

AVEO PHARMACEUTICALS INC

Form 424B5

March 28, 2017

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Filed Pursuant to Rule 424(b)(5)

Registration No. 333-203932

The information in this preliminary prospectus supplement is not complete and may be changed. A registration statement relating to these securities has been declared effective by the Securities and Exchange Commission. This preliminary prospectus supplement and the accompanying prospectus are not an offer to sell these securities and we are not soliciting an offer to buy these securities in any jurisdiction where the offer or sale is not permitted.

Subject to completion, dated March 28, 2017

Preliminary Prospectus Supplement

(To Prospectus dated May 26, 2015)

Shares

AVEO PHARMACEUTICALS, INC.

Common Stock

AVEO Pharmaceuticals, Inc. is offering shares.

Trading Symbol: Nasdaq Global Select Market AVEO

The last reported sale price for our common stock on March 27, 2017 was \$0.65 per share.

This investment involves risk. See **Risk Factors** beginning on page 8 and in our Annual Report on Form 10-K for the year ended December 31, 2016.

| | Per Share | Total |
|--|-----------|-------|
| Public offering price | \$ | \$ |
| Underwriting discount ⁽¹⁾ | \$ | \$ |
| Proceeds, before expenses, to AVEO Pharmaceuticals, Inc. | \$ | \$ |

⁽¹⁾ See Underwriting beginning on page 23 for additional information regarding total underwriter compensation, including expenses for which we have agreed to reimburse the underwriter.

The underwriter expects to deliver the shares to investors on or about March , 2017. We have granted the underwriter an option for a period of 30 days to purchase an additional shares.

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 is truthful or complete. Any representation to the contrary is a criminal offense.

Piper Jaffray

The date of this prospectus supplement is March , 2017

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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 common stock 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 common stock. 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, shares of our common stock only in jurisdictions where offers and sales are permitted. The distribution of this prospectus supplement and the accompanying prospectus and the offering of the common stock 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 the common stock 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 common stock. 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-8 and the risk factors contained in our Annual Report on Form 10-K for the year ended December 31, 2016.

Overview

We are a biopharmaceutical company dedicated to advancing a broad portfolio of targeted therapeutics for oncology and other areas of unmet medical need. Our proprietary platform has delivered unique insights into cancer and related diseases. Our strategy is to leverage these biomarker insights and partner resources to advance the development of our clinical pipeline. We are focused on developing our lead candidate tivozanib in North America as a treatment for renal cell carcinoma, or RCC. In addition, we have entered into partnerships to fund the further development and commercialization of our clinical stage assets, including AV-380, ficlatuzumab, AV-203, and tivozanib for oncology indications outside of North America and for non-oncologic indications worldwide. We are currently seeking a partner to develop the AV-353 platform, a preclinical asset, worldwide for the potential treatment of pulmonary arterial hypertension, or PAH.

Tivozanib

Our pipeline includes our lead candidate tivozanib, an oral, once-daily, vascular endothelial growth factor, or VEGF, 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, colorectal and breast cancers.

Clinical and Regulatory Development in RCC

RCC First Line Phase 3 Trial (TIVO-1): We conducted a global phase 3 clinical trial, which we refer to as the TIVO-1 trial, comparing the efficacy and safety of tivozanib with Nexavar[®] (sorafenib), an approved therapy, for first-line treatment of RCC. The trial met its primary endpoint for progression-free survival, or PFS, but showed a non-statistically significant trend favoring the sorafenib arm in overall survival, or OS. In June 2013, the U.S. Food and Drug Administration, or FDA, issued a complete response letter informing us that it would not approve tivozanib for the first-line treatment of advanced RCC based solely on the data from this trial, and recommended that we perform an additional clinical trial adequately sized to assure the FDA that there is no adverse effect on 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 advanced RCC received tivozanib as second-line treatment subsequent to disease progression on the sorafenib arm in the TIVO-1 first-line RCC trial. We presented the final results at the 2015 American Society of Clinical Oncology (ASCO) Annual Meeting on June 1, 2015. The final results showed a median PFS of 11.0 months and a median OS of 21.6 months, demonstrating the clinically meaningful efficacy of tivozanib in a VEGF treatment refractory population. We believe that the long OS derived from tivozanib following sorafenib that was demonstrated in Study 902 contributed to the discordance in the efficacy results in the TIVO-1 trial between the PFS benefit, which significantly favored tivozanib, and the OS, which trended in favor of sorafenib. However, the FDA did not accept this explanation, finding that the OS results were uninterpretable, and recommended that we perform a second phase 3 trial, as set forth above.

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European Marketing Authorization Application by EUSA. Tivozanib has previously been granted orphan drug designation in Europe for the treatment of RCC. Our licensee, EUSA Pharma (UK) Limited, or EUSA, submitted a marketing authorization application, or MAA, for tivozanib for the treatment of RCC to the European Medicines Agency, or EMA, in February 2016 based primarily on our existing dataset, which includes the results from the TIVO-1 clinical trial of tivozanib in the first-line treatment of RCC, combined with the TIVO-1 extension trial, and one phase 1 and two phase 2 trials in RCC. The EMA validated the MAA in March 2016, confirming that the submission was complete and that it would initiate its review process. EUSA received the Day 120 List of Questions from the Committee for Medicinal Products for Human Use, or CHMP, of the EMA in July 2016, and submitted its responses in November 2016. In January 2017, EUSA received the Day 180 List of Outstanding Issues, or LOI, from the CHMP. The Day 180 LOI signifies that the MAA is not approvable at the present time, and outlines outstanding deficiencies, which are then required to be satisfactorily addressed in an oral explanation and/or in writing prior to a final application decision. EUSA has informed us that it expects to submit written responses to the Day 180 LOI in April 2017, and the EMA has tentatively scheduled EUSA to provide an oral explanation to the CHMP in May 2017.

RCC Third Line Phase 3 Trial (TIVO-3): In May 2016, we initiated enrollment and treatment of patients in a phase 3 trial of tivozanib in the third-line treatment of patients with refractory RCC, which we refer to as the TIVO-3 trial. The TIVO-3 clinical trial was designed to address the OS concerns from the TIVO-1 trial presented in the June 2013 complete response letter from the FDA and to support a request for regulatory approval of tivozanib in the United States as a third-line treatment and as a first-line treatment for RCC. Our trial design, which we reviewed with the FDA, provides for a randomized, controlled, multi-center, open-label phase 3 clinical trial of approximately 322 subjects randomized 1:1 to receive either tivozanib or sorafenib. Subjects enrolled in the trial must have failed two systemic therapies one of which must have been a VEGF TKI. Patients may have received prior immunotherapy, including immune checkpoint (PD-1) inhibitors, reflecting a potentially evolving treatment landscape. The primary objective of the TIVO-3 trial is to show improved PFS, and secondary endpoints include OS, safety and objective response rate. The trial's sites are located in North America and Europe. The TIVO-3 trial does not include a crossover design, meaning that patients who progress in one therapy will not then be offered the opportunity to cross over to the other therapy. We expect to complete enrollment in the TIVO-3 trial in June 2017, and to report top line data in the first quarter of 2018. The TIVO-3 trial passed an initial safety data assessment in February 2017. We expect a pre-planned interim futility analysis to occur mid-year 2017.

