AVEO PHARMACEUTICALS INC
Form 424B4
March 12, 2010
Table of Contents

Filed Pursuant to Rule 424(b)(4)
Registration No. 333-163778

PROSPECTUS

9,000,000 Shares

COMMON STOCK

This is the initial public offering of common stock by AVEO Pharmaceuticals, Inc. AVEO is selling 9,000,000 shares of common stock. Prior to this offering, there has been no public market for our common stock. The initial public offering price of our common stock is $9.00 per share.

Our common stock has been approved for listing on the NASDAQ Global Market under the symbol AVEO.

	Per share	Total
Initial public offering price	**$9.00**	**$81,000,000**
Underwriting discounts and commissions	**$0.63**	**$5,670,000**
Proceeds to AVEO, before expenses	**$8.37**	**$75,330,000**

We have granted the underwriters an option to purchase up to 1,350,000 additional shares of common stock to cover over-allotments.

Investing in our common stock involves risks. See Risk Factors beginning on page 9.

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

The underwriters expect to deliver the shares on or about March 17, 2010.

J.P.Morgan **Morgan Stanley**

Leerink Swann
Canaccord Adams

March 11, 2010

Table of Contents

TABLE OF CONTENTS

You should rely only on the information contained in this prospectus and in any free writing prospectus we may authorize to be delivered or made available to you. We have not authorized anyone to provide you with information that is different. This prospectus may only be used where it is legal to offer and sell shares of our common stock. The information in this prospectus is accurate only as of the date of this prospectus, regardless of the time of delivery of this prospectus or any sale of shares of our common stock.

Until April 5, 2010 (25 days after the commencement of this offering), all dealers that buy, sell or trade shares of our common stock, whether or not participating in this offering, may be required to deliver a prospectus. This delivery requirement is in addition to the dealers obligation to deliver a prospectus when acting as underwriters and with respect to their unsold allotments or subscriptions.

For investors outside the United States: We have not and the underwriters have not done anything that would permit this offering or possession or distribution of this prospectus in any jurisdiction where action for that purpose is required, other than in the United States. Persons outside the United States who come into possession of this prospectus must inform themselves about, and observe any restrictions relating to, the offering of the shares of common stock and the distribution of this prospectus outside the United States.

Table of Contents

PROSPECTUS SUMMARY

This summary highlights information contained elsewhere in this prospectus. This summary does not contain all of the information you should consider before investing in our common stock. You should read this entire prospectus carefully, especially the Risk Factors section beginning on page 9 and our consolidated financial statements and the related notes appearing at the end of this prospectus, before making an investment decision.

Our Company

Overview

We are a biopharmaceutical company focused on discovering, developing and commercializing novel cancer therapeutics. Our product candidates are directed against important mechanisms, or targets, known or believed to be involved in cancer. Tivozanib, our lead product candidate, is a highly potent and selective oral inhibitor of the vascular endothelial growth factor, or VEGF, receptors 1, 2 and 3. Our clinical trials of tivozanib to date have demonstrated a favorable safety and efficacy profile for tivozanib. We have completed a successful 272-patient phase 2 clinical trial of tivozanib in patients with advanced renal cell cancer, or RCC. In this trial, we measured, among other things, each patient s progression-free survival, which refers to the period of time that began when a patient entered the clinical trial and ended when either the patient died or the patient s cancer had grown by a specified percentage or spread to a new location in the body. The overall median progression-free survival of patients in the phase 2 clinical trial was 11.8 months. In a retrospective analysis of the subset of 176 patients in our phase 2 clinical trial who had the clear cell type of RCC and who had undergone prior removal of their affected kidney, referred to as a nephrectomy, both of which are inclusion criteria for our phase 3 clinical trial of tivozanib, the median progression-free survival was 14.8 months. The incidence of side effects in the trial, such as diarrhea, fatigue, rash, mucositis, stomatitis and hand-foot syndrome, which are commonly associated with other VEGF receptor inhibitors, was notably low, with moderate to severe episodes of these side effects occurring in fewer than two percent of treated patients. In December 2009, we initiated patient screening for our phase 3 clinical trial of tivozanib in patients with advanced RCC, in which we plan to enroll 500 patients, which we refer to as the TIVO-1 study. We commenced enrollment of patients in the TIVO-1 study in February 2010. The TIVO-1 study is a randomized, controlled clinical trial of tivozanib compared to Nexavar (sorafenib) in advanced clear cell RCC patients who have undergone a prior nephrectomy, and who have not received any prior VEGF-targeted therapy. Nexavar is an oral VEGF receptor inhibitor approved for the treatment of RCC. In its phase 3 clinical trial in patients with advanced clear cell RCC, 94% of whom had undergone a prior nephrectomy, Nexavar demonstrated a median progression-free survival of 5.5 months. Progression-free survival is the primary endpoint in the TIVO-1 study. The TIVO-1 study is designed so that a difference in progression-free survival of three months or more between the treatment arms would be statistically significant.

