part is this prospectus supplement, which describes the specific terms of this offering and also adds to and updates information contained in the accompanying prospectus and the documents incorporated by reference herein. The second part, the accompanying prospectus, provides more general information. Generally, when we refer to this prospectus, we are referring to both parts of this document combined. To the extent there is a conflict between the information contained in this prospectus supplement and the information contained in the accompanying prospectus or any document incorporated by reference therein filed prior to the date of this prospectus supplement, you should rely on the information in this prospectus supplement; provided that if any statement in one of these documents is inconsistent with a statement in another document having a later date for example, a document incorporated by reference in the accompanying prospectus the statement in the document having the later date modifies or supersedes the earlier statement.

We further note that the representations, warranties and covenants made by us in any agreement that is filed as an exhibit to any document that is incorporated by reference herein were made solely for the benefit of the parties to such agreement, including, in some cases, for the purpose of allocating risk among the parties to such agreements, and should not be deemed to be a representation, warranty or covenant to you. Moreover, such representations, warranties or covenants were accurate only as of the date when made. Accordingly, such representations, warranties and covenants should not be relied on as accurately representing the current state of our affairs.

You should rely only on the information contained in this prospectus supplement or the accompanying prospectus, or incorporated by reference herein. We have not authorized, and the underwriter has not authorized, anyone to provide you with information that is different. The information contained in this prospectus supplement or the accompanying prospectus, or incorporated by reference herein, is accurate only as of the respective dates thereof, regardless of the time of delivery of this prospectus supplement and the accompanying prospectus or of any sale of our securities. It is important for you to read and consider all information contained in this prospectus supplement and the accompanying prospectus, including the documents incorporated by reference herein, in making your investment decision. You should also read and consider the information in the documents to which we have referred you in the sections entitled Where You Can Find More Information and Incorporation by Reference in this prospectus supplement and in the accompanying prospectus.

We are offering to sell, and seeking offers to buy, our securities only in jurisdictions where offers and sales are permitted. The distribution of this prospectus supplement and the accompanying prospectus and the offering of our securities in certain jurisdictions may be restricted by law. Persons outside the United States who come into possession of this prospectus supplement and the accompanying prospectus must inform themselves about, and observe any restrictions relating to, the offering of our securities and the distribution of this prospectus supplement and the accompanying prospectus outside the United States. This prospectus supplement and the accompanying prospectus do not constitute, and may not be used in connection with, an offer to sell, or a solicitation of an offer to buy, any securities offered by this prospectus supplement and the accompanying prospectus by any person in any jurisdiction in which it is unlawful for such person to make such an offer or solicitation.

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PROSPECTUS SUPPLEMENT SUMMARY

This summary does not contain all of the information that you should consider before investing in our securities. You should read this entire prospectus supplement and the accompanying prospectus carefully, including the financial statements and other information incorporated by reference in this prospectus supplement and the accompanying prospectus, before making an investment decision. In addition, please read the Risk Factors section of this prospectus supplement beginning on page S-17 and the risk factors contained in our Annual Report on Form 10-K for the year ended December 31, 2018.

Overview

We are a biopharmaceutical company seeking to advance targeted medicines for oncology and other unmet medical needs. We are working to develop and commercialize our lead candidate tivozanib in North America as a treatment for advanced or metastatic renal cell carcinoma, or RCC. In November 2018, we announced that our phase 3 randomized, controlled, multi-center, open-label trial comparing tivozanib to an approved therapy, sorafenib (Nexavar®), in 350 subjects as a third- and fourth-line treatment for RCC, including subjects with prior checkpoint inhibitor therapy, which we refer to as the TIVO-3 trial, met its primary endpoint of improving progression-free survival, or PFS. Data for the secondary endpoint of the TIVO-3 trial, overall survival, or OS, was not mature as of the time of the final PFS analysis. In January 2019, the U.S. Food and Drug Administration, or FDA, recommended that we not submit a new drug application, or NDA, for tivozanib at this time as the preliminary OS results from the TIVO-3 trial did not allay its concerns about a potential detriment in OS from our previously completed phase 3 trial for tivozanib in the first-line treatment of RCC, which we refer to as the TIVO-1 trial. Following discussion with the FDA, we have extended the timeline for the TIVO-3 trial OS analysis and plan to conduct another interim OS analysis in August 2019. We anticipate reporting the results of this analysis in the fourth quarter of 2019, and plan to provide an update regarding the potential submission of an NDA for tivozanib to the FDA.

We are leveraging several collaborations in the development of tivozanib. We have sublicensed tivozanib, marketed under the brand name FOTIVDA®, for oncological indications in Europe and other territories outside of North America. Through our partner, tivozanib is approved in the European Union, or EU, as well as Norway and Iceland, for the first-line treatment of adult patients with RCC and for adult patients who are vascular endothelial growth factor receptor, or VEGFR, and mTOR pathway inhibitor-naïve following disease progression after one prior treatment with cytokine therapy for RCC. We also have clinical collaborations to study tivozanib in combination with immune checkpoint inhibitors in RCC and in hepatocellular carcinoma, or HCC. We are conducting a 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, which we refer to as the TiNivo trial. Leveraging early monotherapy results in HCC, we have a clinical collaboration to study tivozanib in combination with IMFINZI® (durvalumab), a PD-L1 inhibitor, for the treatment of advanced, unresectable HCC. In addition, a new formulation of tivozanib is in preclinical development for the treatment of age-related macular degeneration.

As part of our strategy, we have also entered into partnerships to help fund the development and commercialization of our other product candidates. Ficlatuzumab, a hepatocyte growth factor, or HGF, inhibitory antibody, is currently being tested in several investigator sponsored studies jointly funded by us and one of our development partners for the potential treatment of squamous cell carcinoma of the head and neck, or HNSCC, acute myeloid leukemia, or AML, and pancreatic cancer. Our partner for AV-203, an anti-ErbB3 monoclonal antibody, is planning to initiate clinical studies in China in 2019 in esophageal squamous cell carcinoma, or ESCC, and has committed to funding the development of AV-203 through proof-of-concept. We have recently regained the rights to AV-380, a humanized IgG1 inhibitory monoclonal antibody targeting growth differentiation factor 15, or GDF15, a divergent member of the TGF-ß family, for the potential treatment of cancer cachexia, and are working to initiate preclinical toxicology studies

in 2019 to support the potential

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filing of an investigational new drug application, or IND, with the FDA. We are evaluating options for the development of our preclinical AV-353 platform which targets the Notch 3 pathway.

Our Product Candidates

Tivozanib

Our pipeline includes our lead candidate tivozanib, an oral, once-daily, VEGFR tyrosine kinase inhibitor, or TKI. Tivozanib is a potent, selective and long half-life inhibitor of all three VEGF receptors and is designed to optimize VEGF blockade while minimizing off-target toxicities, potentially resulting in improved efficacy and minimal dose modifications. Tivozanib has been investigated in several tumor types, including renal cell, hepatocellular, colorectal and breast cancers, as well as in age-related macular degeneration. We have exclusive rights to develop and commercialize tivozanib in all countries outside of Asia and the Middle East under a license from Kyowa Hakko Kirin Co., Ltd. (formerly Kirin Brewery Co., Ltd.), or KHK. We have sublicensed to EUSA Pharma (UK) Limited, or 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 ocular conditions, to which we have retained development rights in all of our licensed territories. We are planning further development of tivozanib as a combination therapy with immune checkpoint inhibitors for the treatment of RCC and HCC.

Clinical and Regulatory Development 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 for PFS with a median PFS in the tivozanib arm of 11.9 months compared with 9.1 months in the sorafenib arm. The trial also showed significant improvement in overall response rate, or ORR, of 33.1% for tivozanib 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. 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 (hazard ratio (HR)=1.245, p=0.105). 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 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 (hazard ratio (HR)=1.147, p=0.276). We believe that an imbalance in subsequent therapy combined with the significant activity seen with tivozanib treatment following sorafenib contributed to the discordance in the efficacy results in the TIVO-1 trial between the PFS and ORR benefit, which significantly favored tivozanib, and the OS, which trended in favor of sorafenib. In 2012, we submitted an NDA to the FDA seeking U.S. marketing approval for tivozanib. In June 2013, the FDA issued a complete response letter informing us that it would not approve tivozanib for the first-line treatment of RCC based solely on the data from this single pivotal trial (TIVO-1), and recommended that we perform an additional clinical trial adequately sized to assure the FDA that tivozanib does not adversely affect OS.

TIVO-1 Extension Study One-way crossover from sorafenib to tivozanib (Study 902): We completed a TIVO-1 extension study in which patients with 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 Study 902 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

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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.

First-Line Approval in Europe: In February 2016, EUSA submitted an application for the use of tivozanib as a first-line treatment for RCC to the EMA based on the data from our TIVO-1 clinical trial, as supported by data from the TIVO-1 extension trial, one phase 1 trial and two phase 2 trials in RCC. In June 2017, following an oral explanation, the Committee for Medicinal Products for Human Use, or CHMP, which is the scientific committee of the EMA, issued an opinion recommending tivozanib for approval. In August 2017, the European Commission granted marketing authorization to EUSA for tivozanib in all 28 countries of the EU, Norway and Iceland. Tivozanib is sold under the brand name FOTIVDA, and is approved 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.

EUSA has commercially launched FOTIVDA in the United Kingdom, Germany, Austria, the Netherlands and Sweden. In November 2017, EUSA initiated product sales in Germany and in November 2018, EUSA received reimbursement approval from the German Federal Association of the Statutory Health Insurances, or GKV-SV, for the first-line treatment of adult patients with RCC. In February 2018, EUSA commercially launched FOTIVDA in the United Kingdom upon receiving reimbursement approval from the United Kingdom s National Institute for Health and Care Excellence, or the NICE, for the first-line treatment of adult patients with RCC. EUSA is working to secure reimbursement approval in Italy, Spain and France and commercially launch FOTIVDA in additional European countries. In January 2019, we were informed by EUSA that the CHMP requested the topline data results from our TIVO-3 trial for review at the CHMP s January 2019 plenary meeting under its post-authorization monitoring procedures. Subsequently, EUSA informed us that the CHMP requested additional data analyses from our TIVO-3 trial. Following its review of these data analyses, the CHMP has determined that the analyses of various factors that may have impacted the preliminary OS data from our TIVO-3 trial do not fully explain the discordance between the PFS results (HR=0.73) and the preliminary OS results (HR=1.12) in the TIVO-3 trial, and that more mature OS data is required prior to drawing a conclusion. Similar to the FDA, the CHMP accepted the proposal to conduct an additional interim OS analysis in August 2019. The CHMP further provided that regulatory action should be considered if the August 2019 interim OS analysis confirms a negative trend in OS.

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.

Third-Line and Fourth-Line Phase 3 Trial (TIVO-3): In May 2016, we initiated enrollment in the TIVO-3 trial, a phase 3 trial of tivozanib in the third- and fourth-line treatment of patients with RCC. The TIVO-3 clinical trial was designed to address the FDA s concern about the negative OS trend expressed in the complete response letter from June 2013. TIVO-3, together with the previously completed TIVO-1 trial of tivozanib in the first-line treatment of RCC, is designed to support a regulatory submission of tivozanib in the United States as a treatment for RCC in multiple lines of therapy. 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 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 in one therapy to cross over to the other therapy.

The TIVO-3 trial enrolled a total of 350 patients. In October 2017, TIVO-3 successfully passed a pre-planned interim futility analysis. Based on the results of the futility analysis, which were reviewed by an

independent statistician, the trial continued as planned without modification. The trial has also passed three semi-annual safety data assessments.

On November 5, 2018, we announced positive topline results for the primary endpoint of the TIVO-3 trial. The trial met its primary endpoint for 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, and PFS for tivozanib was longer than for sorafenib both in patients who received prior checkpoint inhibitor therapy and those who received two prior VEGF TKI therapies. Patients who received prior checkpoint inhibitor therapy had a median PFS of 7.3 months with tivozanib and 5.1 months with sorafenib (HR=0.55, p=0.03). The analysis of the secondary endpoint of OS was not mature at the time of the final PFS analysis and after taking into account the survival status of a group of patients that were previously lost to follow-up, the preliminary OS analysis showed a hazard ratio of 1.12 and a p-value of 0.44. 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, with Grade 3 or higher adverse events 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 event in patients receiving tivozanib was hypertension, an adverse event known to reflect effective VEGF pathway inhibition.

At a meeting in January 2019 with the FDA, the FDA recommended that we not submit an NDA for tivozanib at this time as the preliminary OS results from the TIVO-3 trial did not allay its concerns about a potential detriment in OS outlined in its complete response letter delivered to us in June 2013 regarding the TIVO-1 trial, which had shown a protocol-specified final OS hazard ratio of 1.245. On February 5, 2019, we received final minutes from that meeting with the FDA. The minutes reflect our agreement with the FDA not to submit an NDA for tivozanib at this time and include the FDA s recommendation that we not conduct any exploratory OS analyses. We previously planned to conduct the final OS analysis per protocol in August 2019. However, due to the longer-than-expected median OS in both the tivozanib and sorafenib arms, and following our discussion with the FDA, we plan to designate the OS analysis to be conducted in August 2019 as a second interim analysis. We anticipate reporting the results of this analysis in the fourth quarter of 2019, and plan to provide an update regarding the potential submission of an NDA for tivozanib to the FDA.

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

In March 2017, we initiated enrollment in the TiNivo trial, a phase 1b/2 clinical trial of tivozanib in combination with Opdivo (nivolumab), an immune checkpoint (PD-1) inhibitor, for the treatment of RCC. The TiNivo trial enrolled a total of 28 patients. We are sponsoring the trial, for which Bristol-Myers Squibb, or BMS, has supplied nivolumab. The TiNivo trial is being led by the Institut Gustave Roussy in Paris under the direction of Professor Bernard Escudier, MD, Chairman of the Genitourinary Oncology Committee. The phase 1b portion of the TiNivo trial enrolled six patients. In June 2017, we successfully completed the phase 1 dose escalation portion of the trial, where oral

tivozanib was administered in two escalating dose cohorts in combination with intravenous nivolumab at a constant 240 mg every two weeks. The full dose tivozanib regimen of 1.5 mg daily for 21 days, followed by a 7-day rest period, was selected as the recommended phase 2 dose for the expansion

portion of the trial. On November 3, 2017, the results from the phase 1b portion of the TiNivo trial were presented at the 16th International Kidney Cancer Symposium of the Kidney Cancer Association. The phase 1b portion of the TiNivo trial demonstrated that the combination of tivozanib and nivolumab was well tolerated to the full dose and schedule of single agent tivozanib, with no dose limiting toxicities.

The phase 2 portion of the trial, which enrolled an additional 22 patients, was designed to assess the safety, tolerability, and anti-tumor activity of the combination of tivozanib and nivolumab. On February 10, 2018, we presented preliminary results from the phase 2 portion of the TiNivo trial at the 2018 ASCO Genitourinary Cancers Symposium. On October 22, 2018, we presented updated interim results from all 25 patients treated at full dose at the ESMO 2018 Congress. The combination was generally well tolerated. Treatment-related Grade 3/4 adverse events occurred in 60% of patients, the most common of which was hypertension. Preliminary efficacy was assessed in all 25 patients, who were treated with the full dose and schedule of oral tivozanib in combination with intravenous nivolumab. Of these patients, 13 (52%) had received at least one prior systemic therapy, including two (8%) that had received prior PD-1 therapy, and 12 (48%) were treatment naïve. An ORR was observed in 14 patients (56%) (complete response plus partial response), including one 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. At the time of data collection, 13 patients (52%) remained on study and 18 patients (72%) had tumor shrinkage of at least 25%, with a majority of patients having disease control for at least 48 weeks.

Clinical Development in HCC

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

The trial was designed to evaluate the safety and efficacy of tivozanib in advanced HCC, and enrolled a total of 21 patients at three trial sites. In the phase 1b portion of the trial, which used a modified 3 + 3 dose escalation design, 8 patients were dosed with tivozanib starting at 1.0 mg or 1.5 mg daily for 21 days followed by 7 days off drug. 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.

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

HCC PD-L1 Combination Trial with IMFINZI®: On December 11, 2018, we entered into a clinical supply agreement with a wholly-owned subsidiary of AstraZeneca PLC, or AstraZeneca, to evaluate the safety and efficacy of AstraZeneca s IMFINZI (durvalumab), a human monoclonal antibody directed against programmed death-ligand 1, or PD-L1, in combination with tivozanib as a first-line treatment for patients with advanced, unresectable HCC in a phase 1/2 study. We will serve as the study sponsor; each party will contribute the clinical supply of its study drug; and study costs will be otherwise shared equally. The phase 1 portion of the study is expected to commence in 2019.

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Ficlatuzumab

Ficlatuzumab is a potent HGF inhibitory antibody. HGF is the sole known ligand of the c-Met receptor, which is believed to trigger many activities that are involved in cancer development and metastasis. We have partnered with Biodesix, Inc., or Biodesix, under a worldwide Co-Development and Collaboration Agreement, or the Biodesix Agreement, to develop and commercialize ficlatuzumab. Under the Biodesix Agreement, we and Biodesix each contribute half of the development costs of ficlatuzumab.

Development in HNSCC. We and Biodesix funded an investigator-sponsored phase 1 clinical trial of ficlatuzumab in combination with 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, in addition to being well tolerated. A randomized, phase 2, multicenter, investigator-initiated trial in ERBITUX® (cetuximab) refractory patients to confirm these findings was initiated in the fourth quarter of 2017 under the direction of Julie E. Bauman, MD, MPH, Chief, Division of Hematology/Oncology at the University of Arizona Cancer Center. The phase 2 trial is designed to enroll approximately 60 patients randomized to receive either ficlatuzumab alone or ficlatuzumab and cetuximab.

Development in AML. We and Biodesix are funding an investigator-sponsored phase 1/2 clinical trial of ficlatuzumab in combination with cytarabine in AML. In June 2017, preliminary results from the phase 1 trial were presented at the 2017 ASCO Annual Meeting. This trial, exploring ficlatuzumab in combination with high-dose cytarabine in patients with high risk relapsed or refractory AML, demonstrated early signs of tolerability and activity, including a 50% complete response rate in the eight evaluable patients. The phase 2 portion is ongoing and expected to enroll ten additional patients. On April 1, 2019, data from the phase 1b expansion cohort was presented at the 2019 American Association for Cancer Research Annual Meeting. The data demonstrated a 50% complete response rate in the 18 patients enrolled in the trial, which was substantially consistent with the previously announced phase 1 trial results.

Development in pancreatic cancer. We and Biodesix are funding an investigator-sponsored phase 1/2 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. Preclinical findings demonstrated a beneficial effect of the drug combination of ficlatuzumab and gemcitabine compared to either drug alone in an in-vivo model of PDAC. The trial is designed to determine maximum tolerated dose of ficlatuzumab when combined with gemcitabine and nab-paclitaxel. Secondary outcome measures include response rate and PFS. The trial, which is being conducted under the direction of Kimberly Perez, MD, at the Dana-Farber Cancer Institute, is expected to enroll approximately 24 patients.

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

AV-203

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

recommended phase 2 dose, demonstrated good tolerability and promising early signs of activity, and reached the maximum planned dose of AV-203 monotherapy.

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We have partnered with CANbridge Life Sciences Ltd., or CANbridge, to develop, manufacture and commercialize AV-203 in all countries outside of North America. We have retained the North American rights to AV-203. CANbridge s obligations include conducting and funding clinical development of AV-203 through phase 2 proof-of-concept in ESCC. Following proof-of-concept, we may decide to participate in later-stage worldwide development efforts. In December 2017, CANbridge filed an IND in China seeking regulatory authorization to initiate clinical trials of AV-203, which CANbridge refers to as CAN017, in ESCC. In August 2018, the China National Drug Administration, or CNDA, approved this IND application. CANbridge has advised us that it plans to initiate a phase 1b/extension trial in ESCC in 2019.