RCC PD-1 Combination Trial with Opdivo (TiNivo): In March 2017, we initiated enrollment in a phase 1/2 clinical trial of tivozanib in combination with Opdivo® (nivolumab), an immune checkpoint (PD-1) inhibitor, for the treatment of RCC, which we refer to as the TiNivo trial. Bristol-Myers Squibb is supplying nivolumab for the TiNivo trial, and we are the trial sponsor. In recent clinical trials, TKIs and PD-1 inhibitors have shown promising efficacy in treating RCC in combination. However, several TKI/PD-1 combinations have encountered toxicity levels that we believe are likely to challenge or prohibit such TKIs from safely combining with PD-1 inhibitors for RCC treatment. In our clinical trials, tivozanib has demonstrated a superior tolerability profile relative to certain other TKIs, including lower rates of key potential overlapping toxicities with PD-1 inhibitors. We believe that tivozanib's tolerability profile has the potential to allow tivozanib to combine with PD-1 inhibitors more safely than other TKIs. 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 1 trial will primarily evaluate the safety of tivozanib in combination with nivolumab at escalating doses of tivozanib and, assuming favorable results, is expected to be followed by a phase 2 expansion at the established combination dose. We expect to receive initial data from the phase 1 portion of the TiNivo trial in the first half of 2017.

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Tivozanib Partnerships

In-License from KHK. In 2006, we acquired the exclusive rights to develop and commercialize tivozanib in all countries outside of Asia and the Middle East under a license from Kyowa Hakko Kirin Co., Ltd. (formerly Kirin Brewery Co. Ltd.), or KHK.

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

Ficlatuzumab

Ficlatuzumab is a potent Hepatocyte Growth Factor, or HGF, inhibitory antibody. HGF is the sole known ligand of the c-Met receptor, which is believed to trigger many activities that are involved in cancer development and metastasis. In April 2014, we and Biodesix, Inc., or Biodesix, entered into a worldwide co-development and collaboration agreement, or the Biodesix Agreement, to develop and commercialize ficlatuzumab.

We have completed two phase 1 clinical studies of ficlatuzumab administered as a single agent and in combination with erlotinib, an endothelial growth factor receptor, or EGFR, TKI. We also performed a phase 2 clinical trial evaluating ficlatuzumab in combination with gefitinib, an EGFR TKI, in first-line non-small cell lung cancer, or NSCLC. The phase 2 trial failed to demonstrate a statistically significant benefit in the intent-to-treat, or ITT, population. However, a retrospective exploratory subgroup analysis utilizing Biodesix's companion diagnostic, VeriStrat[®], identified a sub-population of patients who experienced a progression free survival and overall survival benefit from the addition of ficlatuzumab to gefitinib. In December 2014, we and Biodesix initiated the FOCAL trial, a phase 2 confirmatory study of ficlatuzumab in combination with erlotinib in the subset of patients with first-line advanced NSCLC previously identified. After experiencing lower rates of positivity for the two markers and slower than expected enrollment, a blinded look at the FOCAL trial data from enrolled patients found that the patients, who were known to be selected for poor prognosis, experienced materially higher discontinuation rates than observed in both the general ITT population and the retrospective exploratory subgroup population of the prior phase 2 clinical trial. This observation significantly compromised the commercial opportunity and the feasibility of the FOCAL trial. Based on the findings from the interim analysis and the slow enrollment, we and Biodesix agreed in September 2016 to discontinue the FOCAL trial.

We and Biodesix are also funding an investigator-sponsored clinical trial of ficlatuzumab in combination with ERBITUX[®] (cetuximab) in squamous cell carcinoma of the head and neck. We anticipate that we will present preliminary clinical observations from this phase 1 trial at an upcoming scientific conference. We and Biodesix are also funding an investigator-sponsored clinical trial of ficlatuzumab in combination with Cytosar (cytarabine) in acute myeloid leukemia. We anticipate that we will present preliminary clinical observations from this phase 1 trial at an upcoming scientific conference. We continue to evaluate several additional opportunities for the further clinical development of ficlatuzumab.

AV-203

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

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

In March 2016, we entered into a collaboration and license agreement with CANbridge Life Sciences Ltd., or CANbridge, under which we granted CANbridge the exclusive right to develop, manufacture and commercialize AV-203 in all countries other than the United States, Canada and Mexico. CANbridge has begun its work to optimize the manufacturing of AV-203. CANbridge expects that AV-203 will reenter the clinic in 2018.

AV-380

AV-380 is a potent humanized IgG1 inhibitory monoclonal antibody targeting growth differentiating factor-15, or GDF15, a divergent member of the TGF- β 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, and other diseases. We believe that AV-380 represents a unique approach to treating cachexia because it addresses key underlying mechanisms of the syndrome. AV-380 focuses on a significant area of patient need. It is estimated that approximately 30% of all cancer patients die due to cachexia and over half of cancer patients who die do so with cachexia present (*J Cachexia Sarcopenia Muscle* 2010). In the United States alone, the estimated prevalence of cancer cachexia is over 400,000 patients, and the prevalence of cachexia due to cancer, COPD, congestive heart failure, frailty and end stage renal disease combined is estimated to total more than 5 million patients (*Am J Clin Nutr* 2006).

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

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

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

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and neurodegenerative conditions. Publications, including *Nature Medicine* (2009), have implicated the Notch 3 pathway in PAH, a rare and life-threatening disorder that affects approximately 250,000 people worldwide (*Global Data 2016 PAH Opportunity Analyzer; 2012 Decision Resources PAH Report*) and is caused by enlargement of the arterial walls in small arteries between the heart and the lungs, resulting in restricted blood flow. Currently, no known cure for PAH exists. Existing treatments for PAH have focused on controlling symptoms by avoiding vasoconstriction and increasing vasodilation of blood vessels but have not reversed the underlying cause of the disease. However, the results of a recently concluded pre-clinical research study conducted at the University of California at San Diego (and recently presented in a poster at the November 2016 American Heart Association meeting) using one of our anti-Notch3 antibody candidates, generated preclinical data that supports the ability of the antibody to potentially reverse the thickening of vascular smooth muscle cells, which would represent a disease-modifying approach to treatment. A manuscript of the results is being prepared for submission to a peer-reviewed journal.

We are seeking patent protection of our AV-353 platform, which was developed utilizing our research and development platform and have already filed composition of matter patent applications. We are currently seeking a partner to develop the AV-353 platform worldwide for the potential treatment of PAH.

Our Corporate 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 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 AVEO, the Company, we, us, and our refer to AVEO Pharmaceuticals, Inc. and our subsidiaries.

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

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The number of shares of our common stock to be outstanding after this offering is based on 75,862,946 shares of our common stock outstanding as of December 31, 2016. The number of shares of our common stock to be outstanding as used throughout this prospectus supplement, unless otherwise indicated, excludes:

4,858,678 shares of common stock issuable upon exercise of stock options outstanding as of December 31, 2016 at a weighted-average exercise price of \$2.31 per share;

19,453,295 shares of common stock issuable upon exercise of warrants outstanding as of December 31, 2016 at a weighted-average exercise price of \$1.00 per share;

2,746,513 shares of common stock reserved as of December 31, 2016 for future issuance under our equity incentive plans; and

307,282 shares of common stock reserved as of December 31, 2016 for future issuance under our 2010 employee stock purchase plan.

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RISK FACTORS

An investment in our common stock involves a high degree of risk. Before deciding whether to invest in our common stock, you should consider carefully the risks described below and discussed in the section captioned "Risk Factors" included in our Annual Report on Form 10-K for the year ended December 31, 2016, which is incorporated by reference herein in its entirety, 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. Pending their use, we may invest the net proceeds from this offering in a manner that does not produce income or that loses value.

If you purchase shares of common stock in this offering, you will suffer immediate dilution of your investment.