Inhibition of the VEGF pathway has demonstrated benefit for patients with a wide range of cancer types, including RCC, metastatic breast cancer, colorectal cancer, non-small cell lung cancer, liver cancer and brain cancer. Approved VEGF-pathway targeted drugs, including Avastin (bevacizumab), Nexavar and Sutent (sunitinib), accounted for over $6 billion in sales worldwide in 2008, based on 2008 annual reports made publicly available by the companies marketing such drugs. Due to tivozanib s potency and specificity, we believe that it may enable optimal inhibition of the VEGF pathway, while minimizing side effects associated with inhibition of other pathways, referred to as off-target toxicities. We believe this favorable efficacy and safety profile may allow tivozanib to be successfully used as a monotherapy. It may also allow tivozanib to be more readily combined with standard chemotherapy as well as other targeted therapies, potentially increasing the breadth of its clinical utility. In addition to our recently-initiated phase 3 clinical trial of once-daily, oral tivozanib in patients with advanced RCC, we are currently conducting multiple clinical trials of tivozanib including: a phase 1b clinical trial in combination with Torisel (temsirolimus), an approved inhibitor of the receptor known as mammalian target of rapamycin, or mTOR, in patients with advanced RCC; a phase 1b clinical trial in combination with the FOLFOX6 chemotherapy regimen in patients with advanced colorectal cancer and other

Table of Contents

gastrointestinal cancers; a phase 1b clinical trial in combination with paclitaxel in patients with metastatic breast cancer; and a phase 1b clinical trial as a monotherapy in patients with non-small cell lung cancer. We expect that the results of these clinical trials will help to inform our clinical development plans for tivozanib in additional indications. We acquired exclusive rights to develop and commercialize tivozanib worldwide outside of Asia pursuant to a license agreement we entered into with Kirin Brewery Co. Ltd. (now Kyowa Hakko Kirin) in 2006. Under the license agreement, we obtained an exclusive license to research, develop, manufacture and commercialize tivozanib, pharmaceutical compositions thereof and associated biomarkers for the diagnosis, prevention and treatment of any and all human diseases and conditions. Kyowa Hakko Kirin has retained rights to tivozanib in Asia. We have obligations to make milestone, royalty and sublicensing revenue payments to Kyowa Hakko Kirin. For a further discussion of this agreement, please see Business Strategic Partnerships Kyowa Hakko Kirin beginning on page 95.

In addition to tivozanib, we have a pipeline of monoclonal antibodies derived from our Human Response Platform, a novel method of building preclinical models of human cancer, which are intended to more accurately represent cancer biology in patients. AV-299, our next most advanced product candidate, is an antibody which binds to hepatocyte growth factor, or HGF, thereby blocking its function. Through the use of our Human Response Platform, our scientists have identified the HGF/c-Met pathway as being a significant driver of tumor growth. We have completed a phase 1 clinical trial of AV-299 and expect to initiate a phase 2 clinical trial for non-small cell lung cancer in the first half of 2010. In 2007, we entered into an agreement with Schering-Plough Corporation, or Schering-Plough (which subsequently merged with Merck & Co., Inc., or Merck), under which we granted Merck exclusive worldwide rights to co-develop and commercialize AV-299 and under which Merck funds all development and manufacturing expenses, subject to an agreed-upon budget. Under that agreement, we retain the option to co-promote AV-299 in the United States for the first large market oncology indication for which Merck files for marketing approval in the United States.

Our Human Response Platform was designed to overcome many of the limitations of traditional approaches to modeling human cancer. The traditional method of modeling human cancer uses a model referred to as a xenograft. A xenograft model is created by adapting cells from a human tumor to grow in a petri dish, and then injecting these cells in a mouse, where they grow into tumors. However, the resulting tumors differ from the original tumor in important respects, and, accordingly, xenograft models are often poor predictors of the success of cancer drugs in human clinical trials. In our Human Response Platform, we use patented genetic engineering techniques to grow populations of spontaneous tumors in animals containing human-relevant, cancer-causing mutations and tumor variation akin to what is seen in populations of human tumors. Because we believe that these populations of tumors better replicate what is seen in human cancer, we believe that our Human Response Platform provides us with unique insights into cancer biology and mechanisms of drug response and resistance, and represents a significant improvement over traditional approaches. We are utilizing this Human Response Platform alone and with our strategic partners to (i) identify and validate target genes which drive tumor growth, (ii) evaluate drugs which can block the function of these targets and (iii) identify biomarkers, which are indicators of drug response and resistance in patients, in an effort to evaluate which patients are most likely to respond favorably to treatment with such drugs. As of December 31, 2009, we have raised $169.0 million through a number of strategic partnerships based on our Human Response Platform and products derived therefrom with leading cancer companies including Merck, OSI Pharmaceuticals, Inc., or OSI, Schering-Plough (now Merck) and Biogen Idec Inc., or Biogen Idec, comprising $91.5 million of non-dilutive capital in the form of license fees, milestone payments and research and development funding from our strategic partners and $77.5 million in the form of equity sales to our strategic partners.

In addition, we have identified a number of other promising targets for the development of novel cancer therapeutics using our Human Response Platform. We have preclinical antibody discovery programs underway focusing on targets that appear to be important drivers of tumor growth, including the ErbB3 receptor (partnered with Biogen Idec), the RON receptor, the Notch receptors and the Fibroblast Growth Factor receptors.

Table of Contents

Our Strategy

Our objective is to develop and commercialize our product candidates to treat serious unmet medical needs in patients suffering from a variety of cancer types. The critical components of our business strategy are:

- Develop and commercialize our phase 3 clinical product candidate, tivozanib, in multiple cancer types.
- Develop and commercialize our clinical product candidate, AV-299, in collaboration with Merck.
- Build capabilities that will allow us to effectively commercialize our products.
- Leverage our novel Human Response Platform to discover, develop and commercialize a pipeline of first-in-class and best-in-class novel oncology products.
- Establish strategic partnerships to accelerate and maximize the potential of our products and technology while preserving significant commercial rights.