AV-380

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

We believe that AV-380 represents a novel approach to treating cachexia because it has been demonstrated to address key underlying mechanisms of the syndrome. We have established preclinical proof-of-concept for GDF15 as a key driver of cachexia by demonstrating, in animal models, that the administration of GDF15 induces cachexia, and that inhibition of GDF15 reverses cachexia and provides a potential indication of an OS benefit. We have demonstrated preclinical proof-of-concept for AV-380 in multiple cancer cachexia models and have completed cell line development. In connection with the AV-380 program, we have in-licensed certain patents and patent applications from St. Vincent s Hospital Sydney Limited in Sydney, Australia, which we refer to as St. Vincent s.

In August 2015, we entered into a license agreement pursuant to which we granted Novartis International Pharmaceutical Ltd., or Novartis, the exclusive right to develop and commercialize AV-380 and our related antibodies worldwide. On June 29, 2018, Novartis notified us that it would be terminating the agreement, which we refer to as the Novartis License Agreement, without cause, following a change in strategic direction at Novartis. Effective August 28, 2018, we regained worldwide rights to the AV-380 program, and on December 18, 2018, we entered into a new agreement with Novartis, or the AV-380 Transfer Agreement, to further establish and clarify the terms on which Novartis will return the AV-380 program to us to support our continuing development of the AV-380 program. We are working to initiate preclinical toxicology studies in 2019 to support a potential IND filing with the FDA.

AV-353 Platform

The AV-353 platform includes a number of potent inhibitory antibody candidates specific to Notch 3. The Notch 3 pathway is important in cell-to-cell communication involving gene regulation mechanisms that control multiple cell differentiation processes during the entire life cycle. Scientific literature has implicated the Notch 3 receptor pathway in multiple diseases, including cancer, cardiovascular diseases, such as pulmonary arterial hypertension, and neurodegenerative conditions. We are currently evaluating options to develop the AV-353 platform.

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Strategic Partnerships

We have established various strategic partnerships 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 tivozanib in combination with immune checkpoint inhibitors, see Our Product Candidates Tivozanib Clinical and Regulatory Development in RCC RCC PD-1 Combination Trial with Opdivo (TiNivo) and Our Product Candidates Tivozanib Clinical Development in HCC HCC PD-L1 Combination Trial with IMFINZI.

CANbridge

In March 2016, we entered into a collaboration and license agreement with CANbridge, or the CANbridge Agreement, under which we granted CANbridge the exclusive right to develop, manufacture and commercialize AV-203, our proprietary ErbB3 (HER3) inhibitory antibody, for the diagnosis, treatment and prevention of disease in all countries outside of North America. In addition, CANbridge has a right of first negotiation if we determine to outlicense any North American rights. The parties have both agreed not to develop or commercialize any ErbB3 inhibitory antibody other than AV-203 during the term of the CANbridge Agreement. CANbridge has responsibility for all activities and costs associated with the development, manufacture and commercialization of AV-203 in its territories. CANbridge is obligated to use commercially reasonable efforts to develop and obtain regulatory approval for AV-203 in each of China, Japan, the United Kingdom, France, Italy, Spain and Germany. Under the CANbridge Agreement, CANbridge is required to conduct and fund the clinical development of AV-203 through phase 2 proof-of-concept in esophageal squamous cell carcinoma, or ESCC, after which we may elect to contribute to certain worldwide development efforts.

In December 2017, CANbridge filed an IND application with the CNDA for a clinical study of AV-203 in ESCC. CANbridge s IND application was accepted by the CNDA in August 2018. CANbridge has advised us that it plans to initiate a phase 1b/extension trial in ESCC in 2019.

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. In August 2018, CANbridge obtained regulatory approval of its IND application from the CNDA 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.

Pursuant to the CANbridge Agreement, we are eligible to receive up to $40.0 million in potential additional development and regulatory milestone payments and up to $90.0 million in potential commercial milestone payments based on annual net sales of licensed products. Upon commercialization, we are eligible to receive a tiered royalty, with a percentage range in the low double-digits, on net sales of approved licensed products. CANbridge s obligation to pay royalties for each licensed product expires on a country-by-country basis on the later of the expiration of patent rights covering such licensed product in such country, the expiration of regulatory data exclusivity in such country or ten years after the first commercial sale of such licensed product in such country. A percentage of any milestone and royalty payments received by us under the CANbridge Agreement, 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 CNDA 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.

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

EUSA

In December 2015, we entered into a license agreement with EUSA, 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 ocular conditions. EUSA is obligated to use commercially reasonable efforts to seek regulatory approval for and commercialize tivozanib throughout its licensed territories for RCC. EUSA has responsibility for all activities and costs associated with the further development, manufacture, regulatory filings and commercialization of tivozanib in its licensed territories.

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

We are entitled to receive milestone payments of $2.0 million per country upon reimbursement approval, if any, for RCC in each of France, Germany, Italy, Spain and the United Kingdom, which we refer to collectively as the EU5, and 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. In February 2018 and in November 2018, EUSA obtained reimbursement approval from the NICE in the United Kingdom and the GKV-SV in Germany, respectively, for the first-line treatment of RCC. Accordingly, we earned a $2.0 million milestone payment with respect to the reimbursement approval in the United Kingdom that was received from EUSA in March 2018 and a $2.0 million milestone payment with respect to the reimbursement approval in Germany that was received from EUSA in December 2018. 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 tivozanib (FOTIVDA) with the initiation of product sales in Germany. The commercial launch expanded to the United Kingdom following the reimbursement approval by the NICE in February 2018. In

addition, EUSA has launched FOTIVDA in several non-EU5 European countries and is working toward launching FOTIVDA in additional European territories. We recognized approximately $0.5 million and $19,000 in revenue for sales royalties in the years ended December 31, 2018 and 2017, respectively.

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The research and development reimbursement payments under the EUSA Agreement are not subject to the 30% sublicensing payment payable to KHK, subject to certain limitations. We would, however, owe KHK 30% of other, non-research and development payments we may receive from EUSA pursuant to 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 and November 2018 upon EUSA s reimbursement approval for FOTIVDA in the United Kingdom and in Germany, respectively, were subject to the 30% KHK sublicense fee, or $0.6 million, each. We paid the sublicense fees for EUSA s reimbursement approvals in the United Kingdom and Germany in April 2018 and in January 2019, respectively.

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.

Novartis

In August 2015, we entered into the Novartis License Agreement, under which we granted Novartis the exclusive right to develop and commercialize AV-380 and our related antibodies worldwide. Novartis was responsible under the Novartis License Agreement for the development, manufacture and commercialization of our antibodies and any resulting approved therapeutic products. On June 29, 2018, Novartis notified us that it would be terminating our collaboration without cause following a change in strategic direction at Novartis. Effective August 28, 2018, the Novartis License Agreement was terminated, and we regained worldwide rights to the AV-380 program. Novartis termination without cause triggered the termination of all licenses and other rights granted by us to Novartis with regard to the AV-380 program, and the grant by Novartis to us of an irrevocable, exclusive, fully paid-up license, with a right to sub-license, to any patent rights or know-how controlled by Novartis as of the termination date related to the AV-380 program. Following termination, Novartis has initiated the process of transferring the AV-380 program back to us.

On December 18, 2018, we entered into the AV-380 Transfer Agreement to further establish and clarify the terms on which the AV-380 program will be returned to us, and to support our continuing development of the AV-380 program. The AV-380 Transfer Agreement provides for the continued transfer to us of all preclinical, technical, manufacturing and other data developed by Novartis relating to the AV-380 program, as well as cooperation regarding our future regulatory filings relating to AV-380. Pursuant to the AV-380 Transfer Agreement, Novartis also agreed to provide the AV-380 drug supply, valued at approximately $4.0 million, to us at no charge, and to make a one-time payment to us of $2.3 million, which was paid to us in January 2019 and we used to cover the $2.3 million time-based milestone obligation due to St. Vincent s in January 2019 under our license agreement as further described below under the heading St. Vincent s Hospital. The AV-380 Transfer Agreement contains mutual releases by both parties of all claims arising out of the Novartis License Agreement, other than indemnification obligations. Novartis has also agreed that it will not develop, manufacture or commercialize any anti-GDF15 antagonist antibody for three years following the date of the AV-380 Transfer Agreement.

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Biodesix

In April 2014, we entered into a worldwide co-development and collaboration agreement with Biodesix, or the Biodesix Agreement, to develop and commercialize ficlatuzumab. Under the Biodesix Agreement, we and Biodesix are each required to contribute 50% of all clinical, regulatory, manufacturing and other costs to develop ficlatuzumab, and would share equally in any future revenue from development or commercialization, subject to certain exceptions. We retain primary responsibility for clinical development of ficlatuzumab, although all trials are conducted pursuant to a joint development plan.

Under the Biodesix Agreement, we granted Biodesix perpetual, non-exclusive rights to certain intellectual property, including all clinical and biomarker data related to ficlatuzumab, to develop and commercialize VeriStrat®, Biodesix s proprietary companion diagnostic test. Biodesix granted us perpetual, non-exclusive rights to certain intellectual property, including diagnostic data related to VeriStrat, with respect to the development and commercialization of ficlatuzumab; each license includes the right to sublicense, subject to certain exceptions. In October 2016, we amended the Biodesix agreement in connection with the termination of the FOCAL trial, a phase 2 proof-of-concept clinical study of ficlatuzumab in which VeriStrat was used to select clinical trial subjects.

Prior to the first commercial sale of ficlatuzumab, each party has the right to elect to discontinue participating in further development or commercialization efforts with respect to ficlatuzumab, which is referred to as an Opt-Out . If either we or Biodesix elects to Opt-Out, with such party referred to as the Opting-Out Party, then the Opting-Out Party shall not be responsible for any future costs associated with developing and commercializing ficlatuzumab other than any ongoing clinical trials. If we elect to Opt-Out, we will continue to make the existing supply of ficlatuzumab available to Biodesix for the purposes of enabling Biodesix to complete the development of ficlatuzumab, and Biodesix will have the right to commercialize ficlatuzumab. After election of an Opt-Out, the non-opting out party shall have sole decision-making authority with respect to further development and commercialization of ficlatuzumab. Additionally, the Opting-Out Party shall be entitled to receive, if ficlatuzumab is successfully developed and commercialized, a royalty equal to 10% of net sales of ficlatuzumab throughout the world, if any, subject to offsets under certain circumstances. Prior to any Opt-Out, the parties shall share equally in any payments received from a third-party licensee; provided, however, after any Opt-Out, the Opting-Out Party shall be entitled to receive only a reduced portion of such third-party payments. The Biodesix Agreement remains in effect until the expiration of all payment obligations between the parties related to development and commercialization of ficlatuzumab, unless earlier terminated.

We and Biodesix are currently funding several investigator-sponsored clinical trials, including ficlatuzumab in combination with ERBITUX® (cetuximab) in squamous cell carcinoma of the head and neck, ficlatuzumab in combination with Cytosar (cytarabine) in acute myeloid leukemia and ficlatuzumab in combination with nab-paclitaxel and gemcitabine in pancreatic cancer. We continue to evaluate additional opportunities for the further clinical development of ficlatuzumab. Such clinical development, beyond what we are committed to, would require additional manufacturing efforts and costs.

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 Novartis Agreement, we amended and restated the St. Vincent s Agreement and paid St. Vincent s an additional upfront fee of $1.5 million. We are required to make future milestone payments, up to an aggregate total of $14.4 million (exclusive of the $2.3 million milestone payment due in January 2019 described below), upon the earlier of achievement of specified development and regulatory milestones or a specified date for the first indication, and upon the achievement of specified development and regulatory milestones for the second and third indications, for licensed therapeutic products, some of which payments may be increased by a mid to high double-digit percentage rate for milestones payments made after we grant any sublicense, 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. As further described above under the heading Novartis , we 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. 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.

Biogen Idec

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

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Kyowa Hakko Kirin

In December 2006, we entered into a license agreement with KHK, or the KHK Agreement, under which we obtained an exclusive license, with the right to grant sublicenses subject to certain restrictions, to research, develop, manufacture and commercialize tivozanib, pharmaceutical compositions thereof and associated biomarkers in all potential indications. Our exclusive license covers all territories in the world except for Asia and the Middle East, where KHK has retained the rights to tivozanib. Under the KHK Agreement, we obtained exclusive rights in our territory under certain KHK patents, patent applications and know-how related to tivozanib, to research, develop, make, have made, use, import, offer for sale, and sell tivozanib for the diagnosis, prevention and treatment of any and all human diseases and conditions. We and KHK each have access to and can benefit from the other party s clinical data and regulatory filings with respect to tivozanib and biomarkers identified in the conduct of activities under the KHK Agreement.

Under the KHK Agreement, we are obligated to use commercially reasonable efforts to develop and commercialize tivozanib in our territory. Prior to the first anniversary of the first post-marketing approval sale of tivozanib in our territory, neither we nor any of our subsidiaries has the right to conduct certain clinical trials of, seek marketing approval for or commercialize any other cancer product that also works by inhibiting the activity of a VEGF receptor.

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

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

Certain research and development reimbursement payments by EUSA, including the $2.5 million upfront payment in December 2015, the $4.0 million payment in September 2017 upon the receipt of marketing authorization from the European Commission for tivozanib (FOTIVDA) and the $2.0 million payment upon EUSA s election in September 2017 to opt-in to co-develop the TiNivo trial were not subject to sublicense revenue payments to KHK. In addition, if EUSA elects to opt-in to the TIVO-3 trial, the additional research and development reimbursement payment from EUSA of 50% of the total trial costs, up to $20.0 million, would also not be subject to a sublicense revenue payment to KHK, subject to certain limitations. We would, however, owe KHK 30% of other, non-research and development payments we may receive from EUSA pursuant to 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 and

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November 2018 upon EUSA s reimbursement approval for FOTIVDA in the United Kingdom and in Germany, respectively, were subject to the 30% KHK sublicense fee, or $0.6 million each. We paid the sublicense fees for EUSA s reimbursement approvals in the United Kingdom and Germany in April 2018 and in January 2019, respectively.

We are also required to pay tiered royalty payments on net sales we make of tivozanib in our North American territory, which range from the low to mid-teens as a percentage of net sales. The royalty rate escalates within this range based on increasing tivozanib sales. Our royalty payment obligations in a particular country in our territory begin on the date of the first commercial sale of tivozanib in that country, and end on the later of 12 years after the date of first commercial sale of tivozanib in that country or the date of the last to expire of the patents covering tivozanib that have been issued in that country.

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

Our 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 One Broadway, 14th Floor, Cambridge, Massachusetts 02142, and our telephone number is (617) 588-1960. Our internet website is www.aveooncology.com. Information found on, or accessible through, our website is not a part of, and is not incorporated into, this prospectus supplement and the accompanying prospectus, and you should not consider it part of this prospectus supplement and the accompanying prospectus. Our website address is included in this document as an inactive textual reference only. Unless the context otherwise requires, references in this prospectus to we, us, and our refer to AVEO Pharmaceuticals, Inc. and our subsidiaries.

The trademarks, trade names and service marks appearing in this prospectus supplement are the property of their respective owners.

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The Offering

Common stock offered by us pursuant to this prospectus supplement	21,739,131 shares of common stock. This prospect supplement also relates to the offering of shares of our common stock issuable upon exercise of the warrants, as discussed below.
Warrants offered by us pursuant to this prospectus supplement	Warrants to purchase up to 21,739,131 shares of common stock. Each warrant will have an exercise price of $1.25 per share of common stock, will be immediately exercisable and will expire on the second anniversary of its date of issuance. This prospectus supplement also relates to the offering of shares of our common stock issuable upon exercise of the warrants.
Common stock to be outstanding after this offering	160,739,471 shares of common stock, assuming no exercise of the warrants included in this offering.
Underwriter s option to purchase additional securities	We have granted the underwriter an option for a period of 30 days to purchase up to an additional 3,260,869 shares of our common stock and/or to purchase warrants to purchase an aggregate of up to 3,260,869 shares of common stock, in any combinations thereof, from us at the public offering price per share or per warrant, as applicable, less the underwriting discounts and commissions, on the same terms as set forth in this prospectus supplement.
Use of proceeds	We intend to use the net proceeds from this offering for ongoing clinical and preclinical development of our product candidates, as well as for working capital and other general corporate purposes. See Use of Proceeds on page S-22 of this prospectus supplement for more information.
Risk factors	See Risk Factors beginning on page S-17 and the other information included in, or incorporated by reference into, this prospectus supplement and the accompanying prospectus for a discussion of certain factors you should carefully consider before deciding to invest in our securities.
Nasdaq Capital Market symbol	Our common stock is listed on The Nasdaq Capital Market under the symbol AVEO. There is no established trading market for any of the warrants, and we do not expect a market to develop. We do not intend to

apply for a listing for any of the warrants on any securities exchange or other nationally recognized trading system. Without an active trading market, the liquidity of the warrants will be limited.

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The number of shares of our common stock to be outstanding after this offering is based on 126,484,781 shares of our common stock outstanding as of December 31, 2018, as adjusted for the additional 12,515,559 shares of our common stock issued and sold in February 2019 pursuant to our sales agreement with SVB Leerink LLC, or the Leerink Sales Agreement.

The number of shares of our common stock to be outstanding after this offering excludes:

- 9,583,349 shares of common stock issuable upon exercise of stock options outstanding as of December 31, 2018, at a weighted-average exercise price of $2.28 per share;
- 16,839,375 shares of common stock issuable upon exercise of warrants outstanding as of December 31, 2018, and issued in connection with a private placement financing in May 2016, which we refer to as the PIPE Warrants, at an exercise price of $1.00 per share;
- 2,000,000 shares of common stock issuable upon exercise of warrants outstanding as of December 31, 2018, and issued in connection with the settlement of a class-action securities litigation in July 2018, which we refer to as the Settlement Warrants, at an exercise price of $3.00 per share;
- 1,105,666 shares of common stock reserved as of December 31, 2018, for future issuance under our equity incentive plans; and
- 298,308 shares of common stock reserved as of December 31, 2018, for future issuance under our 2010 employee stock purchase plan.

In addition, unless otherwise indicated, all information in this prospectus supplement assumes no exercise of the warrants issued and sold in this offering.

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RISK FACTORS

An investment in our securities involves a high degree of risk. Before deciding whether to invest in our securities, you should consider carefully the risks described below and the risk factors contained in our Annual Report on Form 10-K for the year ended December 31, 2018, together with other information in this prospectus supplement, and the accompanying prospectus, and the information and documents incorporated by reference in this prospectus supplement and the accompanying prospectus, and in any free writing prospectus that we have authorized for use in connection with this offering. If any of these risks actually occurs, our business, financial condition, results of operations or cash flow could be seriously harmed. This could cause the trading price of our common stock to decline, resulting in a loss of all or part of your investment.

Risks Related to This Offering

We have broad discretion in the use of the net proceeds from this offering and may not use them effectively.

Our management will have broad discretion in the application of the net proceeds from this offering and could spend the proceeds in ways that do not improve our results of operations or enhance the value of our common stock. The failure by our management to apply these funds effectively could result in financial losses, and these financial losses could have a material adverse effect on our business, cause the price of our common stock to decline and delay the development of our product candidates. We may invest the net proceeds from this offering, pending their use, in a manner that does not produce income or that loses value.

If you purchase securities in this offering, you will suffer immediate dilution of your investment.

The public offering price of our common stock and the accompanying warrants is substantially higher than the net tangible book value per share of our common stock. Therefore, if you purchase securities in this offering, you will pay an effective price per share of common stock that substantially exceeds our net tangible book value per share after giving effect to this offering. Based on the public offering price of $1.15 per share of common stock and accompanying warrant and assuming no exercise of the warrants included in this offering, no value is attributed to such warrants and such warrants are classified as and accounted for as equity, if you purchase securities in this offering, you will experience immediate dilution of $1.13 per share, representing the difference between the public offering price of the securities and our pro forma as adjusted net tangible book value per share after giving effect to this offering. Furthermore, if any of our outstanding options or warrants are exercised at prices below the public offering price, we grant additional options or other awards under our equity incentive plans or issue additional warrants, the warrants issued in this offering are accounted for as liabilities or we issue additional shares of common stock in the future, you may experience further dilution of your investment. See the section entitled Dilution below for a more detailed illustration of the dilution you would incur if you participate in this offering.

There is no public market for the warrants to purchase common stock being offered by us in this offering.