The public offering price of our common stock is substantially higher than the net tangible book value per share of our common stock. Therefore, if you purchase shares of our common stock in this offering, you will pay a price per share that substantially exceeds our net tangible book value per share after giving effect to this offering. If you purchase common stock in this offering, you will incur an immediate and substantial dilution in net tangible book value of \$ per share, after giving effect to the sale by us of shares in this offering at the public offering price of \$ per share. The exercise of outstanding stock options and warrants may result in 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.

If you purchase shares of common stock 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 per share 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 per share paid by any 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 per share paid by any 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 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.

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CAUTIONARY NOTE REGARDING FORWARD-LOOKING STATEMENTS

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 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, intend, may, plan, project, should, will, would or other words that convey uncertainty of future events or outcomes to 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 ability to maintain compliance with the \$10.0 million financial covenant under our loan agreement with Hercules Technology II, L.P. and Hercules Technology III, L.P., affiliates of Hercules Technology Growth, which we collectively refer to as Hercules;

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 to maintain our third party collaboration agreements and our ability, and the ability of our licensees, to achieve development and commercialization objectives under these arrangements;

our ability, and the ability of our licensees, to demonstrate to the satisfaction of applicable regulatory agencies the safety, efficacy and clinically meaningful benefit of our product candidates;

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our ability to successfully enroll and complete clinical trials of our product candidates, including our TIVO-3 trial;

our ability to maintain compliance with the \$10.0 million financial covenant under our loan agreement with Hercules;

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

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

developments, expenses and outcomes related to our ongoing shareholder litigation;

our ability to successfully implement our strategic plans;

our ability to raise the substantial additional funds required to achieve our goals;

unplanned capital requirements;

adverse general economic and industry conditions;

competitive factors;

our ability to continue as a going concern; and

those risks discussed (i) under the heading "Risk Factors" on page 8 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, 2016 filed with 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.

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USE OF PROCEEDS

We estimate that the net proceeds from our issuance and sale of _____ shares of our common stock in this offering will be approximately \$ _____ million after deducting the estimated underwriting discounts and commissions and estimated offering expenses payable by us. If the underwriter exercises its option to purchase additional shares in full, we estimate that our net proceeds will be approximately \$ _____ million after deducting the estimated underwriting discounts and commissions and estimated offering expenses payable by us.

We intend to use the net proceeds from this offering for working capital and general corporate purposes, including development and pre-commercial expenses incurred in connection with our ongoing phase 3 clinical trial of tivozanib in the third-line treatment of patients with refractory RCC and with our ongoing phase 1/2 clinical trial of tivozanib in combination with Opdivo (nivolumab).

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. Pending use of the proceeds as described above, we intend to invest the proceeds in short-term, interest-bearing, investment-grade securities.

Table of Contents**PRICE RANGE OF COMMON STOCK**

Our common stock is listed on The NASDAQ Global Select Market under the symbol AVEO. The following table sets forth the high and low sale prices per share of our common stock, as reported on The NASDAQ Global Select Market, for the periods indicated.

| | High | Low |
|--|-------------|------------|
| 2015 | | |
| First quarter | \$ 2.02 | \$ 0.78 |
| Second quarter | \$ 3.50 | \$ 1.16 |
| Third quarter | \$ 2.59 | \$ 1.14 |
| Fourth quarter | \$ 1.47 | \$ 0.92 |
| 2016 | | |
| First quarter | \$ 1.27 | \$ 0.82 |
| Second quarter | \$ 1.15 | \$ 0.84 |
| Third quarter | \$ 1.09 | \$ 0.81 |
| Fourth quarter | \$ 0.89 | \$ 0.54 |
| 2017 | | |
| First quarter (through March 27, 2017) | \$ 0.98 | \$ 0.55 |

On March 27, 2017, the last reported sale price of our common stock as reported on the NASDAQ Global Select Market was \$0.65 per share. As of March 17, 2017, there were approximately 57 holders of record of our common stock. We believe that the actual number of stockholders is substantially greater than this number of record holders and includes stockholders who are beneficial owners but whose shares are held in street name by brokers and other nominees. This number of holders of record also does not include stockholders whose shares may be held in trust by other entities.

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.

Table of Contents**CAPITALIZATION**

The following table sets forth our consolidated cash, cash equivalents and marketable securities and capitalization as of December 31, 2016, as follows:

on an actual basis; and

on an as adjusted basis to give effect to our issuance and sale of _____ shares of our common stock in this offering at the public offering price of \$ _____ per share, after deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us.

You should read the following table together with Description of Capital Stock beginning page S-15 of this prospectus supplement, 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, 2016, which is incorporated by reference in this prospectus supplement.

| <u>(in thousands, except share and per share data)</u> | As of December 31, 2016 | |
|--|-------------------------|--------------|
| | Actual | As Adjusted |
| Cash, cash equivalents and marketable securities | \$ 23,348 | \$ |
| Loans payable, net of current portion and discount | \$ 11,879 | \$ 11,879 |
| Stockholders' equity | | |
| Preferred stock, par value \$0.001 per share; 5,000,000 shares authorized, no shares issued or outstanding, actual and as adjusted | \$ | \$ |
| Common stock, par value \$0.001 per share; 200,000,000 shares authorized, actual and as adjusted, 75,862,946 shares issued and outstanding, actual; _____ shares issued and outstanding, as adjusted | \$ 76 | \$ |
| Additional paid-in capital | \$ 519,911 | \$ |
| Accumulated other comprehensive income | \$ 6 | \$ 6 |
| Accumulated deficit | \$ (521,916) | \$ (521,916) |
| Total stockholders' (deficit) equity | \$ (1,923) | \$ |
| Total capitalization | \$ 9,956 | \$ |

The foregoing table does not include:

4,858,678 shares of common stock issuable upon exercise of stock options outstanding as of December 31, 2016 at a weighted-average exercise price of \$2.31 per share;

19,453,295 shares of common stock issuable upon exercise of warrants outstanding as of December 31, 2016 at a weighted-average exercise price of \$1.00 per share;

2,746,513 shares of common stock reserved as of December 31, 2016 for future issuance under our equity incentive plans; and

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307,282 shares of common stock reserved as of December 31, 2016 for future issuance under our 2010 employee stock purchase plan.

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DILUTION

If you purchase our common stock in this offering, your interest will be diluted to the extent of the difference between the public offering price per share and the 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, 2016 was approximately \$(1.9) million, or approximately \$(0.03) per share, based on approximately 75.9 million shares of our common stock then outstanding. After giving effect to the sale of shares of common stock at the public offering price of \$ _____ per share, less the underwriting discounts and commissions and estimated offering expenses payable by us, our as adjusted net tangible book value at December 31, 2016 would be approximately \$ _____ million, or approximately \$ _____ per share. This represents an immediate increase in net tangible book value of \$ _____ per share to existing stockholders and an immediate dilution of \$ _____ per share to investors in this offering.

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

| | |
|---|-----------|
| Public offering price per share | \$ |
| Net tangible book value per share as of December 31, 2016 | \$ (0.03) |
| Increase in net tangible book value per share attributable to new investors | |
| Net tangible book value per share as of December 31, 2016 after giving effect to this offering | \$ |
| Dilution in net tangible book value per share to new investors | \$ |
| If the underwriter exercises in full its option to purchase _____ additional shares of common stock, less the applicable underwriting discounts and commissions and estimated offering expenses payable by us, our as adjusted net tangible book value at December 31, 2016 after giving effect to this offering would be approximately \$ _____ million, or approximately \$ _____ per share, representing an increase in net tangible book value of \$ _____ per share to existing stockholders and immediate dilution in net tangible book value of \$ _____ per share to investors purchasing our common stock in this offering at the public offering price. | |

The calculations in the foregoing table do not include, as of December 31, 2016:

4,858,678 shares of common stock issuable upon exercise of stock options outstanding as of December 31, 2016 at a weighted-average exercise price of \$2.31 per share;

19,453,295 shares of common stock issuable upon exercise of warrants outstanding as of December 31, 2016 at a weighted-average exercise price of \$1.00 per share;

2,746,513 shares of common stock reserved as of December 31, 2016 for future issuance under our equity incentive plans; and

307,282 shares of common stock reserved as of December 31, 2016 for future issuance under our 2010 employee stock purchase plan.