Our Strategic Partnerships

We have entered into the following strategic partnerships where we have granted rights to our product candidates, or have utilized, or granted rights to certain elements of, our Human Response Platform:

- We have a collaboration agreement with Schering-Plough (now Merck), under which we granted Merck worldwide, exclusive rights to develop and commercialize all of our monoclonal antibody antagonists of HGF, including AV-299, for therapeutic and prophylactic use in humans and for veterinary use. We have primary responsibility for certain U.S.-related development activities through completion of the first phase 2 proof-of-concept trial for AV-299. Merck will be responsible for clinical development of AV-299 after completion of such proof-of-concept trial.
- We have a collaboration and license agreement with OSI, which provides for the use of our proprietary *in vivo* models by our scientists, use of our bioinformatics tools and other target validation and biomarker research to further develop and advance OSI s small molecule drug discovery and translational research related to cancer and other diseases. Our strategic partnership with OSI is primarily focused on the identification and validation of genes and targets involved in the processes of epithelial-mesenchymal transition, or mesenchymal-epithelial transition, in cancer.
- We have an exclusive option and license agreement with Biogen Idec regarding the development and commercialization of our discovery-stage ErbB3-targeted antibodies for the potential treatment and diagnosis of cancer and other diseases outside of the United States, Canada and Mexico. We are responsible for developing ErbB3 antibodies through completion of the first phase 2 clinical trial designed in a manner that, if successful, will generate data sufficient to support advancement to a phase 3 clinical trial. Within a specified time period after we complete the phase 2 clinical trial and deliver to Biogen Idec a detailed data package containing the results of the trial, Biogen Idec may elect to obtain a co-exclusive (with us), worldwide license under our relevant intellectual property to develop and manufacture ErbB3 antibody products and an exclusive license under our relevant intellectual property to commercialize ErbB3 antibody products in all countries in the world other than the United States, Canada and Mexico.

We entered into a license and collaboration agreement with Merck to discover and validate small molecule oncology targets. During the research program portion of the collaboration, which concluded in 2006, we used our proprietary cancer models to identify and subsequently validate essential tumor maintenance genes suitable as targets for small molecule drug development. Merck exercised its option to license six targets discovered and validated by us under the research collaboration.

We also entered into a license and research collaboration agreement with Merck relating to the use of our Human Response Platform. The collaboration concluded in 2007 and was focused on the

Table of Contents

identification of genetic profiles that correlate with drug response to certain cancer compounds then under development at Merck, in order to more effectively guide Merck s clinical and market development of these compounds.

Risks Associated with Our Business

Our business is subject to a number of risks of which you should be aware before making an investment decision. These risks are discussed more fully in the Risk Factors section of this prospectus beginning on page 9. In particular:

We currently have no commercial products and we have not received regulatory approval for, nor have we generated commercial revenue from, any of our product candidates.

We are dependent on the success of our lead drug candidate, tivozanib, which is in phase 3 clinical development. Positive results in our phase 2 clinical trial of tivozanib may not be predictive of the results in our phase 3 clinical trial and the results of our phase 3 clinical trial may not be sufficient for approval of tivozanib. We cannot be certain as to what type and how many clinical trials the U.S. Food and Drug Administration, or equivalent foreign regulatory agencies, will require us to conduct in order to gain approval to market tivozanib. If the results of our phase 3 clinical trial are not sufficient for the approval of tivozanib, our business will be adversely affected and the value of your investment could decline.

In order to obtain regulatory approval for the commercial sale of any of our other product candidates, including AV-299, we must demonstrate, through extensive preclinical studies and clinical trials, that the product candidate is safe and effective for use in each target indication, a process that can take many years to complete and that will require us to use substantial resources with highly uncertain results. Problems such as our failure to comply with regulatory requirements, insufficient effectiveness of such product candidates during clinical trials, safety issues, regulatory delays or an inability to enroll and maintain sufficient numbers of patients in our clinical trials could cause us or regulatory authorities to delay, suspend or terminate clinical trials for such product candidates. For these and other reasons, we may never obtain regulatory approval for any of such product candidates. Our failure to meet these ongoing requirements may prevent us from achieving or sustaining profitability.

We have incurred net operating losses since our inception. Our net loss was $44.1 million, $32.5 million and $25.0 million for the years ended December 31, 2009, 2008 and 2007, respectively. As of December 31, 2009, we had an accumulated deficit of $177.7 million. We anticipate that our operating losses will increase over the next several years. In addition, the report of our independent registered public accounting firm with respect to our consolidated financial statements appearing at the end of this prospectus contains an explanatory paragraph stating that our financial results and our need to raise additional financing prior to the end of 2010 raise substantial doubt about our ability to continue as a going concern.

We will need to raise substantial additional funds to achieve our goals. A failure to raise such additional funds may require us to delay, limit, reduce or terminate current or planned activities.

We expect any product candidate that we commercialize with our strategic partners or on our own will compete with existing, market-leading products. For example, even if tivozanib is approved for the treatment of advanced RCC, it would compete with VEGF pathway inhibitors and mTOR inhibitors that are currently approved for the treatment of advanced RCC and other therapies in development. Many of our potential competitors have substantially greater financial, technical and personnel resources and commercial infrastructure than we have.

We currently expect that a substantial portion of our future revenues may be dependent upon our strategic partnerships with OSI, Merck and Biogen Idec. If these strategic partners were to terminate

Table of Contents

their agreements with us, fail to meet their obligations or otherwise decrease their level of efforts, allocation of resources or other commitments under these agreements, our future revenues could decline and the development and commercialization of our product candidates would be interrupted. In addition, if OSI, Merck or Biogen Idec do not achieve some or any of the development, regulatory and commercial milestones or if they do not achieve certain net sales thresholds, in each case, as set forth in their respective agreements, we will not fully realize the expected economic benefits of the agreements.

Our inability to obtain adequate patent protection for our product candidates or technology platform or failure to successfully defend against any claims that our product candidates infringe the rights of third parties could also adversely affect our business. In addition, tivozanib and certain aspects of our Human Response Platform are protected by patents exclusively licensed from other companies. If the licensors terminate the licenses or fail to maintain or enforce the underlying patents, our competitive position will be harmed. Any problems relating to our intellectual property may require us to spend a substantial amount of time and money to resolve.