There is no established public trading market for the warrants being offered in this offering, and we do not expect a market to develop. In addition, we do not intend to apply to list the warrants on any securities exchange or other nationally recognized trading system, including The Nasdaq Capital Market. Without an active trading market, the liquidity of the warrants will be limited.

Holders of warrants purchased in this offering will have no rights as common stockholders until such holders exercise their warrants and acquire our common stock.

Until holders of warrants acquire shares of our common stock upon exercise of the warrants, such holders will have no rights with respect to the shares of our common stock underlying such warrants. Upon exercise of the warrants, the holders thereof will be entitled to exercise the rights of common stockholders only as to matters for which the record date occurs after the exercise date.

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The warrants are speculative in nature.

The warrants do not confer any rights of common stock ownership on their holders, such as voting rights or the right to receive dividends, but rather merely represent the right to acquire shares of common stock at a fixed price for a limited period of time. Specifically, commencing on the date of issuance, holders of the warrants may exercise their right to acquire the common stock subject to such warrants and pay an exercise price per share equal to $1.25, subject to certain adjustments, prior to the second anniversary of the date of issuance, at which time they will be automatically exercised on a cashless basis.

Moreover, following this offering, the market value of the warrants, if any, is uncertain. There can be no assurance that the market value of the warrants will equal or exceed their offering price. The warrants will not be listed or quoted for trading on any market or exchange. There can be no assurance that the market price of the common stock will ever equal or exceed the exercise price of the warrants, and consequently, it may not ever be profitable for holders of the warrants to exercise the warrants.

If you purchase securities in this offering, you may also experience future dilution as a result of future equity offerings.

To raise additional capital, we may in the future offer additional shares of our common stock or other securities convertible into or exchangeable for our common stock at prices that may not be the same as the price paid by investors in this offering. We may sell shares or other securities in any other offering at a price per share that is less than the price paid by investors in this offering, and investors purchasing shares or other securities in the future could have rights superior to existing stockholders. The price per share at which we sell additional shares of our common stock, or securities convertible or exchangeable into common stock, in future transactions may be higher or lower than the price paid by investors in this offering.

Because we do not anticipate paying any cash dividends on our capital stock in the foreseeable future, capital appreciation, if any, will be your sole source of gain.

We have never declared or paid cash dividends on our capital stock. We currently intend to retain all of our future earnings, if any, to finance the growth and development of our business. In addition, the terms of our current debt financing arrangements preclude, and the terms of any future debt agreements may preclude, us from paying dividends. As a result, capital appreciation, if any, of our common stock will be your sole source of gain for the foreseeable future.

Our executive officers, directors and principal stockholders, if they choose to act together, have the ability to control all matters submitted to stockholders for approval.

Upon the closing of this offering, the number of shares of our common stock beneficially owned by our executive officers, directors and principal stockholders and their respective affiliates who owned more than 5% of our outstanding shares of common stock before this offering, will, in the aggregate, represent approximately 21% of our outstanding common stock. As a result, if these stockholders were to choose to act together, they would be able to control all matters submitted to our stockholders for approval, as well as our management and affairs. For example, these persons, if they choose to act together, would control the election of directors and approval of any merger, consolidation or sale of all or substantially all of our assets.

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This concentration of voting power may:

- delay, defer or prevent a change in control;
- entrench our management and the board of directors; or
- delay or prevent a merger, consolidation, takeover or other business combination involving us on terms that other stockholders may desire.

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CAUTIONARY NOTE REGARDING FORWARD-LOOKING STATEMENTS AND INDUSTRY DATA

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

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

our estimates regarding expenses, future revenue, capital requirements and needs for additional financing;

our ability to continue as a going concern; and

our intended use of proceeds from this offering.

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

our ability, and the ability of our licensees, to demonstrate to the satisfaction of applicable regulatory agencies the safety, efficacy and clinically meaningful benefit of our product candidates, including as it relates to the TIVO-3 trial and tivozanib;

our ability to successfully file an NDA with the FDA for tivozanib on the timeline we anticipate, or at all;

our ability to enter into and maintain our third-party collaboration agreements and our ability, and the ability of our strategic partners, to achieve development and commercialization objectives under these arrangements;

the timing and costs of any product candidate seeking and obtaining regulatory approval;

our ability, and the ability of our collaborators, to successfully enroll and complete clinical trials;

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our ability to maintain compliance with regulatory requirements applicable to our product candidates;

our ability to obtain and maintain adequate protection for intellectual property rights relating to our product candidates;

our ability to successfully implement our strategic plans;

our ability to raise the substantial additional funds required to achieve our goals, including those goals pertaining to the development and commercialization of tivozanib;

unplanned capital requirements;

adverse general economic and industry conditions;

competitive factors;

our ability to continue as a going concern; and

those risks discussed (i) under the heading Risk Factors on page S-17 of this prospectus supplement, (ii) in the section titled Risk Factors in our Annual Report on Form 10-K for the year ended December 31, 2018, as filed with the U.S. Securities and Exchange Commission, or the SEC, and (iii) in other filings we make with the SEC from time to time.

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

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

This prospectus summary also includes statistical and other industry and market data that we obtained from industry publications and research, surveys and studies conducted by third parties. All of the market data used in this report involves a number of assumptions and limitations, and you are cautioned not to give undue weight to such data. We believe that the information from these industry publications, surveys and studies is reliable. The industry in which we operate is subject to a high degree of uncertainty and risk due to a variety of important factors, including those risks discussed (i) under the heading Risk Factors on page S-17 of this prospectus supplement, (ii) in the section titled Risk

Factors in our Annual Report on Form 10-K for the year ended December 31, 2018, as filed with the SEC, and (iii) in other filings we make with the SEC from time to time. These and other factors could cause results to differ materially from those expressed in the estimates made by the independent parties and by us.

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USE OF PROCEEDS

We estimate that the net proceeds from this offering will be approximately $22.8 million, or approximately $26.3 million if the underwriter exercises its option to purchase additional securities in this offering in full, in each case after deducting the estimated underwriting discounts and commissions and estimated offering expenses payable by us, and excluding the proceeds, if any, from the exercise of the warrants sold in this offering. If all of the warrants sold in this offering were to be exercised in cash at their exercise price, we would receive additional net proceeds of approximately $27.2 million, or approximately $31.3 million in additional proceeds if the underwriter exercises its option to purchase additional securities in this offering in full. We cannot predict whether or the extent to which the underwriter will exercise its option to purchase additional securities or when or if any of the warrants will be exercised in cash. It is possible that the underwriter s option to purchase additional securities may expire and never be exercised and the warrants may never be exercised in cash.

We intend to use the net proceeds from this offering for ongoing clinical and preclinical development of our product candidates, as well as working capital and other general corporate purposes.

This expected use of net proceeds from this offering represents our intentions based upon our current plans and business conditions, which could change in the future as our plans and business conditions evolve. The amounts and timing of our actual expenditures may vary significantly depending on numerous factors, including the progress of our development, the status of and results from our and our strategic partners clinical trials of our product candidates, as well as any additional collaborations that we may enter into with third parties for our product candidates, and any unforeseen cash needs. As a result, our management will retain broad discretion over the allocation of the net proceeds from this offering. We intend to invest the proceeds, pending their use as described above, in short-term, interest-bearing, investment-grade securities.

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DIVIDEND POLICY

To date, we have paid no cash dividends to our stockholders, and we do not intend to pay cash dividends in the foreseeable future. In addition, the terms of our current debt agreement with Hercules Funding III, LLC and Hercules Capital, Inc., as amended to date, preclude us from paying cash dividends without our lender s prior written consent.

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CAPITALIZATION

The following table sets forth our consolidated cash and cash equivalents and capitalization as of December 31, 2018, as follows:

- on an actual basis;
- on a pro forma basis to give effect to the issuance and sale of 12,515,559 shares of our common stock in February 2019 and approximately $7.5 million in net proceeds received in February 2019 pursuant to the Leerink Sales Agreement; and
- on a pro forma as adjusted basis to give further effect to our issuance and sale of 21,739,131 shares of our common stock and warrants to purchase up to 21,739,131 shares of common stock in this offering at the public offering price of $1.15 per share of common stock and accompanying warrant, after deducting the underwriting discounts and commissions and estimated offering expenses payable by us, and assuming no exercise of the warrants offered hereby, no value is attributed to such warrants and such warrants are classified and accounted for as equity.

You should read the following table together with Description of Capital Stock beginning on page 8 of the accompanying prospectus, and our consolidated financial statements and related notes to those statements and the Management s Discussion and Analysis of Financial Condition and Results of Operations in our Annual Report on Form 10-K for the year ended December 31, 2018, which is incorporated by reference in this prospectus supplement.

	As of December 31, 2018		
(in thousands, except share and per share data)	Actual	Pro forma	Pro forma as adjusted
Cash and cash equivalents	$ 24,427	$ 31,939	$ 54,748
Loans payable, net of current portion and discount	$ 15,779	$ 15,779	$ 15,779
Stockholders deficit			
Preferred stock, par value $0.001 per share; 5,000,000 shares authorized, no shares issued or outstanding, actual, pro forma and pro forma as adjusted	$	$	$
Common stock, par value $0.001 per share; 250,000,000 shares authorized and 126,484,781 shares issued and outstanding, actual; 250,000,000 shares authorized and 139,000,340 shares issued and outstanding, pro forma; and 250,000,000 shares authorized and 160,739,471 shares issued and outstanding, pro forma as adjusted	$ 126	$ 139	$ 161
Additional paid-in capital	$ 567,655	$ 575,154	$ 597,941
Accumulated other comprehensive income	$ 1	$ 1	$ 1
Accumulated deficit	$ (595,009)	$ (595,009)	$ (595,009)

Total stockholders deficit	$ (27,227)	$ (19,715)	$ 3,094
Total capitalization	$ (11,448)	$ (3,936)	$ 18,873

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The foregoing table does not include:

9,583,349 shares of common stock issuable upon exercise of stock options outstanding as of December 31, 2018, at a weighted-average exercise price of $2.28 per share;

16,839,375 shares of common stock issuable upon exercise of the PIPE Warrants outstanding as of December 31, 2018, at an exercise price of $1.00 per share;

2,000,000 shares of common stock issuable upon exercise of the Settlement Warrants outstanding as of December 31, 2018, at an exercise price of $3.00 per share;

1,105,666 shares of common stock reserved as of December 31, 2018, for future issuance under our equity incentive plans; and

298,308 shares of common stock reserved as of December 31, 2018, for future issuance under our 2010 employee stock purchase plan.

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DILUTION

If you purchase our securities in this offering, your interest will be diluted to the extent of the difference between the public offering price per share of common stock and the accompanying warrants and the pro forma as adjusted net tangible book value per share of our common stock after this offering. We calculate net tangible book value per share by subtracting our total liabilities from our total tangible assets and dividing the difference by the number of outstanding shares of our common stock.

Our net tangible book value at December 31, 2018, was approximately $(27.2) million, or approximately $(0.22) per share, based on 126,484,781 shares of our common stock then outstanding. After giving effect to the issuance and sale of 12,515,559 shares of our common stock in February 2019 for approximately $7.5 million in net proceeds received in February 2019 pursuant to the Leerink Sales Agreement, our pro forma net tangible book value at December 31, 2018 would have been approximately $(19.7) million, or approximately $(0.14) per share, based on 139,000,340 shares of our common stock then outstanding. After giving further effect to the issuance and sale of 21,739,131 shares of common stock and warrants to purchase up to 21,739,131 shares of common stock in this offering at the public offering price per share of common stock and accompanying warrant of $1.15, after deducting the underwriting discounts and commissions and estimated offering expenses payable by us, and assuming no exercise of the warrants offered hereby, no value is attributed to such warrants and such warrants are classified and accounted for as equity, our pro forma as adjusted net tangible book value at December 31, 2018, would be approximately $3.1 million, or approximately $0.02 per share. This represents an immediate increase in net tangible book value of $0.16 per share to existing stockholders and an immediate dilution of $1.13 per share to investors in this offering.

The following table illustrates this dilution on a per share basis:

Public offering price per share and accompanying warrant		$ 1.15
Net tangible book value per share as of December 31, 2018	$ (0.22)	
Increase in net tangible book value per share attributable to the issuance and sale of common stock pursuant to Leerink Sales Agreement in February 2019	$ 0.08	
Pro forma net tangible book value per share as of December 31, 2018	$ (0.14)	
Increase in net tangible book value per share to existing stockholders as a result of this offering	$ 0.16	
Pro forma as adjusted net tangible book value per share as of December 31, 2018		$ 0.02
Dilution in net tangible book value per share to new investors in this offering		$ 1.13

If the underwriter exercises its option to purchase additional securities in this offering in full, after deducting the underwriting discounts and commissions and estimated offering expenses payable by us, and assuming no exercise of the warrants offered hereby, no value is attributed to such warrants and such warrants are classified and accounted for as equity, our pro forma as adjusted net tangible book value at December 31, 2018, after giving effect to this offering, would be approximately $6.6 million, or approximately $0.04 per share, representing an increase in net tangible book

value of $0.18 per share to existing stockholders and immediate dilution in net tangible book value of $1.11 per share to investors purchasing our common stock and the accompanying warrants in this offering at the public offering price.

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The calculations in the foregoing table and discussion do not include, as of December 31, 2018:

- 9,583,349 shares of common stock issuable upon exercise of stock options outstanding as of December 31, 2018, at a weighted-average exercise price of $2.28 per share;
- 16,839,375 shares of common stock issuable upon exercise of the PIPE Warrants outstanding as of December 31, 2018, at an exercise price of $1.00 per share;
- 2,000,000 shares of common stock issuable upon exercise of the Settlement Warrants outstanding as of December 31, 2018, at an exercise price of $3.00 per share;
- 1,105,666 shares of common stock reserved as of December 31, 2018, for future issuance under our equity incentive plans; and
- 298,308 shares of common stock reserved as of December 31, 2018, for future issuance under our 2010 employee stock purchase plan.

To the extent that any of our outstanding options or warrants are exercised at prices below the public offering price, we grant additional options or other awards under our equity incentive plans or issue additional warrants, the warrants issued in this offering are accounted for as liabilities or we issue additional shares of common stock in the future, there may be further dilution to new public investors.

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DESCRIPTION OF SECURITIES WE ARE OFFERING

Common Stock

The material terms and provisions of our common stock are described under the heading Description of Capital Stock in the accompanying prospectus.

Warrants

The following is a summary of the material terms and provisions of the warrants that are being offered hereby. This summary is subject to and qualified in its entirety by the forms of warrants, which will be provided to the investors in this offering and will be filed with the SEC as exhibits to a Current Report on Form 8-K in connection with this offering and incorporated by reference into the registration statement of which this prospectus forms a part. Prospective investors should carefully review the terms and provisions of the forms of warrants for a complete description of the terms and conditions of the warrants.

Duration and Exercise Price

The warrants offered hereby will have an exercise price of $1.25 per share. The warrants will be immediately exercisable and may be exercised until the second anniversary of the issuance date, at which time they will be automatically exercised on a cashless basis. The exercise prices and numbers of shares of common stock issuable upon exercise are subject to appropriate adjustment in the event of stock dividends, stock splits, reorganizations or similar events affecting our common stock. The warrants will be issued separately from the shares of common stock offered hereby, and may be transferred separately immediately thereafter. Warrants will be issued in certificated form only.

Exercisability

The warrants will be exercisable, at the option of each holder, in whole or in part, by delivering to us a duly executed exercise notice accompanied by payment in full for the number of shares of our common stock purchased upon such exercise (except in the case of a cashless exercise as discussed below). A holder (together with its affiliates) may not exercise any portion of such holder s warrants to the extent that the holder would own more than 4.99% of our outstanding common stock immediately after exercise, except that upon at least 61 days prior notice from the holder to us, the holder may increase the amount of ownership of outstanding stock after exercising the holder s warrants up to 9.99% of the number of shares of our common stock outstanding immediately after giving effect to the exercise, as such percentage ownership is determined in accordance with the terms of the warrants. Purchasers in this offering may also elect prior to the issuance of warrants to have the initial exercise limitation set at 9.99% of our outstanding common stock.

Cashless Exercise

If, at the time a holder exercises its warrants, a registration statement registering the issuance of the shares of common stock underlying the warrants under the Securities Act of 1933, as amended, or the Securities Act, is not then effective or available for the issuance of such shares, then in lieu of making the cash payment otherwise contemplated to be made to us upon such exercise in payment of the aggregate exercise price, the holder may elect instead to receive upon such exercise (either in whole or in part) the net number of shares of common stock determined according to a formula set forth in the warrant. The warrants will be automatically exercised on a cashless basis on the expiration date.

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Fundamental Transactions

In the event of any fundamental transaction, as described in the warrants and generally including any merger with or into another entity, sale of all or substantially all of our assets, tender offer or exchange offer, or reclassification of our common stock, then upon any subsequent exercise of a warrant, the holder will have the right to receive as alternative consideration, for each share of our common stock that would have been issuable upon such exercise immediately prior to the occurrence of such fundamental transaction, the number of shares of common stock of the successor or acquiring corporation or of our company, if it is the surviving corporation, and any additional consideration receivable upon or as a result of such transaction by a holder of the number of shares of our common stock for which the warrant is exercisable immediately prior to such event.

Transferability

In accordance with its terms and subject to applicable laws and a standard legend with regard to restriction on transfer only in compliance with a public offering or an available exemption therefrom, a warrant may be transferred at the option of the holder upon surrender of the warrant to us together with the appropriate instruments of transfer.

Fractional Shares

No fractional shares of common stock will be issued upon the exercise of the warrants. Rather, the number of shares of common stock to be issued will, at our election, either be rounded up to the nearest whole number or we will pay a cash adjustment in respect of such final fraction in an amount equal to such fraction multiplied by the exercise price.

Trading Market

There is no established trading market for any of the warrants, and we do not expect a market to develop. We do not intend to apply for a listing for any of the warrants on any securities exchange or other nationally recognized trading system. Without an active trading market, the liquidity of the warrants will be limited.

Rights as a Stockholder

Except as otherwise provided in the warrants or by virtue of the holders ownership of shares of our common stock, the holders of warrants do not have the rights or privileges of holders of our common stock, including any voting rights, until such warrant holders exercise their warrants.

Waivers and Amendments

No term of the warrants may be amended or waived without the written consent of the holder of such warrant.

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MATERIAL U.S. TAX CONSIDERATIONS FOR HOLDERS OF OUR COMMON STOCK AND WARRANTS

The following discussion describes the material U.S. federal income tax consequences of the acquisition, ownership and disposition of our common stock and warrants acquired in this offering. This discussion is based on the current provisions of the Internal Revenue Code of 1986, as amended, referred to as the Code, existing and proposed U.S. Treasury regulations promulgated thereunder, and administrative rulings and court decisions in effect as of the date hereof, all of which are subject to change at any time, possibly with retroactive effect. No ruling has been or will be sought from the Internal Revenue Service, or IRS, with respect to the matters discussed below, and there can be no assurance the IRS will not take a contrary position regarding the tax consequences of the acquisition, ownership or disposition of our common stock or warrants, or that any such contrary position would not be sustained by a court.

We assume in this discussion that the shares of our common stock and warrants will be held as capital assets (generally, property held for investment). This discussion does not address all aspects of U.S. federal income taxes that may be relevant to holders in light of their particular circumstances, including the potential application of the Medicare contribution tax on net investment income or the alternative minimum tax, nor does it discuss any aspects of state, local or non-U.S. taxes or gift and estate taxes (except as specifically provided below with respect to non-U.S. holders). This discussion also does not address the special tax rules applicable to particular holders, such as:

- financial institutions;
- brokers or dealers in securities;
- tax-exempt organizations;
- pension plans;
- regulated investment companies;
- persons subject to special tax accounting rules as a result of any item of gross income with respect to our common stock or warrants being taken into account in an applicable financial statement (as defined in the Code);
- owners that hold our common stock or warrants as part of a straddle, hedge, conversion transaction, synthetic security or other integrated investment;
- insurance companies;

controlled foreign corporations, passive foreign investment companies, or corporations that accumulate earnings to avoid U.S. federal income tax; and

certain U.S. expatriates.