To the extent that any of our outstanding options or warrants are exercised, we grant additional options or other awards under our equity incentive plans or issue additional warrants, 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 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 to date, 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 our periodic filings, for the provisions that are important to you.

Our authorized capital stock consists of 200,000,000 shares of common stock, par value \$0.001 per share and 5,000,000 shares of preferred stock, par value \$0.001 per share, all of which preferred stock are undesignated.

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 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 votes cast by the holders of all 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 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 on all matters to be voted upon by stockholders.

Dividends

The holders of common stock, after any preferences of holders of any preferred stock, are entitled to receive dividends when and if declared by the board of directors out of legally available funds.

Liquidation and Dissolution

If we are liquidated or dissolved, the holders of the common stock will be entitled to share in our assets available for distribution to stockholders in proportion to the amount of common stock they own. The amount available for common stockholders is calculated after payment of liabilities. Holders of any preferred stock will receive a preferential share of our assets before the holders of the common stock receive any assets.

Other Rights

Holders of the common stock have no right to:

convert the stock into any other security;

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have the stock redeemed;

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 Global Select 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 designation of the series, the number of authorized shares of the series, dividend rights and terms, conversion rights, voting rights, redemption rights and terms, liquidation preferences and any other rights, powers, preferences and limitations applicable to 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.

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.

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 Global Select 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

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.

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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 at least 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 restated 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.

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

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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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MATERIAL U.S. TAX CONSIDERATIONS FOR NON-U.S. HOLDERS OF COMMON STOCK

The following is a discussion of material U.S. federal income and estate tax considerations relating to the ownership and disposition of our common stock by a non-U.S. holder. For purposes of this discussion, the term *non-U.S. holder* means a beneficial owner (other than a partnership or other pass-through entity) of our common stock that is not, for U.S. federal income tax purposes:

an individual who is a citizen or resident of the United States;

a corporation, or other entity treated as a corporation for U.S. federal income tax purposes, created or organized in or under the laws of the United States or any state thereof or the District of Columbia;

an estate the income of which is subject to U.S. federal income taxation regardless of its source; or

a trust, if a U.S. court is able to exercise primary supervision over the administration of the trust and one or more U.S. persons have authority to control all substantial decisions of the trust or if the trust has a valid election to be treated as a U.S. person under applicable U.S. Treasury Regulations.

This discussion is based on current provisions of the U.S. Internal Revenue Code of 1986, as amended, which we refer to as the Code, existing and proposed U.S. Treasury Regulations promulgated thereunder, current administrative rulings and judicial decisions, all as in effect as of the date of this prospectus supplement and all of which are subject to change or to differing interpretation, possibly with retroactive effect. Any change or differing interpretation could alter the tax consequences to non-U.S. holders described in this prospectus supplement. In addition, the Internal Revenue Service, or the IRS, could challenge one or more of the tax consequences described in this prospectus supplement.

We assume in this discussion that each non-U.S. holder holds shares of our common stock as a capital asset (generally, property held for investment). This discussion does not address all aspects of U.S. federal income and estate taxation that may be relevant to a particular non-U.S. holder in light of that non-U.S. holder's individual circumstances nor does it address the alternative minimum tax, the Medicare tax on net investment income, or any aspects of U.S. state, local or non-U.S. taxes. This discussion also does not consider any specific facts or circumstances that may apply to a non-U.S. holder and does not address the special tax rules applicable to particular non-U.S. holders, such as:

insurance companies;

tax-exempt organizations;

financial institutions;

brokers or dealers in securities;

regulated investment companies;

pension plans;

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controlled foreign corporations;

passive foreign investment companies;

owners that hold our common stock as part of a straddle, hedge, conversion transaction, synthetic security or other integrated investment; and

certain U.S. expatriates.

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

Prospective non-U.S. holders of our common stock 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.

Distributions on our Common Stock

As discussed under **Dividend Policy** above, we do not expect to make cash dividends to holders of our common stock in the foreseeable future. If we pay distributions on our common stock, those distributions generally will constitute dividends for U.S. federal income tax purposes to the extent paid from our current or accumulated earnings and profits, as determined under U.S. federal income tax principles. If a distribution exceeds our current and accumulated earnings and profits, the excess will be treated as a tax-free return of the non-U.S. holder's investment, up to such holder's tax basis in the common stock. Any remaining excess will be treated as capital gain, subject to the tax treatment described below under the heading **Gain on Disposition of Common Stock**. Any distributions will also be subject to the discussions below under the headings **Information Reporting and Backup Withholding** and **FATCA**.

Dividends 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 graduated 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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Gain on Disposition of Common Stock

In general (subject to the discussion below under the headings Information Reporting and Backup Withholding and FATCA), a non-U.S. holder will not be subject to U.S. federal income tax or withholding tax on gain realized upon such holder's sale, exchange or other disposition of shares of our common stock 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 regular graduated rates and in the manner applicable to U.S. persons (as defined in the Code), and if the non-U.S. holder is a foreign corporation, the branch profits tax described above under the heading Distributions on our Common Stock also may apply;

the non-U.S. holder is a non-resident 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) on the net gain derived from the disposition, which may be offset by 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, 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 5-year period ending on the date of the disposition or the period that the non-U.S. holder held our common stock. 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 rule described above.

Information Reporting and Backup Withholding

The gross amount of the distributions on our common stock 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 on our common stock. 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 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 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

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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. Rather, 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.

FATCA

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

Withholding under FATCA generally (1) applies to payments of dividends on our common stock and (2) will apply to payments of gross proceeds from a sale or other disposition of our common stock made after December 31, 2018. Under certain circumstances, a non-U.S. holder may be eligible for refunds or credits of the tax. An intergovernmental agreement between the United States and an applicable foreign country may modify the requirements described in this section. Non-U.S. holders should consult their own tax advisors regarding the possible implications of FATCA on their investment in our common stock and the entities through which they hold our common stock, including, without limitation, the process and deadlines for meeting the applicable requirements to prevent the imposition of the 30% withholding tax under FATCA.

U.S. Federal Estate Tax

Shares of our common stock that are owned or treated as owned by an individual who is a non-U.S. holder (as specially defined for U.S. federal estate tax purposes) at the time of death are considered U.S. *situs* assets and will be included in the individual's gross estate for U.S. federal estate tax purposes. Such shares, therefore, may be subject to U.S. federal estate tax, unless an applicable estate tax or other treaty provides otherwise.

The preceding discussion of material U.S. federal tax considerations is for information only. It is not legal or 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, including the consequences of any proposed changes in applicable laws.

Table of Contents**UNDERWRITING**

Piper Jaffray & Co., or Piper Jaffray, is acting as the sole bookrunner 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 set forth opposite its name below.

| Underwriter | Number of Shares |
|---------------------|---------------------|
| Piper Jaffray & Co. | |

Total

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

We have agreed to indemnify the underwriter against certain liabilities, including liabilities under the Securities Act of 1933, as amended, relating to losses or claims resulting from material misstatements in or omissions from this prospectus supplement, the registration statement of which this prospectus is a part, certain free writing prospectuses that may be used in the offering and in any marketing materials used in connection with this offering and to contribute to payments the underwriter may be required to make in respect of those liabilities.