Our Corporate Information

We were incorporated under the laws of the State of Delaware on October 19, 2001 as GenPath Pharmaceuticals, Inc. and changed our name to AVEO Pharmaceuticals, Inc. on March 1, 2005. Our principal executive offices are located at 75 Sidney Street, Cambridge, Massachusetts, 02139, and our telephone number is (617) 299-5000. Our website address is www.aveopharma.com. The information contained on, or that can be accessed through, our website is not a part of this prospectus. Investors should not rely on any such information in deciding whether to purchase our common stock. We have included our website address in this prospectus solely as an inactive textual reference.

Unless the context otherwise requires, we use the terms AVEO, our company, we, us and our in this prospectus to refer to AV Pharmaceuticals, Inc. and its consolidated subsidiary.

The name AVEO is a registered trademark in the United States, Canada, Europe and Japan, and is solely owned by AVEO Pharmaceuticals, Inc. The AVEO logo is a registered trademark in the United States and is solely owned by AVEO Pharmaceuticals, Inc. The term Human Response Platform is an AVEO-owned common law trademark with registration pending. The symbol indicates a common law trademark. Other service marks, trademarks and trade names appearing in this prospectus are the property of their respective owners.

Table of Contents

THE OFFERING

Common stock offered	9,000,000 shares
Common stock to be outstanding after this offering	29,644,831 shares
Over-allotment option	1,350,000 shares
Use of proceeds	We estimate that the net proceeds from this offering will be approximately $72.6 million, or approximately $83.9 million if the underwriters exercise their over-allotment option in full, after deducting underwriting discounts and commissions and estimated offering expenses payable by us. We expect to use substantially all of the net proceeds from this offering to fund our phase 3 clinical trial of tivozanib, our lead product candidate, with the balance, if any, to be used for working capital and other general corporate purposes. See Use of Proceeds on page 37 for a more complete description of the intended use of proceeds from this offering.
Risk factors	You should read the Risk Factors section of this prospectus beginning on page 9 for a discussion of factors to consider carefully before deciding to invest in shares of our common stock.
NASDAQ Global Market symbol	AVEO

The number of shares of our common stock to be outstanding after this offering is based on 20,644,831 shares of common stock outstanding as of February 1, 2010 after giving effect to the conversion of all of our convertible preferred stock into common stock upon the closing of this offering and excludes:

- 3,248,207 shares of common stock issuable upon exercise of stock options outstanding as of February 1, 2010 at a weighted average exercise price of $4.56 per share;
- 182,200 shares of common stock issuable upon the exercise of warrants outstanding as of February 1, 2010 at a weighted average exercise price of $9.52 per share; and
- an aggregate of 398,611 shares of common stock reserved for future issuance under our stock incentive plans as of February 1, 2010 and an aggregate of 2,125,000 additional shares of common stock that will be available under our 2010 stock incentive plan and 2010 employee stock purchase plan upon the closing of this offering.

Unless otherwise indicated, all information in this prospectus reflects and assumes:

- the implementation of a one-for-four reverse stock split of our common stock on February 18, 2010;

the filing of our restated certificate of incorporation and the adoption of our restated bylaws as of the closing date of this offering;

no exercise by the underwriters of their option to purchase up to 1,350,000 shares of common stock to cover over-allotments;

the conversion of all outstanding shares of our convertible preferred stock into an aggregate of 18,979,155 shares of common stock upon the closing of this offering; and

the conversion of all outstanding warrants to purchase shares of our convertible preferred stock into warrants to purchase an aggregate of 182,200 shares of common stock upon the closing of this offering.

Table of Contents

SUMMARY CONSOLIDATED FINANCIAL DATA

You should read the following summary financial data together with our financial statements, the related notes appearing at the end of this prospectus and the Selected Consolidated Financial Data and Management s Discussion and Analysis of Financial Condition and Results of Operations sections of this prospectus. We derived the summary statements of operations data for the years ended December 31, 2007, 2008 and 2009 and the balance sheet data as of December 31, 2009 from our audited financial statements included in this prospectus. Our historical results for any prior period are not necessarily indicative of results to be expected in any future period, and our results for any interim period are not necessarily indicative of results for a full fiscal year.

The pro forma balance sheet data set forth below gives effect to the conversion of all outstanding shares of our convertible preferred stock into common stock upon the closing of this offering and the pro forma as adjusted balance sheet data also gives effect to our issuance and sale of 9,000,000 shares of common stock in this offering at the initial public offering price of $9.00 per share, after deducting underwriting discounts and commissions and estimated offering expenses payable by us.

	Year Ended December 31,		
	2007	2008	2009
	(in thousands, except per share data)		
Statement of Operations Data:			
Revenue	$ 11,034	$ 19,660	$ 20,719
Operating expenses:			
Research and development	29,248	41,821	51,792
General and administrative	6,502	9,164	10,120
Total operating expenses	35,750	50,985	61,912
Loss from operations	(24,716)	(31,325)	(41,193)
Other income and expense:			
Other income, net		18	(333)
Loss on loan extinguishment		(248)	
Interest expense	(2,437)	(2,086)	(2,811)
Interest income	2,171	1,168	144
Other income (expense), net	(266)	(1,148)	(3,000)
Net loss before taxes	(24,982)	(32,473)	(44,193)
Tax benefit			100
Net loss	$ (24,982)	$ (32,473)	$ (44,093)
Net loss per share applicable to common stockholders-basic and diluted	$ (17.89)	$ (21.08)	$ (27.43)

Table of Contents

	Year Ended December 31,		
	2007	2008	2009
	(in thousands, except per share data)		
Weighted average number of common shares used in net loss per share calculation basic and diluted	1,396	1,541	1,607
Pro forma net loss per share basic and diluted (unaudited)[1]			$ (2.23)
Shares used in computing pro forma net loss per share basic and diluted (unaudited)			19,768

(1) Pro forma basic and diluted net loss per common share is calculated assuming the conversion of all of our outstanding shares of convertible preferred stock into common stock at the beginning of the period or at the original date of issuance, if later.