In addition, this discussion does not address the tax treatment of partnerships or other pass-through entities or persons who hold our common stock or warrants through partnerships or other entities which are pass-through entities for U.S. federal income tax purposes. A partner in a partnership or other pass-through entity that will hold our common stock or warrants should consult his, her or its own tax advisor regarding the tax consequences of the ownership and disposition of our common stock or warrants through a partnership or other pass-through entity, as applicable.

Prospective investors should consult their own tax advisors regarding the U.S. federal, state, local and non-U.S. income and other tax considerations of acquiring, holding and disposing of our common stock and warrants.

For the purposes of this discussion, a U.S. Holder means a beneficial owner of our common stock or warrants that is for U.S. federal income tax purposes (a) an individual citizen or resident of the United States,

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(b) a corporation (or other entity taxable as a corporation for U.S. federal income tax purposes), created or organized in or under the laws of the United States, any state thereof or the District of Columbia, (c) an estate the income of which is subject to U.S. federal income taxation regardless of its source, or (d) a trust if it (1) is subject to the primary supervision of a court within the United States and one or more U.S. persons (within the meaning of Section 7701(a)(30) of the Code) have the authority to control all substantial decisions of the trust or (2) has a valid election in effect under applicable U.S. Treasury regulations to be treated as a U.S. person. A Non-U.S. Holder is a beneficial owner of our common stock or warrants that is neither a U.S. Holder nor a partnership or other pass-through entity for U.S. federal income tax purposes.

Allocation of Purchase Price Between Our Common Stock and Warrants

The common stock and warrants issued pursuant to this offering should be treated for U.S. federal income tax purposes as an investment unit consisting of one share of our common stock and a warrant to purchase one share of common stock. The purchase price for each investment unit will be allocated between these two components in proportion to their relative fair market values at the time the unit is purchased by the holder. This allocation of the purchase price for each unit will establish the holder s initial tax basis for U.S. federal income tax purposes in the share of common stock and the warrant included in each unit. The separation of the share of common stock and the warrant included in each unit should not be a taxable event for U.S. federal income tax purposes. Each holder should consult his, her or its own tax advisor regarding the allocation of the purchase price between the common stock and the warrants for U.S. federal income tax purposes.

Tax Considerations Applicable to U.S. Holders

Exercise and Expiration of Warrants

In general, a U.S. Holder will not recognize gain or loss for U.S. federal income tax purposes upon exercise of a warrant. The U.S. Holder will take a tax basis in the shares acquired on the exercise of a warrant equal to the exercise price of the warrant, increased by the U.S. Holder s adjusted tax basis in the warrant exercised (as determined pursuant to the rules discussed above). The U.S. Holder s holding period in the shares of our common stock acquired on exercise of the warrant will begin on the date of exercise of the warrant, and will not include any period for which the U.S. Holder held the warrant.

In certain circumstances, a U.S. Holder may undertake a cashless exercise of warrants into our common stock. The U.S. federal income tax treatment of a cashless exercise of warrants into our common stock is unclear, and the tax consequences of a cashless exercise could differ from the consequences upon the exercise of a warrant described in the preceding paragraph. U.S. Holders should consult their own tax advisors regarding the U.S. federal income tax consequences of a cashless exercise of warrants.

The lapse or expiration of a warrant will be treated as if the U.S. Holder sold or exchanged the warrant and recognized a capital loss equal to the U.S. Holder s tax basis in the warrant. The deductibility of capital losses is subject to limitations.

Certain Adjustments to and Distributions on Warrants

Under Section 305 of the Code, an adjustment to the number of shares of common stock issued on the exercise of the warrants, or an adjustment to the exercise price of the warrants, may be treated as a constructive distribution to a U.S. Holder of the warrants if, and to the extent that, such adjustment has the effect of increasing such U.S. Holder s proportionate interest in our earnings and profits or assets, depending on the circumstances of such adjustment. An

adjustment made pursuant to a bona fide reasonable adjustment formula that has the effect of preventing dilution should generally not be considered to result in a constructive distribution. Any such constructive distribution would be taxable whether or not there is an actual distribution of cash or other property

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to the holders of warrants. In certain circumstances, if we were to make a distribution in cash or other property with respect to our common stock after the issuance of the warrants, then we may make a corresponding distribution to a warrant holder. The taxation of a distribution received with respect to a warrant is unclear. It is possible such a distribution would be treated as a distribution (or constructive distribution), although other treatments are possible. For more information regarding the tax considerations related to distributions, see the discussion below under Distributions on Our Common Stock. U.S. Holders should consult their tax advisors regarding the proper treatment of any adjustments to the warrants and any distributions with respect to the warrants.

Distributions on Our Common Stock

As described above in the section titled Dividend Policy, we currently do not intend to pay cash dividends in respect of our common stock in the foreseeable future. In the event that we do make distributions on our common stock to a U.S. Holder, those distributions generally will constitute dividends for U.S. tax purposes to the extent paid out of our current or accumulated earnings and profits (as determined under U.S. federal income tax principles). Distributions in excess of our current and accumulated earnings and profits will constitute a return of capital that is applied against and reduces, but not below zero, a U.S. Holder s adjusted tax basis in our common stock. Any remaining excess will be treated as gain realized on the sale or exchange of our common stock as described below under the section titled Disposition of Our Common Stock or Warrants.

Disposition of Our Common Stock or Warrants

Upon a sale or other taxable disposition of our common stock or warrants, a U.S. Holder generally will recognize capital gain or loss in an amount equal to the difference between the amount realized and the U.S. Holder s adjusted tax basis in the common stock or warrants. Capital gain or loss will constitute long-term capital gain or loss if the U.S. Holder s holding period for the common stock or warrants exceeds one year. The deductibility of capital losses is subject to certain limitations. U.S. Holders who recognize losses with respect to a disposition of our common stock or warrants should consult their own tax advisors regarding the tax treatment of such losses.

Information Reporting and Backup Reporting

Information reporting requirements generally will apply to payments of dividends (including constructive dividends) on our common stock and warrants and to the proceeds of a sale or other disposition of our common stock and warrants paid by us to a U.S. Holder unless such U.S. Holder is an exempt recipient, such as a corporation. Backup withholding will apply to those payments if the U.S. Holder fails to provide the holder s taxpayer identification number, or certification of exempt status, or if the holder otherwise fails to comply with applicable requirements to establish an exemption.

Backup withholding is not an additional tax. Rather, any amounts withheld under the backup withholding rules will be allowed as a refund or a credit against the U.S. Holder s U.S. federal income tax liability provided the required information is timely furnished to the IRS. U.S. Holders should consult their own tax advisors regarding their qualification for exemption from information reporting and backup withholding and the procedure for obtaining such exemption.

Tax Considerations Applicable to Non-U.S. Holders

Exercise and Expiration of Warrants

In general, a Non-U.S. Holder will not recognize gain or loss for U.S. federal income tax purposes upon the exercise of warrants into shares of common stock. The U.S. federal income tax treatment of a cashless exercise of warrants into our common stock is unclear. A Non-U.S. Holder should consult his, her, or its own tax advisor regarding the U.S. federal income tax consequences of a cashless exercise of warrants.

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The lapse or expiration of a warrant will be treated as if the Non-U.S. Holder sold or exchanged the warrant and recognized a capital loss equal to the Non-U.S. Holder s tax basis in the warrant. However, a Non-U.S. Holder will not be able to utilize a loss recognized upon lapse or expiration of a warrant against the Non-U.S. Holder s U.S. federal income tax liability unless the loss is effectively connected with the Non-U.S. Holder s conduct of a trade or business within the United States (and, if an income tax treaty applies, is attributable to a permanent establishment or fixed base in the United States) or is treated as a U.S.-source loss and the Non-U.S. Holder is present in the United States for 183 days or more in the taxable year of disposition and certain other conditions are met.

Certain Adjustments to and Distributions on Warrants

As described under U.S. Holders Certain Adjustments to and Distributions on Warrants, an adjustment to the warrants could result in a constructive distribution to a Non-U.S. Holder, which would be treated as described under Distributions on Our Common Stock below, and the tax treatment of distributions on the warrants is unclear. Any resulting withholding tax attributable to deemed dividends would be collected from other amounts payable or distributable to the Non-U.S. Holder. Non-U.S. Holders should consult their tax advisors regarding the proper treatment of any adjustments to and distributions on the warrants.

Distributions on Our Common Stock

As described above in the section titled Dividend Policy, we currently do not intend to pay cash dividends in respect of our common stock in the foreseeable future. In the event that we do make distributions on our common stock to a Non-U.S. Holder, those distributions generally will constitute dividends for U.S. federal income tax purposes as described in U.S. Holders Distributions on Our Common Stock. Any distributions will also be subject to the discussions below titled Information Reporting and Backup Withholding and Foreign Accounts

Any distribution (including a constructive distribution) that is treated as a dividend paid to a Non-U.S. Holder generally will be subject to U.S. federal withholding tax at a 30% rate or such lower rate as may be specified by an applicable income tax treaty between the United States and such holder s country of residence.

Dividends that are treated as effectively connected with a trade or business conducted by a Non-U.S. Holder within the United States, and, if an applicable income tax treaty so provides, that are attributable to a permanent establishment or a fixed base maintained by the Non-U.S. Holder within the United States, are generally exempt from the 30% withholding tax if the Non-U.S. Holder satisfies applicable certification and disclosure requirements (generally including provision of a valid IRS Form W-8ECI (or applicable successor form) certifying that the dividends are effectively connected with the Non-U.S. Holder s conduct of a trade or business within the United States). However, such U.S. effectively connected income, net of specified deductions and credits, is taxed at the same U.S. federal income tax rates applicable to U.S. persons (as defined in the Code). Any U.S. effectively connected income received by a Non-U.S. Holder that is classified as a corporation for U.S. federal income tax purposes may also, under certain circumstances, be subject to an additional branch profits tax at a 30% rate or such lower rate as may be specified by an applicable income tax treaty between the United States and such holder s country of residence.

A Non-U.S. Holder of our common stock who claims the benefit of an applicable income tax treaty between the United States and such holder s country of residence generally will be required to provide a properly executed IRS Form W-8BEN or W-8BEN-E (or successor form) and satisfy applicable certification and other requirements. Non-U.S. Holders are urged to consult their own tax advisors regarding their entitlement to benefits under a relevant income tax treaty and the specific methods available to them to satisfy these requirements.

A Non-U.S. Holder that is eligible for a reduced rate of U.S. withholding tax under an income tax treaty may obtain a refund or credit of any excess amounts withheld by timely filing an appropriate claim with the IRS.

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Disposition of Our Common Stock or Warrants

Subject to the discussions below under the sections titled Information Reporting and Backup Withholding and Foreign Accounts, a Non-U.S. Holder generally will not be subject to U.S. federal income or withholding tax with respect to gain realized on a sale or other disposition of our common stock or warrants unless:

- the gain is effectively connected with the Non-U.S. Holder s conduct of a trade or business in the United States, and if an applicable income tax treaty so provides, the gain is attributable to a permanent establishment or fixed base maintained by the Non-U.S. Holder in the United States; in these cases, the Non-U.S. Holder will be taxed on a net income basis at the same U.S. federal income tax rates applicable to U.S. persons (as defined in the Code), and if the Non-U.S. Holder is a corporation, an additional branch profits tax at a rate of 30%, or a lower rate as may be specified by an applicable income tax treaty, may also apply;

- the Non-U.S. Holder is a nonresident alien present in the United States for 183 days or more in the taxable year of the disposition and certain other requirements are met, in which case the Non-U.S. Holder will be subject to a 30% tax (or such lower rate as may be specified by an applicable income tax treaty between the United States and such holder s country of residence) on the net gain derived from the disposition, which may be offset by certain U.S.-source capital losses of the Non-U.S. Holder, if any; or

- we are, or have been at any time during the five-year period preceding such disposition (or the Non-U.S. Holder s holding period of the common stock or warrants, if shorter), a U.S. real property holding corporation, unless our common stock is regularly traded on an established securities market and the Non-U.S. Holder held no more than 5% of our outstanding common stock, directly or indirectly, during the shorter of the five-year period ending on the date of the disposition or the period that the Non-U.S. Holder held our common stock. Special rules may apply to the determination of the 5% threshold in the case of a holder of warrants. Non-U.S. Holders are urged to consult their own tax advisors regarding the effect of holding our warrants on the calculation of such 5% threshold. Generally, a corporation is a U.S. real property holding corporation if the fair market value of its U.S. real property interests equals or exceeds 50% of the sum of the fair market value of its worldwide real property interests plus its other assets used or held for use in a trade or business. Although there can be no assurance, we believe that we are not currently, and we do not anticipate becoming, a U.S. real property holding corporation for U.S. federal income tax purposes. No assurance can be provided that our common stock will be regularly traded on an established securities market for purposes of the rules described above.

Information Reporting and Backup Withholding

The gross amount of the distributions (including constructive distributions) on our common stock or warrants paid to each Non-U.S. Holder and the tax withheld, if any, with respect to such distributions must be reported annually to the IRS and to each non-U.S. holder. Non-U.S. Holders generally will have to comply with specific certification procedures to establish that the holder is not a U.S. person (as defined in the Code) in order to avoid backup withholding at the applicable rate with respect to dividends (or constructive dividends) on our common stock or warrants. Generally, a Non-U.S. Holder will comply with such procedures if it provides a properly executed IRS Form W-8BEN or W-8BEN-E (or other applicable Form W-8) or otherwise meets documentary evidence requirements for establishing that it is a Non-U.S. Holder, or otherwise establishes an exemption. Dividends paid to Non-U.S. Holders

subject to withholding of U.S. federal income tax, as described above under the heading Distributions on Our Common Stock, will generally be exempt from U.S. backup withholding.

Information reporting and backup withholding generally will apply to the proceeds of a disposition of our common stock or warrants by a Non-U.S. Holder effected by or through the U.S. office of any broker, U.S. or foreign, unless the holder certifies its status as a Non-U.S. Holder and satisfies certain other requirements, or

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otherwise establishes an exemption. Generally, information reporting and backup withholding will not apply to a payment of disposition proceeds to a Non-U.S. Holder where the transaction is effected outside the United States through a non-U.S. office of a broker. However, for information reporting purposes, dispositions effected through a non-U.S. office of a broker with substantial U.S. ownership or operations generally will be treated in a manner similar to dispositions effected through a U.S. office of a broker. Non-U.S. Holders should consult their own tax advisors regarding the application of the information reporting and backup withholding rules to them.

Copies of information returns may be made available to the tax authorities of the country in which the Non-U.S. Holder resides or is incorporated under the provisions of a specific treaty or agreement.

Backup withholding is not an additional tax. Any amounts withheld under the backup withholding rules from a payment to a Non-U.S. Holder can be refunded or credited against the Non-U.S. Holder s U.S. federal income tax liability, if any, provided that an appropriate claim is timely filed with the IRS.

Foreign Accounts

Provisions of the Code commonly known as the Foreign Account Tax Compliance Act, or FATCA, generally impose a 30% withholding tax on dividends (including constructive dividends) on, and gross proceeds from the sale or other disposition of, our common stock and warrants if paid to a non-U.S. entity unless (i) if the non-U.S. entity is a foreign financial institution, the non-U.S. entity undertakes certain due diligence, reporting, withholding, and certification obligations, (ii) if the non-U.S. entity is not a foreign financial institution, the non-U.S. entity identifies certain of its U.S. investors, if any, or (iii) the non-U.S. entity is otherwise exempt under FATCA.

Withholding under FATCA generally applies to payments of dividends (including constructive dividends) on our common stock and warrants. While withholding under FATCA may apply to payments of gross proceeds from a sale or other disposition of our common stock or warrants, under recently proposed U.S. Treasury Regulations, withholding on payments of gross proceeds is not required. Although such regulations are not final, applicable withholding agents may rely on the proposed regulations until final regulations are issued.

An intergovernmental agreement between the United States and an applicable foreign country may modify the requirements described in this section. Under certain circumstances, a holder may be eligible for refunds or credits of the tax. Holders should consult their own tax advisors regarding the possible implications of FATCA on their investment in our common stock or warrants.

U.S. Federal Estate Tax

Common stock owned or treated as owned by an individual who is not a citizen or resident of the United States (as specially defined for U.S. federal estate tax purposes) at the time of death will be included in the individual s gross estate for U.S. federal estate tax purposes and, therefore, may be subject to U.S. federal estate tax, unless an applicable estate tax or other treaty provides otherwise. The foregoing may also apply to warrants. A Non-U.S. Holder should consult his, her, or its own tax advisor regarding the U.S. federal estate tax consequences of the ownership or disposition of shares of our common stock and warrants.

THE PRECEDING DISCUSSION OF MATERIAL U.S. FEDERAL TAX CONSIDERATIONS IS FOR INFORMATION ONLY. IT IS NOT TAX ADVICE. PROSPECTIVE INVESTORS SHOULD CONSULT THEIR OWN TAX ADVISORS REGARDING THE PARTICULAR U.S. FEDERAL, STATE, LOCAL AND NON-U.S. TAX CONSEQUENCES OF PURCHASING, HOLDING AND DISPOSING OF OUR COMMON STOCK OR WARRANTS, INCLUDING THE CONSEQUENCES OF ANY PROPOSED CHANGES IN

APPLICABLE LAWS.

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UNDERWRITING

H.C. Wainwright & Co., LLC is acting as the sole underwriter for this offering. Subject to the terms and conditions set forth in an underwriting agreement between us and the underwriter, we have agreed to sell to the underwriter, and the underwriter has agreed to purchase from us, the number of shares of our common stock and warrants set forth opposite its name below.

Underwriter	Number of Shares	Number of Warrants
H.C. Wainwright & Co., LLC	21,739,131	21,739,131
Total	21,739,131	21,739,131

Subject to the terms and conditions set forth in the underwriting agreement, the underwriter has agreed to purchase all of the shares and the accompanying warrants sold under the underwriting agreement if any of these shares and warrants are purchased.

The underwriter is offering the shares and the accompanying warrants, subject to prior sale, when, as and if issued to and accepted by it, subject to approval of legal matters by its counsel, including the validity of the shares and the accompanying warrants, and other conditions contained in the underwriting agreement, such as the receipt by the underwriter of officers certificates and legal opinions. The underwriter reserves the right to withdraw, cancel or modify offers to the public and to reject orders in whole or in part.

Underwriter s Discounts, Commissions and Expenses

We have been advised by the underwriter that the underwriter proposes to offer our shares of common stock and the accompanying warrants directly to the public at the public offering price set forth on the cover page of this prospectus supplement and to certain dealers that are members of the Financial Industry Regulatory Authority (FINRA). Any securities sold by the underwriter to such securities dealers will be sold at the public offering price less a selling concession not in excess of $0.05175 per share and accompanying warrant. After the public offering of the shares and the accompanying warrants, the offering price and other selling terms may be changed by the underwriter.

None of our securities included in this offering may be offered or sold, directly or indirectly, nor may this prospectus supplement and any other offering material in connection with the offer and sales of any of our shares of common stock and the accompanying warrants be distributed or published in any jurisdiction, except under circumstances that will result in compliance with the applicable rules and regulations of that jurisdiction. Persons who receive this prospectus supplement are advised to inform themselves about and to observe any restrictions relating to this offering of our shares of common stock and warrants and the distribution of this prospectus supplement. This prospectus supplement is neither an offer to sell nor a solicitation of any offer to buy any of our shares of common stock and the accompanying warrants included in this offering in any jurisdiction where that would not be permitted or legal.

The underwriter has advised us that it does not intend to confirm sales to any account over which it exercises discretionary authority.

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The following table summarizes the per share and accompanying warrant underwriting discounts and commissions to the public offering price of our common stock and the accompanying warrants offered pursuant to this prospectus supplement. The information assumes either no exercise or full exercise by the underwriter of its option to purchase additional securities.

	Per Share and Accompanying Warrant	Total Without Option to Purchase Additional Shares and/or the Accompanying Warrants	With Option to Purchase Additional Shares and/or the Accompanying Warrants
Underwriting discounts and commissions	$ 0.0805	$ 1,750,000.05	$ 2,012,500.00

We estimate that the total expenses of the offering, excluding the underwriting discounts and commissions, will be approximately $441,000. These expenses are payable by us. We have agreed to pay the underwriter a non-accountable expense allowance of $35,000. We also have agreed to pay the underwriter up to an additional $75,000 for fees incurred in connection with this offering, including fees of underwriter s counsel, and $10,000 for clearing expenses. These amounts are included in the estimate provided above. In accordance with FINRA Rule 5110, certain of these expense payments are deemed underwriting compensation for this offering.