The underwriter is offering the shares, subject to prior sale, when, as and if issued to and accepted by it, subject to approval of legal matters by their counsel, including the validity of the shares, 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.

Commissions and Discounts

The underwriter has advised us that it proposes initially to offer the shares to the public at the public offering price set forth on the cover page of this prospectus and to dealers at that price less a concession not in excess of \$ _____ per share. After the initial offering, the public offering price, concession or any other term of this offering may be changed.

We have granted to the underwriter an option, exercisable for 30 days from the date of this prospectus, to purchase up to _____ additional shares of our common stock at the public offering price listed on the cover page of this prospectus, less underwriting discounts and commissions.

The following table shows the public offering price, underwriting discounts and commissions and proceeds before expenses to us. The information assumes either no exercise or full exercise by the underwriter of its option to purchase additional shares.

| | Per Share | Total | |
|---|--------------|-------------------|----------------|
| | | Without Option | With Option |
| Public offering price | \$ | \$ | \$ |
| Underwriting discounts and commissions paid by us | \$ | \$ | \$ |
| Proceeds to us, before expenses | \$ | \$ | \$ |

The estimated offering expenses payable by us, exclusive of the underwriting discounts and commissions, are approximately \$ _____. Additionally, we have agreed to reimburse the underwriter for certain of _____.

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its expenses in an amount not to exceed one percent (1.0%) of the gross proceeds of all securities sold pursuant to the underwriting agreement, and separately have agreed to reimburse the underwriter for expenses of up to \$25,000 in connection with the clearance of this offering with the Financial Industry Regulatory Authority, as set forth in the underwriting agreement.

Our common stock is listed on the NASDAQ Global Select Market under the trading symbol AVEO.

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 Piper Jaffray, 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 or otherwise transfer or dispose of, directly or indirectly, any shares of common stock or any securities convertible into, exercisable or exchangeable for or that represent the right to receive common stock (including without limitation, 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 the holder's securities;

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 with 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. 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) upon death by will 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 involving a change of control of the issuer, provided that in the event that 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 Exchange Act of 1934, as amended, or the Exchange Act, is required or shall be made voluntarily in connection with such transfer during the 90-day restricted period. In addition the restrictions will also not apply to (i) the exercise, conversion or exchange of any options or other convertible securities outstanding on the date the lockup agreement was signed (including by net or cashless exercise effected by the delivery or sale of the holder's securities to us to the extent permitted by the instruments representing such options or other convertible securities and including the transfer of shares of common stock to us to satisfy tax withholding obligations in connection therewith), provided that no filing under Section 16(a) of the Exchange Act by any party is required or will be voluntarily made in connection with such exercise, conversion or exchange that reports a disposition of shares of common stock, except to report any transfer of shares of common stock to us to finance a cashless exercise or to satisfy tax withholding obligations as described above, and provided further, that such restrictions shall apply to any of the

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holder's securities issued upon such exercise, conversion or exchange, (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 shall 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, is required or made voluntarily by the holder, us or any other person during the 90-day restricted period or (iii) transfers to us as forfeitures to satisfy tax withholding obligations in connection with the vesting of restricted stock or exercise of options granted pursuant to our equity incentive plans. The restrictions also do not apply to any securities acquired by a holder in the open market after the date of the lock-up agreement, provided that no filing under Section 16(a) of the Exchange Act is required or will be voluntarily made in connection with any subsequent sale, transfer, gift or disposition.

During the 90-day restricted period, we may issue securities (i) 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; (ii) pursuant to the exercise, exchange or conversion of any options, warrants, restricted stock units, rights or convertible securities outstanding on the date of this prospectus supplement or (iii) in connection with a joint venture, collaboration, strategic alliance, licensing, partnering or other commercial relationship.

Piper Jaffray may, in its sole discretion and at any time or from time to time before the termination of the 90-day 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 90-day restricted period.

Price Stabilization and Short Positions

Until the distribution of the shares is completed, SEC rules may limit the underwriter and selling group members from bidding for and purchasing shares of our common stock. However, the underwriter may engage in transactions that stabilize the price of our common stock, such as bids or purchases to peg, fix or maintain that price.

In connection with this offering, the underwriter may purchase and sell shares of our common stock in the open market. These transactions may include short sales, purchases on the open market to cover positions created by short sales and stabilizing transactions. Short sales involve the sale by the underwriter of a greater number of shares than they are required to purchase in this offering. Covered short sales are sales made in an amount not greater than the underwriter's option to purchase additional shares described above. The underwriter may close out any covered short position by either exercising their option to purchase additional shares or purchasing shares in the open market. In determining the source of shares to close out the covered 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 they may purchase shares through the option to purchase additional shares. Naked short sales are sales in excess of the option to purchase additional shares. The underwriter must close out any naked short position by purchasing shares in the open market. A naked short position is more likely to be created if the underwriter is concerned that there may be downward pressure on the price of our common stock in the open market after pricing that could adversely affect investors who purchase in this offering. Stabilizing transactions consist of various bids for or purchases of shares of our common stock made by the underwriter in the open market prior to the closing of this offering.

Similar to other purchase transactions, the underwriter's purchase to cover its short sales may have the effect of raising or maintaining the market price of our common stock or preventing or retarding a decline in the market price of our common stock. As a result, the price of our common stock may be

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higher than the price that might otherwise exist in the open market. The underwriter may conduct these transactions on NASDAQ, in the over-the-counter market or otherwise.

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 our common stock. In addition, neither we nor the underwriter make any representation that the underwriter will engage in these transactions or that these transactions, once commenced, will not be discontinued without notice.

Electronic Offer, Sale and Distributions of Shares

In connection with this offering, the underwriter or securities dealers may distribute prospectuses by electronic means, such as e-mail. In addition, the underwriter may facilitate Internet distribution for this offering to certain of its Internet subscription customers. The underwriter may allocate a limited number of shares for sale to its online brokerage customers. An electronic prospectus is available on the Internet websites maintained by the underwriter. Other than the prospectus in electronic format, the information on the websites of any such underwriter is not part of this prospectus.

Other Relationships

The underwriter and its affiliates are a full service financial institution 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 shares of our common stock may not be made in that Relevant Member State, except that an offer to the public in that Relevant Member State of any shares of our common stock 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

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- (c) in any other circumstances falling within Article 3(2) of the Prospectus Directive, provided that no such offer of shares of our common stock 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 shares of our common stock 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 shares of our common stock to be offered so as to enable an investor to decide to purchase any shares of our common stock, 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.

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

The shares of our common stock 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 the shares of our common stock 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.

Hong Kong

The common shares may not be offered or sold in Hong Kong by means of any document other than (i) in circumstances which do not constitute an offer to the public within the meaning of the Companies

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Ordinance (Cap. 32, Laws of Hong Kong), or (ii) to professional investors within the meaning of the Securities and Futures Ordinance (Cap. 571, Laws of Hong Kong) and any rules made thereunder, or (iii) in other circumstances which do not result in the document being a prospectus within the meaning of the Companies Ordinance (Cap. 32, Laws of Hong Kong) and no advertisement, invitation or document relating to the shares may be issued or may be in the possession of any person for the purpose of issue (in each case whether in Hong Kong or elsewhere), which is directed at, or the contents of which are likely to be accessed or read by, the public in Hong Kong (except if permitted to do so under the laws of Hong Kong) other than with respect to common shares which are or are intended to be disposed of only to persons outside Hong Kong or only to professional investors within the meaning of the Securities and Futures Ordinance (Cap. 571, Laws of Hong Kong) and any rules made thereunder.