	As of December 31, 2009		
	Actual	Pro Forma[a] (unaudited) (in thousands)	Pro Forma as Adjusted[b]
Balance Sheet Data:			
Cash, cash equivalents, and marketable securities	$ 51,301	$ 51,301	$ 123,881
Working capital	18,789	18,789	91,369
Total assets	59,844	59,844	132,424
Loans payable, including current portion	19,745	19,745	19,745
Preferred stock warrant liability	1,459		
Convertible preferred stock	156,705		
Accumulated deficit	(177,725)	(177,725)	(177,725)
Total stockholders deficit	(170,291)	(12,127)	60,453

(a) The pro forma consolidated balance sheet data gives effect to the conversion of all outstanding shares of our convertible preferred stock into 18,979,155 shares of common stock upon the closing of this offering and the conversion of all outstanding preferred stock warrants into warrants for the purchase of 182,200 shares of common stock upon the closing of this offering.

(b) The pro forma as adjusted consolidated balance sheet data also gives further effect to the sale of 9,000,000 shares of our common stock in this offering at the initial public offering price of $9.00 per share, after deducting underwriting discounts and commissions and estimated offering expenses payable by us.

Table of Contents

RISK FACTORS

Investing in our common stock involves a high degree of risk. You should carefully consider the risks and uncertainties described below together with all of the other information contained in this prospectus, including our financial statements and the related notes appearing at the end of this prospectus, before deciding to invest in our common stock. If any of the following risks actually occur, our business, prospects, operating results and financial condition could suffer materially, the trading price of our common stock could decline and you could lose all or part of your investment.

Risks Related to Development, Clinical Testing and Regulatory Approval of Our Drug Candidates

We are dependent on the success of our lead drug candidate, tivozanib, which is in phase 3 development.

To date, we have invested a significant portion of our efforts and financial resources in the research and development of tivozanib. We initiated our phase 3 clinical trial for tivozanib in December 2009 and are currently conducting four phase 1b clinical trials, three of which focus on tivozanib in combination with other known anti-cancer agents.

Our near-term prospects, including our ability to finance our company and to generate strategic partnerships and revenues, will depend heavily on the successful development and commercialization of tivozanib. All of our other potential product candidates, with the exception of AV-299, which we have partnered with Schering-Plough Corporation, or Schering-Plough (now Merck & Co., Inc., or Merck), are in the preclinical research stage. The clinical and commercial success of tivozanib will depend on a number of factors, including the following:

- timely enrollment in our phase 3 clinical trial or our other on-going or planned clinical trials, which may be slower than we currently anticipate, potentially resulting in significant delays;
- our ability to demonstrate to the satisfaction of the U.S. Food and Drug Administration, or FDA, or equivalent foreign regulatory agencies, tivozanib s safety and efficacy through current and future clinical trials;
- the prevalence and severity of adverse side effects;
- timely receipt of necessary marketing approvals from the FDA and similar foreign regulatory authorities;
- achieving and maintaining compliance with all regulatory requirements applicable to the product;
- the availability, relative cost and relative efficacy of alternative and competing treatments;
- the effectiveness of our own or our potential strategic partners marketing, sales and distribution strategy and operations;
- the ability of our third-party manufacturers to manufacture clinical trial supplies of our product candidates and to develop, validate and maintain a commercially viable manufacturing process that is compliant with current good manufacturing practices, or cGMP;
- our ability to successfully launch commercial sales of tivozanib, assuming FDA approval is obtained, whether alone or in collaboration with others;

our ability to avoid third party patent interference or patent infringement claims;

acceptance of tivozanib as safe and effective by patients, the medical community and third-party payors; and

a continued acceptable safety profile of the product following approval.

Table of Contents

Many of these factors are beyond our control. Accordingly, we cannot assure you that we will ever be able to generate revenues through the sale of tivozanib. If we are not successful in commercializing tivozanib, or are significantly delayed in doing so, our business will be materially harmed and the value of your investment could substantially decline.

Positive results in our phase 2 clinical trial of tivozanib may not be predictive of the results in our phase 3 clinical trial. If the results of our phase 3 clinical trial are not positive, or are not sufficient for approval of tivozanib, our business will be adversely affected.

Positive results in early clinical trials of a drug candidate may not be replicated in later clinical trials. A number of companies in the pharmaceutical and biotechnology industries have suffered significant setbacks in late-stage clinical trials even after achieving promising results in earlier-stage development. Although the results of our phase 2 clinical trial of tivozanib for the treatment of advanced RCC were positive, we cannot assure you that the phase 3 clinical trial for the treatment of advanced RCC will achieve positive results. A number of factors could contribute to a lack of positive results in our phase 3 clinical trial of tivozanib.

For example, in our phase 2 clinical trial, we compared tivozanib to treatment with placebo. In our phase 3 clinical trial, the primary endpoint is a comparison of progression-free survival of patients treated with tivozanib to the progression-free survival of patients treated with Nexavar. Nexavar is a VEGF receptor inhibitor which has been approved by the FDA and the European Medicines Agency, or the EMEA, for the treatment of advanced RCC, as well as the treatment of hepatocellular carcinoma. Based on our discussions with the FDA and the EMEA, we have set the number of patients to be enrolled in the clinical trial at a number sufficient to demonstrate that a difference in progression-free survival of three months or more between the treatment arms would be statistically significant. The FDA has advised us that the results of the phase 3 clinical trial will need to show not only that patients treated with tivozanib have a statistically significant improvement in progression-free survival as compared to patients treated with Nexavar, but also that the improvement in progression-free survival of patients treated with tivozanib is clinically meaningful in the context of the safety of the drug. It is not clear how much of an improvement in progression-free survival will be required in order for it to be deemed clinically meaningful in the context of the safety of the drug. The FDA and other regulatory authorities will have substantial discretion in evaluating the results of our phase 3 clinical trial, including with respect to what constitutes a clinically meaningful improvement in progression-free survival. Overall survival is a secondary endpoint in our phase 3 clinical trial. Based on our discussions with the FDA, we do not expect the FDA to require that we show a statistically significant improvement in overall survival in patients treated with tivozanib in order to obtain approval by the FDA; however, if the overall survival data are not positive it may influence how the FDA and other regulatory authorities interpret other data from our phase 3 clinical trial. We did not gather data on overall survival in our phase 2 clinical trial of tivozanib.