After deducting the discounts and commissions due to the underwriter and our estimated offering expenses, we expect our net proceeds from this offering to be approximately $22.8 million.

Our common stock is listed on The Nasdaq Capital Market under the trading symbol AVEO. There is no established trading market for any of the warrants, and we do not expect a market to develop. We do not intend to apply for a listing for any of the warrants on any securities exchange or other nationally recognized trading system. Without an active trading market, the liquidity of the warrants will be limited.

Option to Purchase Additional Shares

We have granted to the underwriter an option, exercisable not later than 30 days after the date of this prospectus supplement, to purchase up to an additional 3,260,869 shares of our common stock at a purchase price of $1.14 per share and/or to purchase up to an additional 3,260,869 warrants at a purchase price of $0.01 per warrant, in each case less underwriting discounts and commissions. If the underwriter exercises this option, it will be obligated, subject to conditions contained in the underwriting agreement, to purchase such number of additional shares and/or warrants as to which it has exercised its option.

No Sales of Similar Securities

We and each of our directors and executive officers have agreed that we and they will not, without the prior written consent of H.C. Wainwright & Co., LLC, subject to certain limited exceptions, directly or indirectly:

offer, pledge, announce the intention to sell, sell, contract to sell, sell any option or contract to purchase, purchase any option or contract to sell, grant any option, right or warrant to purchase, make any short sale in the case of our directors and executive officers only or otherwise transfer or dispose of, directly or indirectly, any shares of common stock or any securities convertible into, exercisable or exchangeable for or, in the case of our directors and executive officers, that represent the right to receive common stock (including without limitation, in the case of our directors and executive officers, common stock which may be deemed to be beneficially owned by the holder in accordance with the rules and regulations of the SEC and securities which may be issued upon exercise of a stock option or warrant) whether now owned or hereafter acquired;

enter into any swap or other agreement that transfers, in whole or in part, any of the economic consequences of ownership of our common stock and, in the case of our directors and executive officers, the holder s securities;

in the case of our directors and executive officers, make any demand for or exercise any right with respect to, the registration of any common stock or any security convertible into or exercisable or exchangeable for common stock in each case that would require us to file a registration statement within the next 90 days of the date of the lock-up agreement; or

publicly disclose the intention to do any of the foregoing,

for a period of 90 days after the public offering date set forth in this prospectus supplement. However, in the case of our directors and executive officers subject to the 90-day restricted period, these restrictions will not apply to transfers of our common stock or any security convertible into or exercisable for our common stock: (i) as a bona fide gift or gifts made by the holder, (ii) to any trust for the direct or indirect benefit of the holder or the holder s immediate family, (iii) by testate succession or intestate succession, (iv) by operation of law, including pursuant to a qualified domestic relations order or in connection with a divorce settlement, (v) pursuant to the underwriting agreement or (vi) in connection with a bona fide third-party tender offer, merger, consolidation or other similar transaction made to all common stock holders, provided that in the event the tender offer, merger, consolidation or other such transaction is not completed, the holder of the common stock shall remain subject to the restrictions; provided, in the case of clauses (i)-(iv), that (x) such transfers do not involve a disposition for value, (y) the transferee agrees in writing to be bound to the 90-day restricted period for subsequent transfers, and (z) no filing by any party under Section 16(a) of the Securities Exchange Act of 1934, as amended, or the Exchange Act, is required or shall be made voluntarily in connection with such transfer. In addition, in the case of our directors and executive officers, the restrictions will also not apply to (i) the exercise, conversion or exchange of any options, warrants, rights or convertible securities outstanding on the date the lockup agreement was signed, including any exercise effected by the delivery or sale of the holder s securities to us (including, without limitation, to finance a cashless exercise); provided that the restrictions will apply to any of the holder s securities issued upon such exercise, conversion or exchange, except to the extent such securities are withheld by us to cover tax liabilities; (ii) the establishment of any contract, instruction or plan that satisfies all of the requirements of Rule 10b5-1(c)(1)(i)(B) under the Exchange Act; provided that no sales of the holder s securities may be made pursuant to such a plan prior to the expiration of the 90-day restricted period, and such a plan may only be established if no public announcement of the establishment or existence thereof and no filing with the SEC or other regulatory authority in respect thereof or transactions thereunder or contemplated thereby, by the holder, us or any other person, is required, and no such announcement or filing is made voluntarily, by the holder, us or any other person, prior to the expiration of the 90-day restricted period; (iii) the transfer of securities to us as forfeitures to satisfy tax withholding obligations in connection with the vesting of restricted stock or exercise of options held by the holder and granted pursuant to our equity incentive plans; provided that if the holder is required to file a report under Section 16(a) of the Exchange Act reporting a reduction in beneficial ownership of shares of our common stock during the 90-day restricted period, the holder is required to include a statement in such report to the effect that the purpose of such transfer was to cover tax withholding obligations of the holder in connection with such vesting or exercise; or (iv) transactions relating to our common stock acquired in open market transactions after the completion of this offering or common stock acquired in this offering.

During the restricted period applicable to us, we may issue securities (i) pursuant to the underwriting agreement, (ii) to our directors, officers, employees and consultants pursuant to our employee benefit plans, equity incentive plans and other employee compensation plans existing on the date of this prospectus supplement; (iii) pursuant to the exercise, exchange or conversion of any options, warrants, rights or convertible securities outstanding on the date of this prospectus supplement or (iv) in connection with a joint venture, collaboration, strategic alliance, licensing, partnering or other commercial relationship.

H.C. Wainwright & Co., LLC may, in its sole discretion and at any time or from time to time before the termination of the applicable restricted period, release all or any portion of the securities subject to lock-up agreements. There are no

existing agreements between the underwriter and any of our stockholders who will execute a lock-up agreement providing consent to the sale of shares prior to the expiration of the applicable restricted period.

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Indemnification

We have agreed to indemnify the underwriter and its officers and directors against certain liabilities, including certain liabilities arising under the Securities Act, and to contribute to payments that the underwriter may be required to make for these liabilities.

Short Positions and Penalty Bids

The underwriter may engage in over-allotment, syndicate covering transactions, and penalty bids or purchases for the purpose of pegging, fixing or maintaining the price of the shares of common stock, in accordance with Regulation M under the Exchange Act.

Over-allotment involves sales by the underwriter of shares in excess of the number of shares the underwriter is obligated to purchase, which creates a syndicate short position. The short position may be either a covered short position or a naked short position. In a covered short position, the number of shares over-allotted by an underwriter is not greater than the number of shares that it may purchase pursuant to its option to purchase additional shares. In a naked short position, the number of shares involved is greater than the number of shares in the option to purchase additional shares. The underwriter may close out any short position by either exercising its option to purchase additional shares and/or purchasing shares in the open market.

Syndicate covering transactions involve purchases of the shares of common stock in the open market after the distribution has been completed in order to cover short positions. In determining the source of shares to close out the short position, the underwriter will consider, among other things, the price of shares available for purchase in the open market as compared to the price at which it may purchase shares through the option to purchase additional shares. If the underwriter sells more shares than could be covered by the option to purchase additional shares, a naked short position, the position can only be closed out by buying shares in the open market. A naked short position is more likely to be created if the underwriter is concerned that there could be downward pressure on the price of the shares in the open market after pricing that could adversely affect investors who purchase in the offering.

Penalty bids permit the underwriter to reclaim a selling concession from a syndicate member when the shares originally sold by the syndicate member are purchased in a stabilizing or syndicate covering transaction to cover syndicate short positions.

These syndicate covering transactions and penalty bids may have the effect of raising or maintaining the market price of our shares of common stock or preventing or retarding a decline in the market price of the common shares. As a result, the price of the shares of common stock may be higher than the price that might otherwise exist in the open market. These transactions may be effected on The Nasdaq Capital Market, and if commenced, they may be discontinued at any time.

Neither we nor the underwriter make any representation or prediction as to the direction or magnitude of any effect that the transactions described above may have on the price of the shares of common stock. In addition, neither we nor the underwriter make any representation that the underwriter will engage in these transactions or that any transaction, once commenced, will not be discontinued without notice.

Electronic Offer, Sale and Distributions of Shares

A prospectus in electronic format may be made available on the Internet sites or through other online services maintained by the underwriter or by its affiliates. In those cases, prospective investors may view offering terms online and prospective investors may be allowed to place orders online. The underwriter may agree with us

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to allocate a specific number of shares and accompanying warrants for sale to online brokerage account holders. Any such allocation for online distributions will be made by the underwriter on the same basis as other allocations.

Other than the prospectus in electronic format, the information on any underwriter s websites and any information contained in any other website maintained by an underwriter is not part of the prospectus or the registration statement of which this prospectus forms a part, has not been approved and/or endorsed by us or the underwriter in its capacity as underwriter and should not be relied upon by investors.

Other Relationships

The underwriter and its affiliates are full-service financial institutions engaged in various activities, which may include securities trading, commercial and investment banking, financial advisory, investment management, investment research, principal investment, hedging, financing and brokerage activities. The underwriter and its affiliates have engaged in, and may in the future engage in, investment banking and other commercial dealings in the ordinary course of business with us or our affiliates. They have received, or may in the future receive, customary fees and commissions for these transactions.

In the ordinary course of their various business activities, the underwriter and its affiliates may make or hold a broad array of investments and actively trade debt and equity securities (or related derivative securities) and financial instruments (including bank loans) for their own account and for the accounts of their customers, and such investment and securities activities may involve securities and/or instruments of the issuer. The underwriter and its affiliates may also make investment recommendations and/or publish or express independent research views in respect of such securities or instruments and may at any time hold, or recommend to clients that they acquire, long and/or short positions in such securities and instruments.

Selling Restrictions

European Economic Area

In relation to each Member State of the European Economic Area which has implemented the Prospectus Directive (each, a Relevant Member State) an offer to the public of any of our securities may not be made in that Relevant Member State, except that an offer to the public in that Relevant Member State of any of our securities may be made at any time under the following exemptions under the Prospectus Directive, if they have been implemented in that Relevant Member State:

(a) to any legal entity which is a qualified investor as defined in the Prospectus Directive;

(b) to fewer than 100 or, if the Relevant Member State has implemented the relevant provision of the 2010 PD Amending Directive, 150, natural or legal persons (other than qualified investors as defined in the Prospectus Directive), as permitted under the Prospectus Directive, subject to obtaining the prior consent of the representatives for any such offer; or

(c) in any other circumstances falling within Article 3(2) of the Prospectus Directive, provided that no such offer of our securities shall result in a requirement for the publication by us or any underwriter of a

prospectus pursuant to Article 3 of the Prospectus Directive.

For the purposes of this provision, the expression an offer to the public in relation to any of our securities in any Relevant Member State means the communication in any form and by any means of sufficient information on the terms of the offer and any of our securities to be offered so as to enable an investor to decide to purchase any of our securities, as the same may be varied in that Member State by any measure implementing the Prospectus Directive in that Member State, the expression Prospectus Directive means Directive 2003/71/EC (and amendments thereto, including the 2010 PD Amending Directive, to the extent implemented in the Relevant Member State), and includes any relevant implementing measure in the Relevant Member State, and the expression 2010 PD Amending Directive means Directive 2010/73/EU.

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United Kingdom

This prospectus is only being distributed to, and is only directed at, persons in the United Kingdom that are qualified investors within the meaning of Article 2(1)(e) of the Prospectus Directive that are also (i) investment professionals falling within Article 19(5) of the Financial Services and Markets Act 2000 (Financial Promotion) Order 2005 (the Order) or (ii) high net worth entities, and other persons to whom it may lawfully be communicated, falling within Article 49(2)(a) to (d) of the Order (each such person being referred to as a relevant person). This prospectus and its contents are confidential and should not be distributed, published or reproduced (in whole or in part) or disclosed by recipients to any other person in the United Kingdom. Any person in the United Kingdom that is not a relevant person should not act or rely on this document or any of its contents.

Canada

Our securities may be sold only to purchasers purchasing, or deemed to be purchasing, as principal that are accredited investors, as defined in National Instrument 45-106 Prospectus Exemptions or subsection 73.3(1) of the Securities Act (Ontario), and are permitted clients, as defined in National Instrument 31-103 Registration Requirements, Exemptions and Ongoing Registrant Obligations. Any resale of our securities must be made in accordance with an exemption from, or in a transaction not subject to, the prospectus requirements of applicable securities laws.

Securities legislation in certain provinces or territories of Canada may provide a purchaser with remedies for rescission or damages if the prospectus (including any amendment thereto) contains a misrepresentation, provided that the remedies for rescission or damages are exercised by the purchaser within the time limit prescribed by the securities legislation of the purchaser s province or territory. The purchaser should refer to any applicable provisions of the securities legislation of the purchaser s province or territory for particulars of these rights or consult with a legal advisor.

Pursuant to section 3A.3 (or, in the case of securities issued or guaranteed by the government of a non-Canadian jurisdiction, section 3A.4) of National Instrument 33-105 Underwriting Conflicts (NI 33-105), the underwriter is not required to comply with the disclosure requirements of NI 33-105 regarding underwriter conflicts of interest in connection with this offering.

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LEGAL MATTERS

The validity of the shares of common stock and the accompanying warrants offered hereby will be passed upon for us by Wilmer Cutler Pickering Hale and Dorr LLP, Boston, Massachusetts. Sheppard, Mullin, Richter & Hampton LLP, New York, New York has acted as counsel for the underwriter in connection with certain matters relating to this offering.

EXPERTS

Ernst & Young LLP, independent registered public accounting firm, has audited our consolidated financial statements included in our Annual Report on Form 10-K for the year ended December 31, 2018, and the effectiveness of our internal control over financial reporting as of December 31, 2018, as set forth in their reports (which contains an explanatory paragraph describing conditions that raise substantial doubt about our ability to continue as a going concern as described in Note 1 to the consolidated financial statements), which are incorporated by reference in this prospectus supplement and elsewhere in the registration statement. Our financial statements are incorporated by reference in reliance on Ernst & Young LLP s reports, given on their authority as experts in accounting and auditing.

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WHERE YOU CAN FIND MORE INFORMATION

We file annual, quarterly and current reports, proxy statements and other information with the SEC. Our SEC filings are available to the public over the Internet at the SEC s website at http://www.sec.gov. Copies of certain information filed by us with the SEC are also available on our website at http://www.aveooncology.com. Our website is not a part of this prospectus supplement and is not incorporated by reference in this prospectus.

This prospectus supplement is part of a registration statement we filed with the SEC. This prospectus supplement and the accompanying prospectus omit some information contained in the registration statement in accordance with SEC rules and regulations. You should review the information and exhibits in the registration statement for further information about us and our consolidated subsidiaries and the securities we are offering. Statements in this prospectus supplement and in the accompanying prospectus concerning any document we filed as an exhibit to the registration statement or that we otherwise filed with the SEC are not intended to be comprehensive and are qualified by reference to these filings. You should review the complete document to evaluate these statements.

INCORPORATION BY REFERENCE

The SEC allows us to incorporate by reference into this prospectus supplement much of the information we file with the SEC, which means that we can disclose important information to you by referring you to those publicly available documents. The information that we incorporate by reference is considered to be part of this prospectus supplement and the accompanying prospectus. Because we are incorporating by reference future filings with the SEC, this prospectus supplement and the accompanying prospectus are continually updated and those future filings may modify or supersede some of the information included or incorporated in this prospectus supplement and the accompanying prospectus. This means that you must look at all of the SEC filings that we incorporate by reference to determine if any of the statements in this prospectus supplement or the accompanying prospectus or in any document previously incorporated by reference have been modified or superseded. This prospectus supplement and the accompanying prospectus incorporate by reference the documents listed below (File No. 001-34655) and any future filings we make with the SEC under Sections 13(a), 13(c), 14 or 15(d) of the Exchange Act (in each case, other than those documents or the portions of those documents not deemed to be filed) until the offering of the securities under the registration statement is terminated or completed:

- our Annual Report on Form 10-K for the fiscal year ended December 31, 2018;
- the information included in our definitive proxy statement on Schedule 14A for the 2018 Annual Meeting of Stockholders, filed on April 27, 2018, to the extent incorporated by reference into Part III of the Annual Report on Form 10-K for the fiscal year ended December 31, 2017;
- our Current Reports on Form 8-K dated February 6, 2019, March 1, 2019, March 21, 2019 and April 3, 2019; and
- the description of our common stock contained in our registration statement on Form 8-A filed on March 9, 2010, including any amendments or reports filed for the purpose of updating such description.

You may request a copy of these filings, at no cost, by writing or telephoning us at the following address or telephone number:

AVEO Pharmaceuticals, Inc.

One Broadway, 14th Floor

Cambridge, Massachusetts 02142

Attention: Investor Relations

Telephone: (617) 588-1960

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PROSPECTUS

$200,000,000

Common Stock

Preferred Stock

Debt Securities

Warrants

Units

We may offer and sell securities from time to time in one or more offerings of up to $200,000,000 in aggregate offering price. This prospectus describes the general terms of these securities and the general manner in which these securities will be offered. We will provide the specific terms of these securities in supplements to this prospectus. The prospectus supplements will also describe the specific manner in which these securities will be offered and may also supplement, update or amend information contained in this document. You should read this prospectus and any applicable prospectus supplement before you invest.

We may offer these securities in amounts, at prices and on terms determined at the time of offering. The securities may be sold directly to you, through agents, or through underwriters and dealers. If agents, underwriters or dealers are used to sell the securities, we will name them and describe their compensation in a prospectus supplement.

Our common stock is listed on The NASDAQ Capital Market under the symbol AVEO.

Investing in these securities involves significant risks. See Risk Factors included in any accompanying prospectus supplement and in the documents incorporated by reference in this prospectus for a discussion of the factors you should carefully consider before deciding to purchase these securities.

Neither the Securities and Exchange Commission nor any state securities commission has approved or disapproved of these securities or passed upon the adequacy or accuracy of this prospectus. Any representation to the contrary is a criminal offense.

The date of this prospectus is December 15, 2017

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ABOUT THIS PROSPECTUS

This prospectus is part of a registration statement that we filed with the Securities and Exchange Commission, which we refer to as the SEC, utilizing a shelf registration process. Under this shelf registration process, we may from time to time sell any combination of the securities described in this prospectus in one or more offerings for an aggregate initial offering price of up to $200,000,000.

This prospectus provides you with a general description of the securities we may offer. Each time we sell securities, we will provide one or more prospectus supplements that will contain specific information about the terms of the offering. The prospectus supplement may also add, update or change information contained in this prospectus. You should read both this prospectus and the accompanying prospectus supplement together with the additional information described under the heading Where You Can Find More Information beginning on page 2 of this prospectus.

You should rely only on the information contained in or incorporated by reference in this prospectus, any accompanying prospectus supplement or in any related free writing prospectus filed by us with the SEC. We have not authorized anyone to provide you with different information. This prospectus and any accompanying prospectus supplement do not constitute an offer to sell or the solicitation of an offer to buy any securities other than the securities described in this prospectus or such accompanying prospectus supplement or an offer to sell or the solicitation of an offer to buy such securities in any circumstances in which such offer or solicitation is unlawful. You should assume that the information appearing in this prospectus, any prospectus supplement, the documents incorporated by reference and any related free writing prospectus is accurate only as of their respective dates. Our business, financial condition, results of operations and prospects may have changed materially since those dates.

Unless the context otherwise indicates, references in this prospectus to we, our, us, AVEO and the Company ref collectively, to AVEO Pharmaceuticals, Inc., a Delaware corporation, and its subsidiaries.

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WHERE YOU CAN FIND MORE INFORMATION

We file annual, quarterly and current reports, proxy statements and other information with the SEC. Our SEC filings are available to the public over the Internet at the SEC s website at http://www.sec.gov. Copies of certain information filed by us with the SEC are also available on our website at http://www.aveooncology.com/. Our website is not a part of this prospectus and is not incorporated by reference in this prospectus. You may also read and copy any document we file at the SEC s Public Reference Room, 100 F Street, N.E., Washington, D.C. 20549. Please call the SEC at 1-800-SEC-0330 for further information on the operation of the Public Reference Room.