Singapore

This prospectus has not been registered as a prospectus with the Monetary Authority of Singapore. Accordingly, this prospectus and any other document or material in connection with the offer or sale, or invitation for subscription or purchase, of the common shares may not be circulated or distributed, nor may the common shares be offered or sold, or be made the subject of an invitation for subscription or purchase, whether directly or indirectly, to persons in Singapore other than (i) to an institutional investor under Section 274 of the Securities and Futures Act, Chapter 289 of Singapore (the SFA), (ii) to a relevant person pursuant to Section 275(1), or any person pursuant to Section 275(1A), and in accordance with the conditions specified in Section 275 of the SFA or (iii) otherwise pursuant to, and in accordance with the conditions of, any other applicable provision of the SFA, in each case subject to compliance with conditions set forth in the SFA.

Where the common shares are subscribed or purchased under Section 275 of the SFA by a relevant person which is:

- (a) a corporation (which is not an accredited investor (as defined in Section 4A of the SFA)) the sole business of which is to hold investments and the entire share capital of which is owned by one or more individuals, each of whom is an accredited investor; or
- (b) a trust (where the trustee is not an accredited investor) whose sole purpose is to hold investments and each beneficiary of the

shares, debentures and units of shares and debentures of that corporation or the beneficiaries' rights and interest (howsoever described) in that trust shall not be transferred within six months after that corporation or that trust has acquired the common shares pursuant to an offer made under Section 275 of the SFA except:

- (a) to an institutional investor (for corporations, under Section 274 of the SFA) or to a relevant person defined in Section 275(2) of the SFA, or to any person pursuant to an offer that is made on terms that such shares, debentures and units of shares and debentures of that corporation or such rights and interest in that trust are acquired at a consideration of not less than \$200,000 (or its equivalent in a foreign currency) for each transaction, whether such amount is to be paid for in cash or by exchange of securities or other assets, and further for corporations, in accordance with the conditions specified in Section 275 of the SFA;
- (b) where no consideration is or will be given for the transfer; or
- (c) where the transfer is by operation of law.

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Switzerland

The common shares may not be publicly offered in Switzerland and will not be listed on the SIX Swiss Exchange (the SIX) or on any other stock exchange or regulated trading facility in Switzerland. This document has been prepared without regard to the disclosure standards for issuance prospectuses under art. 652a or art. 1156 of the Swiss Code of Obligations or the disclosure standards for listing prospectuses under art. 27 ff. of the SIX Listing Rules or the listing rules of any other stock exchange or regulated trading facility in Switzerland. Neither this document nor any other offering or marketing material relating to the common shares or the offering may be publicly distributed or otherwise made publicly available in Switzerland.

Neither this document nor any other offering or marketing material relating to the offering, or the common shares have been or will be filed with or approved by any Swiss regulatory authority. In particular, this document will not be filed with, and the offer of common shares will not be supervised by, the Swiss Financial Market Supervisory Authority FINMA, and the offer of common shares has not been and will not be authorized under the Swiss Federal Act on Collective Investment Schemes (CISA). Accordingly, no public distribution, offering or advertising, as defined in CISA, its implementing ordinances and notices, and no distribution to any non-qualified investor, as defined in CISA, its implementing ordinances and notices, shall be undertaken in or from Switzerland, and the investor protection afforded to acquirers of interests in collective investment schemes under CISA does not extend to acquirers of common shares.

United Arab Emirates

This offering has not been approved or licensed by the Central Bank of the United Arab Emirates (the UAE), Securities and Commodities Authority of the UAE and/or any other relevant licensing authority in the UAE including any licensing authority incorporated under the laws and regulations of any of the free zones established and operating in the territory of the UAE, in particular the Dubai Financial Services Authority (DFSA), a regulatory authority of the Dubai International Financial Centre (DIFC). The offering does not constitute a public offer of securities in the UAE, DIFC and/or any other free zone in accordance with the Commercial Companies Law, Federal Law No 8 of 1984 (as amended), DFSA Offered Securities Rules and NASDAQ Dubai Listing Rules, accordingly, or otherwise. The common shares may not be offered to the public in the UAE and/or any of the free zones.

The common shares may be offered and issued only to a limited number of investors in the UAE or any of its free zones who qualify as sophisticated investors under the relevant laws and regulations of the UAE or the free zone concerned.

France

This prospectus (including any amendment, supplement or replacement thereto) is not being distributed in the context of a public offering in France within the meaning of Article L. 411-1 of the French Monetary and Financial Code (Code monétaire et financier).

This prospectus has not been and will not be submitted to the French Autorité des marchés financiers (the AMF) for approval in France and accordingly may not and will not be distributed to the public in France.

Pursuant to Article 211-3 of the AMF General Regulation, French residents are hereby informed that:

- (a) the transaction does not require a prospectus to be submitted for approval to the AMF;
- (b) persons or entities referred to in Point 2°, Section II of Article L.411-2 of the Monetary and Financial Code may take part in the transaction solely for their own account, as provided in Articles D. 411-1, D. 734-1, D. 744-1, D. 754-1 and D. 764-1 of the Monetary and Financial Code; and

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- (c) the financial instruments thus acquired cannot be distributed directly or indirectly to the public otherwise than in accordance with Articles L. 411-1, L. 411-2, L. 412-1 and L. 621-8 to L. 621-8-3 of the Monetary and Financial Code.

This prospectus is not to be further distributed or reproduced (in whole or in part) in France by the recipients of this prospectus. This prospectus has been distributed on the understanding that such recipients will only participate in the issue or sale of our common stock for their own account and undertake not to transfer, directly or indirectly, our common stock to the public in France, other than in compliance with all applicable laws and regulations and in particular with Articles L. 411-1 and L. 411-2 of the French Monetary and Financial Code.

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LEGAL MATTERS

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

EXPERTS

The consolidated financial statements of AVEO Pharmaceuticals, Inc. appearing in AVEO Pharmaceuticals Inc.'s Annual Report (Form 10-K) for the year ended December 31, 2016, and the effectiveness of AVEO Pharmaceuticals Inc.'s internal control over financial reporting as of December 31, 2016, have been audited by Ernst & Young LLP, independent registered public accounting firm, as set forth in its reports thereon (which contains an explanatory paragraph describing conditions that raise substantial doubt about the Company's ability to continue as a going concern as described in Note 1 to the consolidated financial statements), which conclude, among other things, that AVEO Pharmaceuticals, Inc. did not maintain effective internal control over financial reporting as of December 31, 2016, based on Internal Control - Integrated Framework issued by the Committee of Sponsoring Organizations of the Treadway Commission (2013 framework), because of the effects of the material weakness described therein, included therein, and incorporated herein by reference. Such financial statements have been incorporated herein by reference in reliance upon such reports given on the authority of such firm 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. 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 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:

Annual Report on Form 10-K for the fiscal year ended December 31, 2016;

The information included in our definitive proxy statement on Schedule 14A for the 2016 Annual Meeting of Stockholders, filed on April 14, 2016, to the extent incorporated by reference into Part III of the Annual Report on Form 10-K for the fiscal year ended December 31, 2015;

Our Current Reports on Form 8-K dated May 31, 2016, January 5, 2017, and January 12, 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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\$100,000,000

PROSPECTUS

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 \$100,000,000 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 Global Select Market under the symbol AVEO.