We cannot be certain as to what type and how many clinical trials the FDA, or equivalent foreign regulatory agencies, will require us to conduct in order to gain approval to market tivozanib. Prior to approving a new drug, the FDA generally requires that the efficacy of the drug be demonstrated in two adequate and well-controlled clinical trials. In some situations the FDA approves drugs on the basis of a single well-controlled clinical trial. Based on our discussions with the FDA and the EMEA, we believe we will be required to conduct only a single phase 3 clinical trial of tivozanib in advanced RCC. All of the VEGF inhibitor drugs approved by the FDA and the EMEA to date in advanced RCC, including Votrient, which was approved by the FDA in October 2009, have been approved on the basis of a single phase 3 clinical trial. However, if the FDA or EMEA determines that our phase 3 clinical trial results are not statistically significant and do not demonstrate a clinically meaningful benefit and an acceptable safety profile, or if the FDA or EMEA requires us to conduct additional phase 3 clinical trials of tivozanib in order to gain approval, we will incur significant additional development costs, commercialization of tivozanib would be prevented or delayed and our business would be adversely affected.

Table of Contents

If we do not obtain regulatory approval for tivozanib, AV-299 or any other product candidates, our business will be adversely affected.

Tivozanib, AV-299 and any other product candidate we seek to develop will be subject to extensive governmental regulations relating to, among other things, development, clinical trials, manufacturing and commercialization. In order to obtain regulatory approval for the commercial sale of any product candidate, we must demonstrate through extensive preclinical studies and clinical trials that the product candidate is safe and effective for use in each target indication, and that our production process yields a consistent and stable product. This process can take many years to complete, requiring the expenditure of substantial resources with highly uncertain results. We may never obtain regulatory approval for tivozanib, AV-299 or any other product candidate we may develop.

We have recently completed a phase 2 clinical trial of our lead product candidate, tivozanib, and have initiated a phase 3 clinical trial of tivozanib for the treatment of RCC. We are also conducting phase 1b clinical trials of tivozanib in various combinations and dosing regimens in RCC and additional solid tumor indications, including breast cancer and colorectal cancer. In addition to tivozanib, we have a pipeline of monoclonal antibodies derived from our Human Response Platform, a novel method of building preclinical models of human cancer, which are intended to more accurately represent cancer biology in patients. Our first product candidate derived from our Human Response Platform, AV-299, is expected to enter a phase 2 clinical trial for non-small cell lung cancer in the first half of 2010. The results to date from preclinical studies, our phase 1 and phase 2 clinical trials of tivozanib and our phase 1 clinical trials of AV-299 may not be predictive of results in future preclinical studies and clinical trials. A failure of one or more preclinical or clinical trials can occur at any stage of testing. Moreover, there can be no assurance that we will demonstrate the required safety and efficacy to obtain regulatory approvals for either of these product candidates.

Even though tivozanib has been generally well-tolerated in the limited number of patients who have been treated with it, there is no guarantee that unacceptable side effects or other risks will not occur with the exposure of a larger number of patients. If tivozanib, AV-299 or any other product candidate is not shown to be safe and effective in humans through clinical trials, we will not be able to obtain regulatory approval for such product candidate, and the resulting delays in developing other product candidates and conducting related preclinical studies and clinical trials, as well as the potential need for additional financing, would have a material adverse effect on our business, financial condition and results of operations.

If we are not successful in discovering, developing and commercializing additional product candidates, our ability to expand our business and achieve our strategic objectives would be impaired.

Although a substantial amount of our efforts will focus on the continued clinical testing and potential approval of tivozanib as well as the continued development of AV-299, a key element of our strategy is to discover, develop and commercialize a portfolio of antibody-based products. We are seeking to do so through our internal research programs and intend to explore strategic partnerships for the development of new products. All of our other potential product candidates remain in the discovery and preclinical study stages. Research programs to identify product candidates require substantial technical, financial and human resources, whether or not any product candidates are ultimately identified. Our research programs may initially show promise in identifying potential product candidates, yet fail to yield product candidates for clinical development for many reasons, including the following:

- the research methodology used may not be successful in identifying potential product candidates;
- competitors may develop alternatives that render our product candidates obsolete;
- a product candidate may on further study be shown to have harmful side effects or other characteristics that indicate it is unlikely to be effective or otherwise does not meet applicable regulatory criteria;
- a product candidate may not be capable of being produced in commercial quantities at an acceptable cost, or at all; and
- a product candidate may not be accepted as safe and effective by patients, the medical community or third-party payors.

11

Table of Contents

Any failure or delay in completing clinical trials for our product candidates may prevent us from obtaining regulatory approval or commercializing product candidates on a timely basis, or at all, which would require us to incur additional costs and delay receipt of any product revenue.