This prospectus is part of a registration statement we filed with the SEC. This prospectus omits some information contained in the registration statement in accordance with SEC rules and regulations. You should review the information and exhibits in the registration statement for further information about us and our consolidated subsidiaries and the securities we are offering. Statements in this prospectus concerning any document we filed as an exhibit to the registration statement or that we otherwise filed with the SEC are not intended to be comprehensive and are qualified by reference to these filings. You should review the complete document to evaluate these statements.

INCORPORATION BY REFERENCE

The SEC allows us to incorporate by reference much of the information we file with the SEC, which means that we can disclose important information to you by referring you to those publicly available documents. The information that we incorporate by reference in this prospectus is considered to be part of this prospectus. Because we are incorporating by reference future filings with the SEC, this prospectus is continually updated and those future filings may modify or supersede some of the information included or incorporated in this prospectus. This means that you must look at all of the SEC filings that we incorporate by reference to determine if any of the statements in this prospectus or in any document previously incorporated by reference have been modified or superseded. This prospectus incorporates by reference the documents listed below (File No. 001-34655) and any future filings we make with the SEC under Sections 13(a), 13(c), 14 or 15(d) of the Securities Exchange Act of 1934, as amended, or the Exchange Act (in each case, other than those documents or the portions of those documents not deemed to be filed) between the date of the initial registration statement and the effectiveness of the registration statement and following the effectiveness of the registration statement until the offering of the securities under the registration statement is terminated or completed:

- Annual Report on Form 10-K for the fiscal year ended December 31, 2016, including the information specifically incorporated by reference into the Annual Report on Form 10-K from our Definitive Proxy Statement on Schedule 14A, filed with the SEC on April 27, 2017, as amended and supplemented by the Definitive Additional Materials on Schedule 14A that we filed with the SEC on April 27, 2017 and May 17, 2017;

- Quarterly Reports on Form 10-Q for the fiscal quarters ended March 31, 2017, June 30, 2017 and September 30, 2017;

- Current Reports on Form 8-K filed on January 4, 2017, January 5, 2017, January 12, 2017, March 29, 2017, April 12, 2017, May 17, 2017, June 23, 2017, June 27, 2017, August 17, 2017, and November 20, 2017; and

The description of our common stock contained in our Registration Statement on Form 8-A filed on March 9, 2010, including any amendments or reports filed for the purpose of updating such description.

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You may request a copy of these filings, at no cost, by writing or telephoning us at the following address or telephone number:

AVEO Pharmaceuticals, Inc.

One Broadway, 14th Floor

Cambridge, Massachusetts 02142

Attention: Investor Relations

Telephone: (617) 588-1960

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CAUTIONARY NOTE REGARDING FORWARD-LOOKING STATEMENTS

This prospectus and the information incorporated by reference in this prospectus include forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, as amended, or the Securities Act, and Section 21E of the Exchange Act. These statements are based on current expectations, estimates, forecasts and projections about the industry in which we operate and the beliefs and assumptions of our management. Words such as expects, anticipates, targets, goals, projects, intends, plans, believes, seeks, estimates, continues, and may such words and similar expressions are intended to identify such forward-looking statements. In addition, any statements that refer to projections regarding our future financial performance; trends in our business; our capital needs and capital expenditures; our market position and competitive changes in the marketplace for our product candidates and any products; our ability to innovate new product candidates; our collaborators, licensees and other strategic partners; intellectual property and litigation matters; potential acquisitions and divestitures; key personnel; the effect of new accounting pronouncements and other characterizations of future events or circumstances are forward-looking statements. You are cautioned that these forward-looking statements are only predictions and are subject to risks, uncertainties and assumptions, including: risks inherent in pharmaceutical research and development, such as adverse results in our clinical development activities and our ability to obtain any necessary financing to conduct our planned activities, decisions made by the U.S. Food and Drug Administration and other regulatory authorities with respect to the development and commercialization of our drug candidates and those of our collaborators and licensees; risks relating to our ability to obtain, maintain and enforce intellectual property rights for our drug candidates; risks arising as a result of our dependence on our existing and future strategic partners, and other risk factors that are referenced in the section of any accompanying prospectus supplement entitled Risk Factors. You should also carefully review the risk factors and cautionary statements described in the other documents we file from time to time with the SEC, specifically our most recent Annual Report on Form 10-K, our Quarterly Reports on Form 10-Q and our Current Reports on Form 8-K. We undertake no obligation to revise or update any forward-looking statements, except to the extent required by law.

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ABOUT AVEO PHARMACEUTICALS, INC.

Company Overview

We are a biopharmaceutical company dedicated to advancing a broad portfolio of targeted therapeutics for oncology and other areas of unmet medical need. We are focused on seeking to develop and commercialize our lead candidate tivozanib (FOTIVDA®), a potent, selective, long half-life inhibitor of vascular endothelial growth factor 1, 2 and 3 receptors, in North America as a treatment for renal cell carcinoma, or RCC, and other cancers. We are leveraging multiple partnerships aimed at developing and commercializing tivozanib in oncology indications outside of North America, and at progressing our pipeline of novel therapeutic candidates in cancer and cachexia (wasting syndrome). Tivozanib (FOTIVDA®) is approved by the European Commission for the treatment of adult patients with advanced RCC in the European Union plus Norway and Iceland.

Company Information

We were incorporated in 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 One Broadway, 14th Floor, Cambridge, Massachusetts 02142, and our telephone number is (617) 588-1960. Our website is located at www.aveooncology.com. Information found on, or accessible through, our website is not a part of, and is not incorporated into, this prospectus, and you should not consider it part of this prospectus.

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CONSOLIDATED RATIOS OF EARNINGS TO FIXED CHARGES AND RATIOS OF EARNINGS TO COMBINED FIXED CHARGES AND PREFERRED STOCK DIVIDENDS

The following table sets forth our ratio of earnings to fixed charges for each of the periods indicated. You should read this table in conjunction with the consolidated financial statements and notes incorporated by reference in this prospectus.

	Nine Months Ended	Fiscal Year Ended				
	September 30, 2017	December 31, 2016	December 31, 2015	December 31, 2014	December 31, 2013	December 31, 2012
Consolidated ratios of earnings to fixed charges	N/A	N/A	N/A	N/A	N/A	N/A
Consolidated ratios of earnings to combined fixed charges and preferred stock dividends	N/A	N/A	N/A	N/A	N/A	N/A

For purposes of calculating the ratios above, earnings consist of income before income taxes plus fixed charges. Fixed charges include interest expense, non-cash interest expense, and an estimate of the interest expense within rental expense.

Our earnings were insufficient to cover fixed charges for the periods listed above, and we are unable to disclose a ratio of earnings to fixed charges or ratio of earnings to combined fixed charges and preferred stock dividends for such periods. The dollar amount in thousands of the deficiency in earnings available for fixed charges for the nine months ended September 30, 2017 and the fiscal years ended December 31, 2016, 2015, 2014, 2013 and 2012 was approximately $68,423, $26,786, $15,001, $52,739, $107,029 and $114,394, respectively.

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USE OF PROCEEDS

We intend to use the net proceeds from the sale of any securities offered under this prospectus for general corporate purposes unless otherwise indicated in the applicable prospectus supplement. General corporate purposes may include the repayment and refinancing of debt; working capital and capital expenditures; research and development expenses, including clinical trial costs; general and administrative expenses; and the potential acquisition of, or investment in, companies, technologies, products or assets that complement our business. We have not determined the amount of net proceeds to be used specifically for such purposes. As a result, management will retain broad discretion over the allocation of net proceeds.

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DESCRIPTION OF CAPITAL STOCK

The following description of our capital stock is intended as a summary only and therefore is not a complete description of our capital stock. This description is based upon, and is qualified by reference to, our restated certificate of incorporation, as amended, or certificate of incorporation, our second amended and restated by-laws, or by-laws, and applicable provisions of Delaware corporate law. You should read our certificate of incorporation and by-laws, which are filed as exhibits to the registration statement of which this prospectus forms a part, for the provisions that are important to you.

Our authorized capital stock consists of 250,000,000 shares of common stock, par value $0.001 per share, and 5,000,000 shares of preferred stock, par value $0.001 per share. At our 2017 annual meeting of stockholders, held on June 21, 2017, we received stockholder approval for a proposed amendment to our certificate of incorporation to effect a reverse stock split of our common stock by a ratio of not less than 1-for-3 and not more than 1-for-15, such ratio and the implementation and timing of such reverse stock split to be determined in the discretion of our board of directors provided that the board of directors must determine to effect the reverse stock split and such amendment must be filed with the Secretary of State of the State of Delaware no later than December 19, 2017. As of November 30, 2017, no such reverse stock split has been effected.

Common Stock

Annual Meeting. Annual meetings of our stockholders are held on the date designated in accordance with our by-laws. Written notice must be mailed to each stockholder entitled to vote not less than ten nor more than 60 days before the date of the meeting. The presence in person or by proxy of the holders of record of a majority in voting power of our issued and outstanding shares entitled to vote at such meeting constitutes a quorum for the transaction of business at meetings of the stockholders. Special meetings of the stockholders, unless otherwise prescribed by statute or by our certificate of incorporation, may be called for any purpose or purposes, by the chairman of our board of directors, our board of directors, or our chief executive officer. Except as may be otherwise provided by applicable law, our certificate of incorporation or our by-laws, all elections, other than elections of directors, and all other questions shall be decided by the affirmative vote of the holders of a majority in voting power of the shares of our stock which are present in person or by proxy and voting affirmatively or negatively on such matter. Except as may be provided by applicable law, our certificate of incorporation or our by-laws, each director shall be elected by the vote of the plurality of the votes cast by the stockholders entitled to vote with respect to that director s election at any meeting for the election of directors at which a quorum is present.

Voting Rights. Each holder of common stock is entitled to one vote for each share held of record on all matters to be voted upon by stockholders.

Dividends. Subject to the rights, powers and preferences of any outstanding preferred stock, and except as provided by law or in our certificate of incorporation, dividends may be declared and paid or set aside for payment on the common stock out of legally available assets or funds when and as declared by the board of directors.

Liquidation, Dissolution and Winding Up. Subject to the rights, powers and preferences of any outstanding preferred stock, in the event of our liquidation, dissolution or winding up, our net assets will be distributed pro rata to the holders of our common stock.

Other Rights. Holders of the common stock have no right to:

convert the stock into any other security;

have the stock redeemed;

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purchase additional stock; or

maintain their proportionate ownership interest.

The common stock does not have cumulative voting rights. Holders of shares of the common stock are not required to make additional capital contributions.

Transfer Agent and Registrar. Computershare Trust Company, N.A. is transfer agent and registrar for the common stock.

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

Preferred Stock

We are authorized to issue blank check preferred stock, which may be issued in one or more series upon authorization of our board of directors. Our board of directors is authorized to fix the designations, powers, preferences and the relative, participating, optional or other special rights and any qualifications, limitations and restrictions of the shares of each series of preferred stock. The authorized shares of our preferred stock are available for issuance without further action by our stockholders, unless such action is required by applicable law or the rules of any stock exchange on which our securities may be listed. Under the certificate of incorporation, the number of authorized preferred stock may be increased or decreased (but not below the number of shares outstanding) by the affirmative vote of the holders of a majority of the voting power of the capital stock entitled to vote thereon, voting as a single class. If the approval of our stockholders is not required for the issuance of shares of our preferred stock, our board may determine not to seek stockholder approval. The specific terms of any series of preferred stock offered pursuant to this prospectus will be described in the prospectus supplement relating to that series of preferred stock.

A series of our preferred stock could, depending on the terms of such series, impede the completion of a merger, tender offer or other takeover attempt. Our board of directors will make any determination to issue preferred shares based upon its judgment as to the best interests of our stockholders. Our directors, in so acting, could issue preferred stock having terms that could discourage an acquisition attempt through which an acquirer may be able to change the composition of our board of directors, including a tender offer or other transaction that some, or a majority, of our stockholders might believe to be in their best interests or in which stockholders might receive a premium for their stock over the then-current market price of the stock.

The preferred stock has the terms described below unless otherwise provided in the prospectus supplement relating to a particular series of preferred stock. You should read the prospectus supplement relating to the particular series of preferred stock being offered for specific terms, including:

the designation and stated value per share of the preferred stock and the number of shares offered;

the amount of liquidation preference per share;

the price at which the preferred stock will be issued;

the dividend rate, or method of calculation of dividends, the dates on which dividends will be payable, whether dividends will be cumulative or noncumulative and, if cumulative, the dates from which dividends will commence to accumulate;

any redemption or sinking fund provisions;

if other than the currency of the United States, the currency or currencies including composite currencies in which the preferred stock is denominated and/or in which payments will or may be payable;

any conversion provisions; and

any other rights, preferences, privileges, limitations and restrictions on the preferred stock.

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The preferred stock will, when issued, be fully paid and non-assessable. Unless otherwise specified in the prospectus supplement, each series of preferred stock will rank equally as to dividends and liquidation rights in all respects with each other series of preferred stock. The rights of holders of shares of each series of preferred stock will be subordinate to those of our general creditors.

We may, at our option, with respect to any series of preferred stock, elect to offer fractional interests in shares of preferred stock, and provide for the issuance of depositary receipts representing depositary shares, each of which will represent a fractional interest in a share of the series of preferred stock. The fractional interest will be specified in the prospectus supplement relating to a particular series of preferred stock.

Rank. Unless otherwise specified in the prospectus supplement, the preferred stock will, with respect to dividend rights and rights upon our liquidation, dissolution or winding up of our affairs, rank:

- senior to our common stock and to all equity securities ranking junior to such preferred stock with respect to dividend rights or rights upon our liquidation, dissolution or winding up of our affairs;

- on a parity with all equity securities issued by us, the terms of which specifically provide that such equity securities rank on a parity with the preferred stock with respect to dividend rights or rights upon our liquidation, dissolution or winding up of our affairs; and

- junior to all equity securities issued by us, the terms of which specifically provide that such equity securities rank senior to the preferred stock with respect to dividend rights or rights upon our liquidation, dissolution or winding up of our affairs.

The term equity securities does not include convertible debt securities.

Dividends. Holders of the preferred stock of each series will be entitled to receive, when, as and if declared by our board of directors, cash dividends at such rates and on such dates described in the prospectus supplement. Different series of preferred stock may be entitled to dividends at different rates or based on different methods of calculation. The dividend rate may be fixed or variable or both. Dividends will be payable to the holders of record as they appear on our stock books on record dates fixed by our board of directors, as specified in the applicable prospectus supplement.

Dividends on any series of preferred stock may be cumulative or noncumulative, as described in the applicable prospectus supplement. If our board of directors does not declare a dividend payable on a dividend payment date on any series of noncumulative preferred stock, then the holders of that noncumulative preferred stock will have no right to receive a dividend for that dividend payment date, and we will have no obligation to pay the dividend accrued for that period, whether or not dividends on that series are declared payable on any future dividend payment dates. Dividends on any series of cumulative preferred stock will accrue from the date we initially issue shares of such series or such other date specified in the applicable prospectus supplement.

No dividends may be declared or paid or funds set apart for the payment of any dividends on any parity securities unless full dividends have been paid or set apart for payment on the preferred stock. If full dividends are not paid, the preferred stock will share dividends pro rata with the parity securities.

No dividends may be declared or paid or funds set apart for the payment of dividends on any junior securities unless full dividends for all dividend periods terminating on or prior to the date of the declaration or payment will have been paid or declared and a sum sufficient for the payment set apart for payment on the preferred stock.

Liquidation Preference. Upon any voluntary or involuntary liquidation, dissolution or winding up of our affairs, then, before we make any distribution or payment to the holders of any common stock or any other class or series of our capital stock ranking junior to the preferred stock in the distribution of assets upon any

liquidation, dissolution or winding up of our affairs, the holders of each series of preferred stock shall be entitled to receive out of assets legally available for distribution to stockholders, liquidating distributions in the amount of the liquidation preference per share set forth in the prospectus supplement, plus any accrued and unpaid dividends thereon. Such dividends will not include any accumulation in respect of unpaid noncumulative dividends for prior dividend periods. Unless otherwise specified in the prospectus supplement, after payment of the full amount of their liquidating distributions, the holders of preferred stock will have no right or claim to any of our remaining assets. Upon any such voluntary or involuntary liquidation, dissolution or winding up, if our available assets are insufficient to pay the amount of the liquidating distributions on all outstanding preferred stock and the corresponding amounts payable on all other classes or series of our capital stock ranking on parity with the preferred stock and all other such classes or series of shares of capital stock ranking on parity with the preferred stock in the distribution of assets, then the holders of the preferred stock and all other such classes or series of capital stock will share ratably in any such distribution of assets in proportion to the full liquidating distributions to which they would otherwise be entitled.

Upon any such liquidation, dissolution or winding up and if we have made liquidating distributions in full to all holders of preferred stock, we will distribute our remaining assets among the holders of any other classes or series of capital stock ranking junior to the preferred stock according to their respective rights and preferences and, in each case, according to their respective number of shares. For such purposes, our consolidation or merger with or into any other corporation, trust or entity, or the sale, lease or conveyance of all or substantially all of our property or assets will not be deemed to constitute a liquidation, dissolution or winding up of our affairs.

Redemption. If so provided in the applicable prospectus supplement, the preferred stock will be subject to mandatory redemption or redemption at our option, as a whole or in part, in each case upon the terms, at the times and at the redemption prices set forth in such prospectus supplement.

The prospectus supplement relating to a series of preferred stock that is subject to mandatory redemption will specify the number of shares of preferred stock that shall be redeemed by us in each year commencing after a date to be specified, at a redemption price per share to be specified, together with an amount equal to all accrued and unpaid dividends thereon to the date of redemption. Unless the shares have a cumulative dividend, such accrued dividends will not include any accumulation in respect of unpaid dividends for prior dividend periods. We may pay the redemption price in cash or other property, as specified in the applicable prospectus supplement. If the redemption price for preferred stock of any series is payable only from the net proceeds of the issuance of shares of our capital stock, the terms of such preferred stock may provide that, if no such shares of our capital stock shall have been issued or to the extent the net proceeds from any issuance are insufficient to pay in full the aggregate redemption price then due, such preferred stock shall automatically and mandatorily be converted into the applicable shares of our capital stock pursuant to conversion provisions specified in the applicable prospectus supplement. Notwithstanding the foregoing, we will not redeem any preferred stock of a series unless:

- if that series of preferred stock has a cumulative dividend, we have declared and paid or contemporaneously declare and pay or set aside funds to pay full cumulative dividends on the preferred stock for all past dividend periods and the then current dividend period; or

- if such series of preferred stock does not have a cumulative dividend, we have declared and paid or contemporaneously declare and pay or set aside funds to pay full dividends for the then current dividend period.

In addition, we will not acquire any preferred stock of a series unless:

if that series of preferred stock has a cumulative dividend, we have declared and paid or contemporaneously declare and pay or set aside funds to pay full cumulative dividends on all outstanding shares of such series of preferred stock for all past dividend periods and the then current dividend period; or

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if that series of preferred stock does not have a cumulative dividend, we have declared and paid or contemporaneously declare and pay or set aside funds to pay full dividends on the preferred stock of such series for the then current dividend period.

However, at any time we may purchase or acquire preferred stock of that series (1) pursuant to a purchase or exchange offer made on the same terms to holders of all outstanding preferred stock of such series or (2) by conversion into or exchange for shares of our capital stock ranking junior to the preferred stock of such series as to dividends and upon liquidation.

If fewer than all of the outstanding shares of preferred stock of any series are to be redeemed, we will determine the number of shares that may be redeemed pro rata from the holders of record of such shares in proportion to the number of such shares held or for which redemption is requested by such holder or by any other equitable manner that we determine. Such determination will reflect adjustments to avoid redemption of fractional shares.