Investing in these securities involves certain risks. See Risk Factors on page 5 and any of 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.

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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 May 26, 2015

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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 \$100,000,000.

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** refer, collectively, to AVEO Pharmaceuticals, Inc., a Delaware corporation, and its subsidiaries.

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.

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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, 2014, including the information specifically incorporated by reference into the Annual Report on Form 10-K from our definitive proxy statement for the 2015 Annual Meeting of Stockholders;

Current Reports on Form 8-K filed on January 7, 2015, January 23, 2015, February 27, 2015, March 6, 2015 (solely with respect to item 8.01), March 19, 2015, March 24, 2015, April 8, 2015 (solely with respect to item 8.01) and April 22, 2015; 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.

650 East Kendall Street

Cambridge, Massachusetts 02142

Attention: Investor Relations

Telephone: (617) 299-5810

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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 and Section 21E of the Exchange Act regarding, among other things, our future discovery and development efforts, our collaborations, our future operating results and financial position, our business strategy, and other objectives for our operations. You can identify these forward-looking statements by their use of words such as anticipate, believe, estimate, expect, forecast, intend, plan, target, will and other words and terms of similar meaning. You also can identify them by the fact that they do not relate strictly to historical or current facts. There are a number of important risks and uncertainties that could cause our actual results to differ materially from those indicated by forward-looking statements. These risks and uncertainties include those inherent in pharmaceutical research and development, such as adverse results in our drug discovery, preclinical trials and clinical development activities, our dependence on our existing and future strategic partners, our ability to obtain any necessary financing to conduct our planned activities, decisions made by the U.S. Food and Drug Administration and other regulatory authorities with respect to the development and commercialization of our drug candidates, our ability to obtain, maintain and enforce intellectual property rights for our drug candidates and other risk factors. You are cautioned that these forward-looking statements are only predictions and are subject to risks, uncertainties and assumptions 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. Unless required by law, we do not undertake any obligation to publicly update any forward-looking statements.

AVEO

Company Overview

AVEO Pharmaceuticals, Inc. is a biopharmaceutical company committed to developing targeted therapies through biomarker-driven insights to provide substantial improvements in patient outcomes where significant unmet medical needs exist. AVEO's proprietary platform has delivered unique insights into cancer and related disease. Our strategy is to leverage these biomarker insights and partner resources to advance the development of our clinical pipeline. We currently are exploring partnership opportunities to fund the further development of three of our four development programs, including our lead program for tivozanib. We have a pipeline of product candidates which include:

Tivozanib, a potent, selective long half-life vascular endothelial growth factor tyrosine kinase inhibitor of all three vascular endothelial growth factors.

Ficlatuzumab, a potent Hepatocyte Growth Factor, or HGF, antibody that inhibits the activity of the HGF/c-Met pathway.

AV-203, a potent, high affinity inhibitor of ErbB3 function that has demonstrated anti-tumor activity in multiple preclinical models and early signs of clinical activity.

AV-380, a potent humanized IgG1 inhibitory monoclonal antibody in preclinical development targeting growth differentiating factor-15, a divergent member of the TGF- β family, for the potential treatment or prevention of cachexia.

Pursuant to our agreement with Bodesix, Inc., or Bodesix, we are conducting a phase 2 trial to develop ficlatuzumab in combination with erlotinib in patients with advanced non-small cell lung cancer with a Bodesix companion diagnostic test. We are currently exploring partnering opportunities to advance the development of our other clinical stage assets.

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We have devoted substantially all of our resources to the research and development of our product candidates. We have not generated any revenue from the commercial sales of our product candidates since our inception and do not expect to generate any revenue from the commercial sales of our product candidates in the immediate term. We expect to continue to devote substantial resources on executing on our clinical development strategy.

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 650 East Kendall Street, Cambridge, Massachusetts 02142, and our telephone number is (617) 299-5000.

Table of Contents**RISK FACTORS**

An investment in our common stock involves a high degree of risk. Before deciding whether to invest in our common stock, you should consider carefully the risks discussed under the sections captioned "Risk Factors" contained in our most recent Annual Report on Form 10-K, as well as our subsequent Quarterly Reports on Form 10-Q and other filings we make with the SEC from time to time, which are incorporated by reference herein in their entirety, together with other information in this prospectus, the information and documents incorporated by reference in this 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.

CONSOLIDATED RATIOS OF EARNINGS TO FIXED CHARGES

The following table sets forth our ratio of earnings to fixed charges and the ratio of earnings to combined fixed charges and preferred stock dividends 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.

| | December 31, 2014 | December 31, 2013 | Fiscal Year Ended December 31, 2012 | December 31, 2011 | December 31, 2010 |
|---|----------------------|----------------------|---|----------------------|----------------------|
| Consolidated ratios of earnings to fixed charges ⁽¹⁾ | N/A | N/A | N/A | 8.2 | N/A |

⁽¹⁾ Our ratios of earnings to combined fixed charges and preferred stock dividends for the periods indicated above are the same as our ratios of earnings to fixed charges set forth above.

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.

We did not record earnings for any of the fiscal years ended December 31, 2014, 2013, 2012 and 2010. Accordingly, our earnings were insufficient to cover fixed charges for such periods 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 of the deficiency in earnings available for fixed charges for the fiscal years ended December 31, 2014, 2013, 2012 and 2010 was approximately \$52,739,000, \$107,029,000, \$114,394,000, and \$58,789,000, respectively.

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 repayment and refinancing of debt, working capital and capital expenditures, research and development expenses, including clinical trial costs, general and administrative expenses, and 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, 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 100,000,000 shares of common stock, par value \$0.001 per share and 5,000,000 shares of preferred stock, par value \$0.001 per share, all of which preferred stock are undesignated. At our 2015 annual meeting of stockholders, to be held on May 28, 2015 we are seeking stockholder approval to increase the number of shares of common stock authorized for issuance under our certificate of incorporation to 200,000,000.

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 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 entitled to vote thereon. 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 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 on all matters to be voted upon by stockholders.

Dividends. The holders of common stock, after any preferences of holders of any preferred stock, are entitled to receive dividends when and if declared by the board of directors out of legally available funds.

Liquidation and Dissolution. If we are liquidated or dissolved, the holders of the common stock will be entitled to share in our assets available for distribution to stockholders in proportion to the amount of common stock they own. The amount available for common stockholders is calculated after payment of liabilities. Holders of any preferred stock will receive a preferential share of our assets before the holders of the common stock receive any assets.

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

convert the stock into any other security;

have the stock redeemed;

purchase additional stock; or

maintain their proportionate ownership interest.

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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 Global Select 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. As of March 31, 2015 no shares of preferred stock were outstanding. Our board of directors is authorized to fix the designation of the series, the number of authorized shares of the series, dividend rights and terms, conversion rights, voting rights, redemption rights and terms, liquidation preferences and any other rights, powers, preferences and limitations applicable to 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.

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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.

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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

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.

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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

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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.

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 Global Select 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. 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 at least 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 restated 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.

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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.

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.

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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 the 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. Together, the senior indenture and the subordinated indenture are referred to as the indentures and, together, the senior trustee and the subordinated trustee are referred to as the trustees. This prospectus briefly outlines some of the provisions of the indentures. The following summary of the material provisions of the indentures is qualified in its entirety by the provisions of the indentures, including definitions of certain terms used in the indentures. Wherever we refer to particular sections or defined terms of 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.