We cannot predict whether we will encounter problems with any of our ongoing or planned clinical trials that will cause us or regulatory authorities to delay, suspend or terminate those clinical trials. The completion of clinical trials for product candidates may be delayed or halted for many reasons, including:

- delays or failure in reaching agreement on acceptable clinical trial contracts or clinical trial protocols with prospective sites;
- failure of our third-party contractors or our investigators to comply with regulatory requirements or otherwise meet their contractual obligations in a timely manner;
- delays or failure in obtaining the necessary approvals from regulators or institutional review boards in order to commence a clinical trial at a prospective trial site, or their suspension or termination of a clinical trial once commenced;
- our inability, or the inability of our strategic partners or licensees, to manufacture or obtain from third parties materials sufficient to complete our preclinical studies and clinical trials;
- delays in patient enrollment, and variability in the number and types of patients available for clinical trials, or high drop-out rates of patients in our clinical trials;
- difficulty in maintaining contact with patients after treatment, resulting in incomplete data;
- poor effectiveness of our product candidates during clinical trials;
- safety issues, including serious adverse events associated with our product candidates;
- governmental or regulatory delays and changes in regulatory requirements, policy and guidelines; or
- varying interpretations of data by the FDA and similar foreign regulatory agencies.

Clinical trials often require the enrollment of large numbers of patients, and suitable patients may be difficult to identify and recruit. For example, we plan to enroll 500 patients in our phase 3 clinical trial of tivozanib. Our ability to enroll sufficient numbers of patients in our clinical trials depends on many factors, including the size of the patient population, the nature of the protocol, the proximity of patients to clinical sites, the eligibility criteria for the trial, competing clinical trials and the availability of approved effective drugs. There are a number of approved treatments for advanced RCC, including drugs that work by inhibiting the VEGF pathway. The availability of these approved treatments and the requirement in our phase 3 clinical trial that patients not have been treated with drugs that inhibit the VEGF pathway could make it more difficult to enroll patients or could delay enrollment in our phase 3 clinical trial. Moreover, we are aware of a number of ongoing clinical trials in RCC which will compete for eligible patients with our tivozanib clinical trials and may delay enrollment in our clinical trials.

In addition, patients may withdraw from a clinical trial for a variety of reasons. If we fail to enroll and maintain the number of patients for which the clinical trial was designed, the statistical power of that clinical trial may be reduced which would make it harder to demonstrate that the

product candidate being tested in such clinical trial is safe and effective. Additionally, we may not be able to enroll a sufficient number of qualified patients in a timely or cost-effective manner.

We, the FDA, applicable regulatory authorities or institutional review boards may suspend or terminate clinical trials of a product candidate at any time if we or they believe the patients participating in such clinical trials are being exposed to unacceptable health risks or for other reasons.

Significant clinical trial delays could allow our competitors to obtain marketing approval before we do or shorten the patent protection period during which we may have the exclusive right to commercialize our product candidates. Our product development costs also will increase if we experience delays in completing clinical

Table of Contents

trials. In addition, it is impossible to predict whether legislative changes will be enacted, or whether FDA regulations, guidance or interpretations will be changed, or what the impact of such changes, if any, may be. If we experience any such problems, we may not have the financial resources to continue development of the product candidate that is affected or the development of any of our other product candidates.

Even if we receive regulatory approval for any of our product candidates, we will be subject to ongoing FDA obligations and continued regulatory review, which may result in significant additional expense. Additionally, our product candidates, if approved, could be subject to labeling and other restrictions and market withdrawal and we may be subject to penalties if we fail to comply with regulatory requirements or experience unanticipated problems with our products.

Any regulatory approvals that we or our strategic partners receive for our product candidates may also be subject to limitations on the approved indicated uses for which the product may be marketed or to the conditions of approval, or contain requirements for potentially costly post-marketing testing, including phase 4 clinical trials, and surveillance to monitor the safety and efficacy of the product candidate. In addition, if the FDA approves any of our product candidates, the manufacturing processes, labeling, packaging, distribution, adverse event reporting, storage, advertising, promotion and recordkeeping for the product will be subject to extensive and ongoing regulatory requirements. These requirements include submissions of safety and other post-marketing information and reports, registration, as well as continued compliance with cGMP and good clinical practices, or GCP, for any clinical trials that we conduct post-approval. Later discovery of previously unknown problems with a product, including adverse events of unanticipated severity or frequency, or with our third-party manufacturers or manufacturing processes, or failure to comply with regulatory requirements, may result in, among other things:

- restrictions on the marketing or manufacturing of the product, withdrawal of the product from the market, or voluntary or mandatory product recalls;
- fines, warning letters or holds on clinical trials;
- refusal by the FDA to approve pending applications or supplements to approved applications filed by us or our strategic partners, or suspension or revocation of product license approvals;
- product seizure or detention, or refusal to permit the import or export of products; and
- injunctions or the imposition of civil or criminal penalties.

The FDA s policies may change and additional government regulations may be enacted that could prevent, limit or delay regulatory approval of our product candidates. We cannot predict the likelihood, nature or extent of government regulation that may arise from future legislation or administrative action, either in the United States or abroad. If we are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies, or if we are not able to maintain regulatory compliance, we may lose any marketing approval that we may have obtained and we may not achieve or sustain profitability, which would adversely affect our business.

Failure to obtain regulatory approval in jurisdictions outside the United States will prevent us from marketing our products abroad.

We intend to market our products, if approved, in international markets, which will require separate regulatory approvals and compliance with numerous and varying regulatory requirements. The approval procedures vary among countries and may involve requirements for additional testing, and the time required to obtain approval may differ from that required to obtain FDA approval. In addition, in many countries outside the United States, a product candidate must be approved for reimbursement before it can be approved for sale in that country. In some cases, the price that we intend to charge for our product is also subject to approval. Approval by the FDA does not ensure approval by regulatory authorities in other countries or jurisdictions, and approval by one foreign regulatory authority does not ensure approval by regulatory authorities in other foreign countries or by the FDA. The foreign regulatory approval process may include all of the risks associated with obtaining FDA

Table of Contents

approval. We may not obtain foreign regulatory approvals on a timely basis, if at all. We and our future strategic partners may not be able to file for regulatory approvals and may not receive necessary approvals to commercialize our products in any market.