Unless otherwise specified in the prospectus supplement, we will mail notice of redemption at least 30 days but not more than 60 days before the redemption date to each holder of record of preferred stock to be redeemed at the address shown on our stock transfer books. Each notice shall state:

the redemption date;

the number of shares and series of preferred stock to be redeemed;

the redemption price;

the place or places where certificates for such preferred stock are to be surrendered for payment of the redemption price;

that dividends on the shares to be redeemed will cease to accrue on such redemption date;

the date on which the holder s conversion rights, if any, as to such shares shall terminate; and

the specific number of shares to be redeemed from each such holder if fewer than all the shares of any series are to be redeemed.

If notice of redemption has been given and we have set aside the funds necessary for such redemption in trust for the benefit of the holders of any shares called for redemption, then from and after the redemption date, dividends will cease to accrue on such shares, and all rights of the holders of such shares will terminate, except the right to receive the redemption price.

Voting Rights. Holders of preferred stock will not have any voting rights, except as required by law or as indicated in the applicable prospectus supplement.

Unless otherwise provided for under the terms of any series of preferred stock, no consent or vote of the holders of shares of preferred stock or any series thereof shall be required for any amendment to our certificate of incorporation that would increase the number of authorized shares of preferred stock or the number of authorized shares of any series thereof or decrease the number of authorized shares of preferred stock or the number of authorized shares of any series thereof (but not below the number of authorized shares of preferred stock or such series, as the case may be, then outstanding).

Conversion Rights. The terms and conditions, if any, upon which any series of preferred stock is convertible into our common stock will be set forth in the applicable prospectus supplement relating thereto. Such terms will include the number of shares of common stock into which the shares of preferred stock are convertible, the conversion price, rate or manner of calculation thereof, the conversion period, provisions as to whether conversion will be at our option or at the option of the holders of the preferred stock, the events requiring an adjustment of the conversion price and provisions affecting conversion in the event of the redemption.

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Transfer Agent and Registrar. The transfer agent and registrar for the preferred stock will be set forth in the applicable prospectus supplement.

Effects of Authorized but Unissued Stock

Authorized but unissued shares of common stock and preferred stock are available for future issuance without stockholder approval, subject to any limitations imposed by the listing standards of the NASDAQ Capital Market. These additional shares may be used for a variety of corporate finance transactions, acquisitions and employee benefit plans. The existence of authorized but unissued and unreserved common stock and preferred stock could make more difficult or discourage an attempt to obtain control of us by means of a proxy contest, tender offer, merger or otherwise. In addition, if we issue preferred stock, the issuance could adversely affect the voting power of holders of common stock and the likelihood that such holders will receive dividend payments and payments upon liquidation.

Provisions of Our Certificate of Incorporation and By-laws and Delaware Law That May Have Anti-Takeover Effects

Board of Directors. We do not have a classified board of directors. All of our directors are elected annually. The number of directors comprising our board of directors is fixed from time to time by the board of directors.

Removal of Directors by Stockholders. Members of our board of directors may be removed from office at any time with or without cause by the affirmative vote of the holders of a majority of the outstanding shares entitled to vote at an election of directors.

Stockholder Nomination of Directors. Our by-laws provide that a stockholder must notify us in writing of any stockholder nomination of a director not earlier than the close of business on the 120th day, and not later than the close of business on the 90th day prior to the first anniversary of the preceding year s annual meeting; provided, that, in the case of the annual meeting of stockholders, if the date of the annual meeting is more than 20 days before or more than 60 days after such anniversary date, notice by the stockholder to be timely must be so delivered not earlier than the close of business on the 120th day prior to the date of such annual meeting and not later than the close of business on the later of (x) the 90th day prior to such annual meeting and (y) the 10th day following the day on which public announcement of the date of such annual meeting is first made by us. Our by-laws also provide that, subject to certain limitations, if a stockholder (or a qualified representative of the stockholder) does not appear at a meeting of stockholders to present a nomination, such nomination shall be disregarded, notwithstanding that proxies in respect of such vote may have been received by us.

No Action By Written Consent. Our certificate of incorporation and our by-laws provide that our stockholders may not act by written consent and may only act at duly called meetings of stockholders.

Delaware Business Combination Statute. Section 203 of the General Corporation Law of the State of Delaware, which we refer to as the DGCL, is applicable to us. Section 203 of the DGCL restricts some types of transactions and business combinations between a corporation and a 15% stockholder. A 15% stockholder is generally considered by Section 203 to be a person owning 15% or more of the corporation s outstanding voting stock. Section 203 refers to a 15% stockholder as an interested stockholder. Section 203 restricts these transactions for a period of three years from the date the stockholder acquires 15% or more of our outstanding voting stock. With some exceptions, unless the transaction is approved by the board of directors and the holders of at least two-thirds of the outstanding voting stock of the corporation, Section 203 prohibits significant business transactions such as:

a merger with, disposition of significant assets to or receipt of disproportionate financial benefits by the interested stockholder, and

any other transaction that would increase the interested stockholder s proportionate ownership of any class or series of our capital stock.

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The shares held by the interested stockholder are not counted as outstanding when calculating the two-thirds of the outstanding voting stock needed for approval.

The prohibition against these transactions does not apply if:

- prior to the time that any stockholder became an interested stockholder, the board of directors approved either the business combination or the transaction in which such stockholder acquired 15% or more of our outstanding voting stock, or
- the interested stockholder owns at least 85% of our outstanding voting stock as a result of a transaction in which such stockholder acquired 15% or more of our outstanding voting stock. Shares held by persons who are both directors and officers or by some types of employee stock plans are not counted as outstanding when making this calculation.

Super-Majority Voting. The DGCL provides generally that the affirmative vote of a majority of the shares entitled to vote on any matter is required to amend a corporation s certificate of incorporation or by-laws, unless a corporation s certificate of incorporation or by-laws, as the case may be, requires a greater percentage. Our by-laws may be amended or repealed by a majority vote of our board of directors or the affirmative vote of the holders of at least 75% of the votes that all our stockholders would be entitled to cast in any annual election of directors. In addition, the affirmative vote of the holders of at least 75% of the votes that all our stockholders would be entitled to cast in any annual election of directors is required to amend or repeal or to adopt any provisions inconsistent with any of the provisions of our certificate of incorporation described in this paragraph.

Directors Liability

Our certificate of incorporation limits the personal liability of directors for breach of fiduciary duty to the maximum extent permitted by the DGCL. Our certificate of incorporation provides that no director will have personal liability to us or to our stockholders for monetary damages for breach of fiduciary duty or other duty as a director. However, these provisions do not eliminate or limit the liability of any of our directors:

- for any breach of their duty of loyalty to us or our stockholders;
- for acts or omissions not in good faith or which involve intentional misconduct or a knowing violation of law;
- for voting or assenting to unlawful payments of dividends or other distributions; or
- for any transaction from which the director derived an improper personal benefit.

Any amendment to or repeal of these provisions will not eliminate or reduce the effect of these provisions in respect of any act or failure to act, or any cause of action, suit or claim that would accrue or arise prior to any amendment or repeal or adoption of an inconsistent provision. If the DGCL is amended to provide for further limitations on the

personal liability of directors of corporations, then the personal liability of our directors will be further limited to the greatest extent permitted by the DGCL.

In addition, our certificate of incorporation provides that we must indemnify our directors and officers and we must advance expenses, including attorneys fees, to our directors and officers in connection with legal proceedings, subject to very limited exceptions.

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DESCRIPTION OF DEBT SECURITIES

We may offer debt securities which may be senior or subordinated. We refer to the senior debt securities and the subordinated debt securities collectively as debt securities. The following description summarizes the general terms and provisions of the debt securities. We will describe the specific terms of the debt securities and the extent, if any, to which the general provisions summarized below apply to any series of debt securities in the prospectus supplement relating to the series and any applicable free writing prospectus that we authorize to be delivered. When we refer to we, our, us, AVEO, and the Company, in this section, we mean AVEO Pharmaceuticals, Inc., excluding, unless context otherwise requires or as otherwise expressly stated, our subsidiaries.

We may issue senior debt securities from time to time, in one or more series under a senior indenture to be entered into between us and a senior trustee to be named in a prospectus supplement, which we refer to as the senior trustee. We may issue subordinated debt securities from time to time, in one or more series under a subordinated indenture to be entered into between us and a subordinated trustee to be named in a prospectus supplement, which we refer to as the subordinated trustee. The forms of senior indenture and subordinated indenture are filed as exhibits to the registration statement of which this prospectus forms a part. The senior indenture and the subordinated indenture are referred to individually as an indenture and together as the indentures and the senior trustee and the subordinated trustee are referred to individually as a trustee and together as the trustees. This section summarizes some of the provisions of the indentures and is qualified in its entirety by the specific text of the indentures, including definitions of terms used in the indentures. Wherever we refer to particular sections of, or defined terms in, the indentures, those sections or defined terms are incorporated by reference in this prospectus or the applicable prospectus supplement. You should review the indentures that are filed as exhibits to the registration statement of which this prospectus forms a part for additional information.

Neither indenture will limit the amount of debt securities that we may issue. The applicable indenture will provide that debt securities may be issued up to an aggregate principal amount authorized from time to time by us and may be payable in any currency or currency unit designated by us or in amounts determined by reference to an index.

General

The senior debt securities will constitute our unsecured and unsubordinated general obligations and will rank equally in right of payment with our other unsecured and unsubordinated obligations. The subordinated debt securities will constitute our unsecured and subordinated general obligations and will be junior in right of payment to our senior indebtedness (including senior debt securities), as described under the heading Certain Terms of the Subordinated Debt Securities Subordination. The debt securities will be structurally subordinated to all existing and future indebtedness and other liabilities of our subsidiaries unless such subsidiaries expressly guarantee such debt securities.

The debt securities will be our unsecured obligations. Any secured debt or other secured obligations will be effectively senior to the debt securities to the extent of the value of the assets securing such debt or other obligations.

The applicable prospectus supplement and/or free writing prospectus will include any additional or different terms of the debt securities of any series being offered, including the following terms:

- the title and type of the debt securities;

whether the debt securities will be senior or subordinated debt securities, and, with respect to any subordinated debt securities the terms on which they are subordinated;

the initial aggregate principal amount of the debt securities;

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the price or prices at which we will sell the debt securities;

the maturity date or dates of the debt securities and the right, if any, to extend such date or dates;

the rate or rates, if any, at which the debt securities will bear interest, or the method of determining such rate or rates;

the date or dates from which such interest will accrue, the interest payment dates on which such interest will be payable or the method of determination of such dates;

the right, if any, to extend the interest payment periods and the duration of that extension;

the manner of paying principal and interest and the place or places where principal and interest will be payable;

provisions for a sinking fund, purchase fund or other analogous fund, if any;

any redemption dates, prices, obligations and restrictions on the debt securities;

the currency, currencies or currency units in which the debt securities will be denominated and the currency, currencies or currency units in which principal and interest, if any, on the debt securities may be payable;

any conversion or exchange features of the debt securities;

whether the debt securities will be subject to the defeasance provisions in the indenture;

whether the debt securities will be issued in definitive or global form or in definitive form only upon satisfaction of certain conditions;

whether the debt securities will be guaranteed as to payment or performance;

any special tax implications of the debt securities;

any events of defaults or covenants in addition to or in lieu of those set forth in the indenture; and

any other material terms of the debt securities.

When we refer to principal in this section with reference to the debt securities, we are also referring to premium, if any.

We may from time to time, without notice to or the consent of the holders of any series of debt securities, create and issue further debt securities of any such series ranking equally with the debt securities of such series in all respects (or in all respects other than (1) the payment of interest accruing prior to the issue date of such further debt securities or (2) the first payment of interest following the issue date of such further debt securities). Such further debt securities may be consolidated and form a single series with the debt securities of such series and have the same terms as to status, redemption or otherwise as the debt securities of such series.

You may present debt securities for exchange and you may present debt securities for transfer in the manner, at the places and subject to the restrictions set forth in the debt securities and the applicable prospectus supplement. We will provide you those services without charge, although you may have to pay any tax or other governmental charge payable in connection with any exchange or transfer, as set forth in the indenture.

Debt securities may bear interest at a fixed rate or a floating rate. Debt securities bearing no interest or interest at a rate that at the time of issuance is below the prevailing market rate (original issue discount securities) may be sold at a discount below their stated principal amount. U.S. federal income tax considerations applicable to any such discounted debt securities or to certain debt securities issued at par which are treated as having been issued at a discount for U.S. federal income tax purposes will be described in the applicable prospectus supplement.

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We may issue debt securities with the principal amount payable on any principal payment date, or the amount of interest payable on any interest payment date, to be determined by reference to one or more currency exchange rates, securities or baskets of securities, commodity prices or indices. You may receive a payment of principal on any principal payment date, or a payment of interest on any interest payment date, that is greater than or less than the amount of principal or interest otherwise payable on such dates, depending on the value on such dates of the applicable currency, security or basket of securities, commodity or index. Information as to the methods for determining the amount of principal or interest payable on any date, the currencies, securities or baskets of securities, commodities or indices to which the amount payable on such date is linked and certain related tax considerations will be set forth in the applicable prospectus supplement.

Certain Terms of the Senior Debt Securities

Covenants. Unless we indicate otherwise in a prospectus supplement with respect to a particular series of senior debt securities, the senior debt securities will not contain any financial or restrictive covenants, including covenants restricting either us or any of our subsidiaries from incurring, issuing, assuming or guaranteeing any indebtedness secured by a lien on any of our or our subsidiaries property or capital stock, or restricting either us or any of our subsidiaries from entering into sale and leaseback transactions.

Consolidation, Merger and Sale of Assets. Unless we indicate otherwise in a prospectus supplement with respect to a particular series of senior debt securities, we may not consolidate with or merge into any other person, in a transaction in which we are not the surviving corporation, or convey, transfer or lease our properties and assets substantially as an entirety to any person, in either case, unless:

- the successor entity, if any, is a U.S. corporation, limited liability company, partnership or trust;
- the successor entity assumes our obligations on the senior debt securities and under the senior indenture;
- immediately after giving effect to the transaction, no default or event of default shall have occurred and be continuing; and
- we have delivered to the senior trustee an officer s certificate and an opinion of counsel, each stating that the consolidation, merger, conveyance, transfer or lease and, if a supplemental indenture is required in connection with such transaction, such supplemental indenture, comply with the senior indenture and all conditions precedent provided for in the senior indenture relating to such transaction have been complied with.

The restrictions described in the bullets above do not apply (1) to our consolidation with or merging into one of our affiliates, if our board of directors determines in good faith that the purpose of the consolidation or merger is principally to change our state of incorporation or our form of organization to another form or (2) if we merge with or into a single direct or indirect wholly-owned subsidiary of ours.

The surviving business entity will succeed to, and be substituted for, us under the senior indenture and the senior debt securities and, except in the case of a lease, we shall be released from all obligations under the senior indenture and the senior debt securities.

No Protection in the Event of a Change in Control. Unless we indicate otherwise in a prospectus supplement with respect to a particular series of senior debt securities, the senior debt securities will not contain any provisions that may afford holders of the senior debt securities protection in the event we have a change in control or in the event of a highly leveraged transaction (whether or not such transaction results in a change in control).

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Events of Default. Unless we indicate otherwise in a prospectus supplement with respect to a particular series of senior debt securities, the following are events of default under the senior indenture with respect to senior debt securities of each series:

- failure to pay interest on any senior debt securities of such series when due and payable, if that default continues for a period of 30 days (or such other period as may be specified for such series);
- failure to pay principal on the senior debt securities of such series when due and payable whether at maturity, upon redemption, by declaration or otherwise (and, if specified for such series, the continuance of such failure for a specified period);
- default in the performance of or breach of any of our covenants or agreements in the senior indenture applicable to senior debt securities of such series, other than a covenant breach which is specifically dealt with elsewhere in the senior indenture, and that default or breach continues for a period of 90 days after we receive written notice from the trustee or from the holders of 25% or more in aggregate principal amount of the senior debt securities of such series;
- certain events of bankruptcy or insolvency, whether or not voluntary; and
- any other event of default provided for in such series of senior debt securities as may be specified in the applicable prospectus supplement.

The default by us under any other debt, including any other series of debt securities, is not a default under the senior indenture.

If an event of default other than an event of default specified in the fourth bullet point above occurs with respect to a series of senior debt securities and is continuing under the senior indenture, then, and in each such case, either the trustee or the holders of not less than 25% in aggregate principal amount of such series then outstanding under the senior indenture (each such series voting as a separate class) by written notice to us and to the trustee, if such notice is given by the holders, may, and the trustee at the request of such holders shall, declare the principal amount of and accrued interest on such series of senior debt securities to be immediately due and payable, and upon this declaration, the same shall become immediately due and payable.

If an event of default specified in the fourth bullet point above occurs and is continuing, the entire principal amount of and accrued interest on each series of senior debt securities then outstanding shall automatically become immediately due and payable.

Unless otherwise specified in the prospectus supplement relating to a series of senior debt securities originally issued at a discount, the amount due upon acceleration shall include only the original issue price of the senior debt securities, the amount of original issue discount accrued to the date of acceleration and accrued interest, if any.

Upon certain conditions, declarations of acceleration may be rescinded and annulled and past defaults may be waived by the holders of a majority in aggregate principal amount of all the senior debt securities of such series affected by

the default, each series voting as a separate class. Furthermore, subject to various provisions in the senior indenture, the holders of a majority in aggregate principal amount of a series of senior debt securities, by notice to the trustee, may waive a continuing default or event of default with respect to such senior debt securities and its consequences, except a default in the payment of principal of or interest on such senior debt securities (other than any such default in payment resulting solely from an acceleration of the senior debt securities) or in respect of a covenant or provision of the senior indenture which cannot be modified or amended without the consent of the holders of each such senior debt security. Upon any such waiver, such default shall cease to exist, and any event of default with respect to such senior debt securities shall be deemed to have been cured, for every purpose of the senior indenture; but no such waiver shall extend to any subsequent or other default or event of default or impair any right consequent thereto.

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The holders of a majority in aggregate principal amount of a series of senior debt securities may direct the time, method and place of conducting any proceeding for any remedy available to the trustee or exercising any trust or power conferred on the trustee with respect to such senior debt securities. However, the trustee may refuse to follow any direction that conflicts with law or the senior indenture, that may involve the trustee in personal liability or that the trustee determines in good faith may be unduly prejudicial to the rights of holders of such series of senior debt securities not joining in the giving of such direction and may take any other action it deems proper that is not inconsistent with any such direction received from holders of such series of senior debt securities. A holder may not pursue any remedy with respect to the senior indenture or any series of senior debt securities unless:

- the holder gives the trustee written notice of a continuing event of default;
- the holders of at least 25% in aggregate principal amount of such series of senior debt securities make a written request to the trustee to pursue the remedy in respect of such event of default;
- the requesting holder or holders offer the trustee indemnity satisfactory to the trustee against any costs, liability or expense;
- the trustee does not comply with the request within 60 days after receipt of the request and the offer of indemnity; and
- during such 60-day period, the holders of a majority in aggregate principal amount of such series of senior debt securities do not give the trustee a direction that is inconsistent with the request.

These limitations, however, do not apply to the right of any holder of a senior debt security of any affected series to receive payment of the principal of and interest on such senior debt security in accordance with the terms of such debt security, or to bring suit for the enforcement of any such payment in accordance with the terms of such debt security, on or after the due date for the senior debt securities, which right shall not be impaired or affected without the consent of the holder.

The senior indenture requires certain of our officers to certify, on or before a fixed date in each year in which any senior debt security is outstanding, as to their knowledge of our compliance with all covenants, agreements and conditions under the senior indenture.

Satisfaction and Discharge. We can satisfy and discharge our obligations to holders of any series of debt securities if:

- we have paid or caused to be paid the principal of and interest on all senior debt securities of such series (with certain limited exceptions) when due and payable;
- we deliver to the senior trustee for cancellation all senior debt securities of such series theretofore authenticated under the senior indenture (with certain limited exceptions); or

all senior debt securities of such series have become due and payable or will become due and payable within one year (or are to be called for redemption within one year under arrangements satisfactory to the senior trustee) and we deposit in trust an amount of cash or a combination of cash and U.S. government or U.S. government agency obligations (or in the case of senior debt securities denominated in a foreign currency, foreign government securities or foreign government agency securities) sufficient to make interest, principal and any other payments on the debt securities of that series on their various due dates;

and if, in any such case, we also pay or cause to be paid all other sums payable under the senior indenture, as and when the same shall be due and payable and we deliver to the senior trustee an officer s certificate and an opinion of counsel, each stating that these conditions have been satisfied.