None of the indentures 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 pari passu 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 debt securities issued under the subordinated indenture the terms on which they are subordinated;

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the aggregate principal amount of the debt securities;

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, per year, 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 manner of determination of such interest payment dates and the related record 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 and upon what terms the debt securities may be defeased;

any events of default or covenants in addition to or in lieu of those set forth 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; and

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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.

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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.

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, 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, 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 (subject to certain exceptions provided for in the senior indenture);

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

certain other conditions are met.

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).

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 for any series of senior debt securities:

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);

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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 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 an existing 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 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.

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.

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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 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 pay or cause to be paid, as and when due and payable, the principal of and any interest on all senior debt securities of such series outstanding under the senior indenture; 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) and we deposit in trust a combination of cash and U.S. government or U.S. 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.

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. 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 discharge and covenant defeasance will apply to any series of debt securities issued under the indentures.

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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 a combination of cash and U.S. government or U.S. 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 of 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 a combination of cash and U.S. government or U.S. 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.

Modification and Waiver. We and the trustee may amend or supplement the senior indenture or the senior debt securities 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;

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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, delete from or revise the conditions, limitations and restrictions on the authorized amount, terms, purposes of issue, authentication and delivery of any series of senior debt securities;

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 all series affected by the amendment or modification (voting together as a single class); 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 of 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;

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

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

waives an uncured default in the payment of principal of or interest on the senior debt securities (except in the case of a rescission of acceleration as described above);

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changes the provisions relating to the waiver of past defaults or changes 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; or

reduces the above-stated percentage of outstanding senior debt securities of such series whose holders must consent to a supplemental indenture or modifies or 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 years after the date upon which such principal, premium or interest 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.

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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 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 debt 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;

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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 depository or its nominee as the owner of the debt securities, units or warrants represented by these global securities. The depository 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 depository or its nominee identified in the applicable prospectus supplement and registered in the name of that depository 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 depository for the global security, the nominees of the depository or any successors of the depository or those nominees.

If not described below, any specific terms of the depository 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 depository arrangements.

Ownership of beneficial interests in a global security will be limited to persons, called participants, that have accounts with the depository or persons that may hold interests through participants. Upon the issuance of a global security, the depository 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 depository, 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 depository, or its nominee, is the registered owner of a global security, that depository 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 depository 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

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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 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 time to time in one or more transactions:

at a fixed price, or prices, which may be changed from time to time;

at market prices prevailing at the time of sale;

at prices related to such prevailing market prices; or

at negotiated prices.

Each prospectus supplement will describe the method of distribution of the securities and any applicable restrictions.

The prospectus supplement with respect to the securities of a particular series will describe the terms of the offering of the securities, including the following:

the name of the agent or any underwriters;

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the public offering or purchase price and the proceeds we will receive from the sale of the securities;

any discounts and commissions to be allowed or re-allowed or paid to the agent or underwriters;

all other items constituting underwriting compensation;

any discounts and commissions to be allowed or re-allowed or paid to dealers; and

any exchanges on which the securities will be listed.

If any underwriters or agents are utilized in the sale of the securities in respect of which this prospectus is delivered, we will enter into an underwriting agreement or other agreement with them at the time of sale to them, and we will set forth in the prospectus supplement relating to such offering the names of the underwriters or agents and the terms of the related agreement with them.

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If a dealer is utilized in the sale of the securities in respect of which this prospectus is delivered, we will sell such securities to the dealer, as principal. The dealer may then resell such securities to the public at varying prices to be determined by such dealer at the time of resale.

If we offer securities in a subscription rights offering to our existing security holders, we may enter into a standby underwriting agreement with dealers, acting as standby underwriters. We may pay the standby underwriters a commitment fee for the securities they commit to purchase on a standby basis. If we do not enter into a standby underwriting arrangement, we may retain a dealer-manager to manage a subscription rights offering for us.

Remarketing firms, agents, underwriters, dealers and other persons may be entitled under agreements which they may enter into with us to indemnification by us against certain civil liabilities, including liabilities under the Securities Act, and may be customers of, engage in transactions with or perform services for us in the ordinary course of business.

If so indicated in the applicable prospectus supplement, we will authorize underwriters or other persons acting as our agents to solicit offers by certain institutions to purchase securities from us pursuant to delayed delivery contracts providing for payment and delivery on the date stated in the prospectus supplement. Each contract will be for an amount not less than, and the aggregate amount of securities sold pursuant to such contracts shall not be less nor more than, the respective amounts stated in the prospectus supplement. Institutions with whom the contracts, when authorized, may be made include commercial and savings banks, insurance companies, pension funds, investment companies, educational and charitable institutions and other institutions, but shall in all cases be subject to our approval. Delayed delivery contracts will not be subject to any conditions except that:

the purchase by an institution of the securities covered under that contract shall not at the time of delivery be prohibited under the laws of the jurisdiction to which that institution is subject; and

if the securities are also being sold to underwriters acting as principals for their own account, the underwriters shall have purchased such securities not sold for delayed delivery. The underwriters and other persons acting as our agents will not have any responsibility in respect of the validity or performance of delayed delivery contracts.

Certain agents, underwriters and dealers, and their associates and affiliates may be customers of, have borrowing relationships with, engage in other transactions with, and/or perform services, including investment banking services, for us or one or more of our respective affiliates in the ordinary course of business.

In order to facilitate the offering of the securities, any underwriters may engage in transactions that stabilize, maintain or otherwise affect the price of the securities or any other securities the prices of which may be used to determine payments on such securities. Specifically, any underwriters may overallocate in connection with the offering, creating a short position for their own accounts. In addition, to cover overallocations or to stabilize the price of the securities or of any such other securities, the underwriters may bid for, and purchase, the securities or any such other securities in the open market. Finally, in any offering of the securities through a syndicate of underwriters, the underwriting syndicate may reclaim selling concessions allowed to an underwriter or a dealer for distributing the securities in the offering if the syndicate repurchases previously distributed securities in transactions to cover syndicate short positions, in stabilization transactions or otherwise. Any of these activities may stabilize or maintain the market price of the securities above independent market levels. Any such underwriters are not required to engage in these activities and may end any of these activities at any time.

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Under Rule 15c6-1 of the Exchange Act, trades in the secondary market generally are required to settle in three business days, unless the parties to any such trade expressly agree otherwise. The applicable prospectus supplement may provide that the original issue date for your securities may be more than three scheduled business days after the trade date for your securities. Accordingly, in such a case, if you wish to trade securities on any date prior to the third business day before the original issue date for your securities, you will be required, by virtue of the fact that your securities initially are expected to settle more than three scheduled business days after the trade date for your securities, to make alternative settlement arrangements to prevent a failed settlement.

The securities may be new issues of securities and may have no established trading market. The securities may or may not be listed on a national securities exchange. We can make no assurance as to the liquidity of or the existence of trading markets for any of the securities.

In compliance with the guidelines of the Financial Industry Regulatory Authority, or FINRA, the aggregate maximum discount, commission or agency fees or other items constituting underwriting compensation to be received by any FINRA member or independent broker-dealer will not exceed 8% of the proceeds from any offering pursuant to this prospectus and any applicable prospectus supplement.

LEGAL MATTERS

Unless the applicable prospectus supplement indicates otherwise, the validity of the securities in respect of which this prospectus is being delivered will be passed upon by Wilmer Cutler Pickering Hale and Dorr LLP, Boston, Massachusetts.

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, 2014, and the effectiveness of our internal control over financial reporting as of December 31, 2014, as set forth in their reports, which are incorporated by reference in this prospectus 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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Shares

AVEO PHARMACEUTICALS, INC.

Common Stock

PROSPECTUS SUPPLEMENT

Piper Jaffray

March , 2017