Under current U.S. federal income tax law, the deposit and our legal release from the debt securities would be treated as though we took back your debt securities and gave you your share of the cash and debt securities or

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bonds deposited in trust. In that event, you could recognize gain or loss on the debt securities you give back to us. Purchasers of the debt securities should consult their own advisers with respect to the tax consequences to them of such deposit and discharge, including the applicability and effect of tax laws other than the U.S. federal income tax law.

Defeasance. Unless the applicable prospectus supplement provides otherwise, the following discussion of legal defeasance and covenant defeasance will apply to any series of debt securities issued under the indentures.

Legal Defeasance. We can legally release ourselves from any payment or other obligations on the debt securities of any series, called legal defeasance , if certain conditions are met, including the following:

- We deposit in trust for your benefit and the benefit of all other direct holders of the debt securities of the same series cash or a combination of cash and U.S. government or U.S. government agency obligations (or, in the case of senior debt securities denominated in a foreign currency, foreign government or foreign government agency obligations) that will generate enough cash to make interest, principal and any other payments on the debt securities of that series on their various due dates.

- There is a change in current U.S. federal income tax law or a U.S. Internal Revenue Service ruling that lets us make the above deposit without causing you to be taxed on the debt securities any differently than if we did not make the deposit and instead repaid the debt securities ourselves when due. Under current U.S. federal income tax law, the deposit and our legal release from the debt securities would be treated as though we took back your debt securities and gave you your share of the cash and debt securities or bonds deposited in trust. In that event, you could recognize gain or loss on the debt securities you give back to us.

- We deliver to the trustee a legal opinion of our counsel confirming the tax law change or ruling described above.

If we accomplish legal defeasance, as described above, you would have to rely solely on the trust deposit for repayment of the debt securities. You could not look to us for repayment in the event of any shortfall.

Covenant Defeasance. Without any change in current U.S. federal tax law, we can make the same type of deposit described above and be released from some of the covenants in the debt securities, called covenant defeasance . In that event, you would lose the protection of those covenants but would gain the protection of having money and securities set aside in trust to repay the debt securities. In order to achieve covenant defeasance, we must do the following (among other things):

- We must deposit in trust for your benefit and the benefit of all other direct holders of the debt securities of the same series cash or a combination of cash and U.S. government or U.S. government agency obligations (or, in the case of senior debt securities denominated in a foreign currency, foreign government or foreign government agency obligations) that will generate enough cash to make interest, principal and any other payments on the debt securities of that series on their various due dates.

We must deliver to the trustee a legal opinion of our counsel confirming that under current U.S. federal income tax law we may make the above deposit without causing you to be taxed on the debt securities any differently than if we did not make the deposit and instead repaid the debt securities ourselves when due.

If we accomplish covenant defeasance, you could still look to us for repayment of the debt securities if there were a shortfall in the trust deposit. In fact, if one of the events of default occurred (such as our bankruptcy) and the debt securities become immediately due and payable, there may be such a shortfall. Depending on the events causing the default, you may not be able to obtain payment of the shortfall.

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Modification and Waiver. We and the trustee may amend or supplement the senior indenture or the senior debt securities of any series without the consent of any holder:

to convey, transfer, assign, mortgage or pledge any assets as security for the senior debt securities of one or more series;

to evidence the succession of a corporation, limited liability company, partnership or trust to us, and the assumption by such successor of our covenants, agreements and obligations under the senior indenture or to otherwise comply with the covenant relating to mergers, consolidations and sales of assets;

to comply with requirements of the SEC in order to effect or maintain the qualification of the senior indenture under the Trust Indenture Act of 1939, as amended, or the Trust Indenture Act;

to add to our covenants such new covenants, restrictions, conditions or provisions for the protection of the holders, and to make the occurrence, or the occurrence and continuance, of a default in any such additional covenants, restrictions, conditions or provisions an event of default;

to cure any ambiguity, defect or inconsistency in the senior indenture or in any supplemental indenture or to conform the senior indenture or the senior debt securities to the description of senior debt securities of such series set forth in this prospectus or any applicable prospectus supplement;

to provide for or add guarantors with respect to the senior debt securities of any series;

to establish the form or forms or terms of the senior debt securities as permitted by the senior indenture;

to evidence and provide for the acceptance of appointment under the senior indenture by a successor trustee, or to make such changes as shall be necessary to provide for or facilitate the administration of the trusts in the senior indenture by more than one trustee;

to add to, change or eliminate any of the provisions of the senior indenture in respect of one or more series of senior debt securities, provided that any such addition, change or elimination shall (a) neither (1) apply to any senior debt security of any series created prior to the execution of such supplemental indenture and entitled to the benefit of such provision nor (2) modify the rights of the holder of any such senior debt security with respect to such provision or (b) become effective only when there is no senior debt security described in clause (a)(1) outstanding;

to make any change to the senior debt securities of any series so long as no senior debt securities of such series are outstanding; or

to make any change that does not adversely affect the rights of any holder in any material respect.

Other amendments and modifications of the senior indenture or the senior debt securities issued may be made, and our compliance with any provision of the senior indenture with respect to any series of senior debt securities may be waived, with the consent of the holders of a majority of the aggregate principal amount of the outstanding senior debt securities of each series affected by the amendment or modification (voting as separate series); provided, however, that each affected holder must consent to any modification, amendment or waiver that:

extends the final maturity of any senior debt securities of such series;

reduces the principal amount of any senior debt securities of such series;

reduces the rate, or extends the time for payment of, interest on any senior debt securities of such series;

reduces the amount payable upon the redemption of any senior debt securities of such series;

changes the currency of payment of principal of or interest on any senior debt securities of such series;

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reduces the principal amount of original issue discount securities payable upon acceleration of maturity or the amount provable in bankruptcy;

waives a continuing default in the payment of principal of or interest on the senior debt securities (other than any such default in payment resulting solely from an acceleration of the senior debt securities);

changes the provisions relating to the waiver of past defaults or impairs the right of holders to receive payment or to institute suit for the enforcement of any payment or conversion of any senior debt securities of such series on or after the due date therefor;

modifies any of the provisions of these restrictions on amendments and modifications, except to increase any required percentage or to provide that certain other provisions cannot be modified or waived without the consent of the holder of each senior debt security of such series affected by the modification;

adversely affects the right to convert or exchange senior debt securities into common stock or other property in accordance with the terms of the senior debt securities; or

reduces the above-stated percentage of outstanding senior debt securities of such series whose holders must consent to a supplemental indenture or modifies, amends or waives certain provisions of or defaults under the senior indenture.

It shall not be necessary for the holders to approve the particular form of any proposed amendment, supplement or waiver, but it shall be sufficient if the holders consent approves the substance thereof. After an amendment, supplement or waiver of the senior indenture in accordance with the provisions described in this section becomes effective, the trustee must give to the holders affected thereby certain notice briefly describing the amendment, supplement or waiver. Any failure by the trustee to give such notice, or any defect therein, shall not, however, in any way impair or affect the validity of any such amendment, supplemental indenture or waiver.

No Personal Liability of Incorporators, Stockholders, Officers, Directors. The senior indenture provides that no recourse shall be had under any obligation, covenant or agreement of ours in the senior indenture or any supplemental indenture, or in any of the senior debt securities or because of the creation of any indebtedness represented thereby, against any of our incorporators, stockholders, officers or directors, past, present or future, or of any predecessor or successor entity thereof under any law, statute or constitutional provision or by the enforcement of any assessment or by any legal or equitable proceeding or otherwise. Each holder, by accepting the senior debt securities, waives and releases all such liability.

Concerning the Trustee. The senior indenture provides that, except during the continuance of an event of default, the trustee will not be liable except for the performance of such duties as are specifically set forth in the senior indenture. If an event of default has occurred and is continuing, the trustee will exercise such rights and powers vested in it under the senior indenture and will use the same degree of care and skill in its exercise as a prudent person would exercise under the circumstances in the conduct of such person s own affairs.

The senior indenture and the provisions of the Trust Indenture Act incorporated by reference therein contain limitations on the rights of the trustee thereunder, should it become a creditor of ours or any of our subsidiaries, to

obtain payment of claims in certain cases or to realize on certain property received by it in respect of any such claims, as security or otherwise. The trustee is permitted to engage in other transactions, provided that if it acquires any conflicting interest (as defined in the Trust Indenture Act), it must eliminate such conflict or resign.

We may have normal banking relationships with the senior trustee in the ordinary course of business.

Unclaimed Funds. All funds deposited with the trustee or any paying agent for the payment of principal, premium, interest or additional amounts in respect of the senior debt securities that remain unclaimed for two

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years after the date upon which such amounts became due and payable will be repaid to us. Thereafter, any right of any holder of senior debt securities to such funds shall be enforceable only against us, and the trustee and paying agents will have no liability therefor.

Governing Law. The senior indenture and the senior debt securities will be governed by, and construed in accordance with, the internal laws of the State of New York.

Certain Terms of the Subordinated Debt Securities

Other than the terms of the subordinated indenture and subordinated debt securities relating to subordination or otherwise as described in the prospectus supplement relating to a particular series of subordinated debt securities, the terms of the subordinated indenture and subordinated debt securities are identical in all material respects to the terms of the senior indenture and senior debt securities.

Additional or different subordination terms may be specified in the prospectus supplement applicable to a particular series.

Subordination. The indebtedness evidenced by the subordinated debt securities is subordinate to the prior payment in full of all of our senior indebtedness, as defined in the subordinated indenture. During the continuance beyond any applicable grace period of any default in the payment of principal, premium, interest or any other payment due on any of our senior indebtedness, we may not make any payment of principal of or interest on the subordinated debt securities (except for certain sinking fund payments). In addition, upon any payment or distribution of our assets upon any dissolution, winding-up, liquidation or reorganization, the payment of the principal of and interest on the subordinated debt securities will be subordinated to the extent provided in the subordinated indenture in right of payment to the prior payment in full of all our senior indebtedness. Because of this subordination, if we dissolve or otherwise liquidate, holders of our subordinated debt securities may receive less, ratably, than holders of our senior indebtedness. The subordination provisions do not prevent the occurrence of an event of default under the subordinated indenture.

The term senior indebtedness of a person means with respect to such person the principal of, premium, if any, interest on, and any other payment due pursuant to any of the following, whether outstanding on the date of the subordinated indenture or incurred by that person in the future:

- all of the indebtedness of that person for money borrowed;
- all of the indebtedness of that person evidenced by notes, debentures, bonds or other securities sold by that person for money;
- all of the lease obligations that are capitalized on the books of that person in accordance with generally accepted accounting principles;
- all indebtedness of others of the kinds described in the first two bullet points above and all lease obligations of others of the kind described in the third bullet point above that the person, in any manner, assumes or

guarantees or that the person in effect guarantees through an agreement to purchase, whether that agreement is contingent or otherwise; and

all renewals, extensions or refundings of indebtedness of the kinds described in the first, second or fourth bullet point above and all renewals or extensions of leases of the kinds described in the third or fourth bullet point above;

unless, in the case of any particular indebtedness, renewal, extension or refunding, the instrument creating or evidencing it or the assumption or guarantee relating to it expressly provides that such indebtedness, renewal, extension or refunding is not superior in right of payment to the subordinated debt securities. Our senior debt securities constitute senior indebtedness for purposes of the subordinated indenture.

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DESCRIPTION OF WARRANTS

We may issue warrants to purchase common stock, preferred stock or debt securities. We may offer warrants separately or together with one or more additional warrants, common stock, preferred stock or debt securities, or any combination of those securities in the form of units, as described in the applicable prospectus supplement. If we issue warrants as part of a unit, the accompanying prospectus supplement will specify whether those warrants may be separated from the other securities in the unit prior to the expiration date of the warrants. The applicable prospectus supplement will also describe the following terms of any warrants:

- the specific designation and aggregate number of, and the offering price at which we will issue, the warrants;
- the currency or currency units in which the offering price, if any, and the exercise price are payable;
- the date on which the right to exercise the warrants will begin and the date on which that right will expire or, if you may not continuously exercise the warrants throughout that period, the specific date or dates on which you may exercise the warrants;
- whether the warrants are to be sold separately or with other securities as parts of units;
- whether the warrants will be issued in definitive or global form or in any combination of these forms, although, in any case, the form of a warrant included in a unit will correspond to the form of the unit and of any security included in that unit;
- any applicable material U.S. federal income tax consequences;
- the identity of the warrant agent for the warrants and of any other depositaries, execution or paying agents, transfer agents, registrars or other agents;
- the proposed listing, if any, of the warrants or any securities purchasable upon exercise of the warrants on any securities exchange;
- the designation and terms of any equity securities purchasable upon exercise of the warrants;
- the designation, aggregate principal amount, currency and terms of any debt securities that may be purchased upon exercise of the warrants;

if applicable, the designation and terms of the preferred stock with which the warrants are issued and the number of warrants issued with each security;

if applicable, the date from and after which any warrants issued as part of a unit and the related debt securities, preferred stock, or common stock will be separately transferable;

the number of shares of common stock or preferred stock purchasable upon exercise of a warrant and the price at which those shares may be purchased;

if applicable, the minimum or maximum amount of the warrants that may be exercised at any one time;

information with respect to book-entry procedures, if any;

the anti-dilution provisions of, and other provisions for changes to or adjustment in the exercise price of, the warrants, if any;

any redemption or call provisions; and

any additional terms of the warrants, including terms, procedures and limitations relating to the exchange or exercise of the warrants.

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DESCRIPTION OF UNITS

We may issue units comprised of one or more of the other securities that may be offered under this prospectus, in any combination. The following, together with the additional information we may include in the applicable prospectus supplement, summarizes the material terms and provisions of the units that we may offer under this prospectus. While the terms summarized below will apply generally to any units we may offer, we will describe the particular terms of any series of units in more detail in the applicable prospectus supplement.

Each unit will be issued so that the holder of the unit is also the holder of each security included in the unit. Thus, the holder of a unit will have the rights and obligations of a holder of each included security. The unit agreement under which a unit is issued may provide that the securities included in the unit may not be held or transferred separately at any time, or at any time before a specified date.

Any applicable prospectus supplement will describe:

- the material terms of the units and of the securities comprising the units, including whether and under what circumstances those securities may be held or transferred separately;
- any material provisions relating to the issuance, payment, settlement, transfer or exchange of the units or of the securities comprising the units; and
- any material provisions of the governing unit agreement that differ from those described above.

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FORMS OF SECURITIES

Each debt security, unit and warrant will be represented either by a certificate issued in definitive form to a particular investor or by one or more global securities representing the entire issuance of securities. Unless the applicable prospectus supplement provides otherwise, certificated securities in definitive form and global securities will be issued in registered form. Definitive securities name you or your nominee as the owner of the security, and in order to transfer or exchange these securities or to receive payments other than interest or other interim payments, you or your nominee must physically deliver the securities to the trustee, registrar, paying agent or other agent, as applicable. Global securities name a depositary or its nominee as the owner of the debt securities, units or warrants represented by these global securities. The depositary maintains a computerized system that will reflect each investor s beneficial ownership of the securities through an account maintained by the investor with its broker/dealer, bank, trust company or other representative, as we explain more fully below.

Global Securities

We may issue the debt securities, units and warrants in the form of one or more fully registered global securities that will be deposited with a depositary or its nominee identified in the applicable prospectus supplement and registered in the name of that depositary or nominee. In those cases, one or more global securities will be issued in a denomination or aggregate denominations equal to the portion of the aggregate principal or face amount of the securities to be represented by global securities. Unless and until it is exchanged in whole for securities in definitive registered form, a global security may not be transferred except as a whole by and among the depositary for the global security, the nominees of the depositary or any successors of the depositary or those nominees.

If not described below, any specific terms of the depositary arrangement with respect to any securities to be represented by a global security will be described in the prospectus supplement relating to those securities. We anticipate that the following provisions will apply to all depositary arrangements.

Ownership of beneficial interests in a global security will be limited to persons, called participants, that have accounts with the depositary or persons that may hold interests through participants. Upon the issuance of a global security, the depositary will credit, on its book-entry registration and transfer system, the participants accounts with the respective principal or face amounts of the securities beneficially owned by the participants. Any dealers, underwriters or agents participating in the distribution of the securities will designate the accounts to be credited. Ownership of beneficial interests in a global security will be shown on, and the transfer of ownership interests will be effected only through, records maintained by the depositary, with respect to interests of participants, and on the records of participants, with respect to interests of persons holding through participants. The laws of some states may require that some purchasers of securities take physical delivery of these securities in definitive form. These laws may impair your ability to own, transfer or pledge beneficial interests in global securities.

So long as the depositary, or its nominee, is the registered owner of a global security, that depositary or its nominee, as the case may be, will be considered the sole owner or holder of the securities represented by the global security for all purposes under the applicable indenture, warrant agreement or unit agreement. Except as described below, owners of beneficial interests in a global security will not be entitled to have the securities represented by the global security registered in their names, will not receive or be entitled to receive physical delivery of the securities in definitive form and will not be considered the owners or holders of the securities under the applicable indenture, unit agreement or warrant agreement. Accordingly, each person owning a beneficial interest in a global security must rely on the procedures of the depositary for that global security and, if that person is not a participant, on the procedures of the participant through which the person owns its interest, to exercise any rights of a holder under the applicable indenture, unit agreement or warrant agreement. We understand that under existing industry practices, if we request

any action of holders or if an owner of a beneficial interest in a global security desires to give or take any action that a holder is entitled to give or take

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under the applicable indenture, unit agreement or warrant agreement, the depositary for the global security would authorize the participants holding the relevant beneficial interests to give or take that action, and the participants would authorize beneficial owners owning through them to give or take that action or would otherwise act upon the instructions of beneficial owners holding through them.

Principal, premium, if any, and interest payments on debt securities, and any payments to holders with respect to warrants or units, represented by a global security registered in the name of a depositary or its nominee will be made to the depositary or its nominee, as the case may be, as the registered owner of the global security. None of us, or any trustee, warrant agent, unit agent or other agent of ours, or any agent of any trustee, warrant agent or unit agent will have any responsibility or liability for any aspect of the records relating to payments made on account of beneficial ownership interests in the global security or for maintaining, supervising or reviewing any records relating to those beneficial ownership interests.

We expect that the depositary for any of the securities represented by a global security, upon receipt of any payment to holders of principal, premium, interest or other distribution of underlying securities or other property on that registered global security, will immediately credit participants accounts in amounts proportionate to their respective beneficial interests in that global security as shown on the records of the depositary. We also expect that payments by participants to owners of beneficial interests in a global security held through participants will be governed by standing customer instructions and customary practices, as is now the case with the securities held for the accounts of customers or registered in street name, and will be the responsibility of those participants.

If the depositary for any of the securities represented by a global security is at any time unwilling or unable to continue as depositary or ceases to be a clearing agency registered under the Exchange Act, and a successor depositary registered as a clearing agency under the Exchange Act is not appointed by us within 90 days, we will issue securities in definitive form in exchange for the global security that had been held by the depositary. Any securities issued in definitive form in exchange for a global security will be registered in the name or names that the depositary gives to the relevant trustee, warrant agent, unit agent or other relevant agent of ours or theirs. It is expected that the depositary s instructions will be based upon directions received by the depositary from participants with respect to ownership of beneficial interests in the global security that had been held by the depositary.

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PLAN OF DISTRIBUTION

We may sell securities:

through underwriters;

through dealers;

through agents;

directly to purchasers; or

through a combination of any of these methods of sale.

In addition, we may issue the securities as a dividend or distribution or in a subscription rights offering to our existing security holders. This prospectus may be used in connection with any offering of our securities through any of these methods or other methods described in the applicable prospectus supplement.

We may directly solicit offers to purchase securities, or agents may be designated to solicit such offers. We will, in the prospectus supplement relating to such offering, name any agent that could be viewed as an underwriter under the Securities Act, and describe any commissions that we must pay. Any such agent will be acting on a best efforts basis for the period of its appointment or, if indicated in the applicable prospectus supplement, on a firm commitment basis.

The distribution of the securities may be effected from