Risks Related to Our Financial Position and Capital Requirements

We have incurred net operating losses since our inception and anticipate that we will continue to incur substantial operating losses for the foreseeable future. We may never achieve or sustain profitability, which would depress the market price of our common stock, and could cause you to lose all or a part of your investment.

We have incurred net losses since our inception, including net losses of $44.1 million, $32.5 million and $25.0 million for the years ended December 31, 2009, 2008 and 2007, respectively. As of December 31, 2009, we had an accumulated deficit of $177.7 million. We do not know whether or when we will become profitable. To date, we have not commercialized any products or generated any revenues from the sale of products, and we do not expect to generate any product revenues in the foreseeable future. Our losses have resulted principally from costs incurred in our discovery and development activities. We anticipate that our operating losses will substantially increase over the next several years as we execute our plan to expand our discovery, research, development and commercialization activities, including the phase 3 clinical development and planned commercialization of our lead product candidate, tivozanib.

If we do not successfully develop and obtain regulatory approval for our existing and future pipeline product candidates and effectively manufacture, market and sell any product candidates that are approved, we may never generate product sales, and even if we do generate product sales, we may never achieve or sustain profitability on a quarterly or annual basis. Our failure to become and remain profitable would depress the market price of our common stock and could impair our ability to raise capital, expand our business, diversify our product offerings or continue our operations. A decline in the market price of our common stock also could cause you to lose all or a part of your investment.

In addition, the report of our independent registered public accounting firm with respect to our consolidated financial statements appearing at the end of this prospectus contains an explanatory paragraph stating that our operating losses and negative cash flows from operations since inception, and our need to raise additional financing and/or financial support prior to December 31, 2010 in order to continue to fund our operations, raise substantial doubt about our ability to continue as a going concern. We believe that the successful completion of this offering will eliminate this doubt and enable us to continue as a going concern; however, if we are unable to raise sufficient capital in this offering, we will need to obtain alternative financing or significantly modify our operational plans for us to continue as a going concern. Further, even if we successfully complete and receive the net proceeds from this offering, given our planned expenditures for the next several years, including, without limitation, expenditures in connection with our phase 3 clinical trial of tivozanib, it is possible that our independent registered public accounting firm may conclude, in connection with the preparation of our financial statements for fiscal year 2010 or any other subsequent period, that there is substantial doubt regarding our ability to continue as a going concern as of December 31, 2010 or as of the end of any other subsequent period.

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

Since our inception, most of our resources have been dedicated to the discovery and preclinical and clinical development of our product candidates. In particular, we initiated a phase 3 clinical trial of tivozanib in December 2009, which will require substantial funds to complete. We believe that we will continue to expend substantial resources for the foreseeable future developing tivozanib and other new and existing antibody product candidates. These expenditures will include costs associated with research and development, acquiring new

Table of Contents

technologies, conducting preclinical and clinical trials, obtaining regulatory approvals and manufacturing products, as well as marketing and selling any products approved for sale. In addition, other unanticipated costs may arise. Because the outcome of our planned and anticipated clinical trials is highly uncertain, we cannot reasonably estimate the actual amounts necessary to successfully complete the development and commercialization of our product candidates.

We believe that the net proceeds from this offering, together with our existing cash and cash equivalents, marketable securities, committed research and development funding and milestone payments that we expect to receive under our existing strategic partnership and license agreements, along with payments we believe that we will receive under new strategic partnerships we assume we will enter into under our current projected operating plan, will allow us to fund our operating plan through at least the second quarter of 2012. However, our operating plan may change as a result of many factors currently unknown to us, and we may need to seek additional funds sooner than planned, through public or private equity or debt financings or other sources, such as strategic partnerships. In addition, we may seek additional capital due to favorable market conditions or strategic considerations even if we believe we have sufficient funds for our current or future operating plans.

Our future capital requirements depend on many factors, including:

- the number and characteristics of the product candidates we pursue;
- the scope, progress, results and costs of researching and developing our product candidates, and conducting preclinical and clinical trials;
- the timing of, and the costs involved in, obtaining regulatory approvals for our product candidates;
- the cost of commercialization activities if any of our product candidates are approved for sale, including marketing, sales and distribution costs;
- the cost of manufacturing our product candidates and any products we successfully commercialize;
- our ability to establish and maintain strategic partnerships, licensing or other arrangements and the financial terms of such agreements;
- the costs involved in preparing, filing, prosecuting, maintaining, defending and enforcing patent claims, including litigation costs and the outcome of such litigation; and
- the timing, receipt and amount of sales of, or royalties on, our future products, if any.

Additional funds may not be available when we need them, on terms that are acceptable to us, or at all. If adequate funds are not available to us on a timely basis, we may be required to:

- delay, limit, reduce or terminate preclinical studies, clinical trials or other development activities for one or more of our product candidates;
- delay, limit, reduce or terminate our research and development activities; or

delay, limit, reduce or terminate our establishment of sales and marketing capabilities or other activities that may be necessary to commercialize our product candidates.

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

We may seek additional capital through a combination of private and public equity offerings, debt financings, strategic partnerships and alliances and licensing arrangements. To the extent that we raise additional capital through the sale of equity or convertible debt securities, your ownership interest will be diluted, and the terms may include liquidation or other preferences that adversely affect your rights as a stockholder. Debt financing, if available, may involve agreements that include covenants limiting or restricting our ability to take certain actions, such as incurring debt, making capital expenditures or declaring dividends. If we raise additional funds through strategic partnerships and alliances and licensing arrangements with third parties, we may have to relinquish valuable rights to our technologies or product candidates, or grant licenses on terms that are not

Table of Contents

favorable to us. If we are unable to raise additional funds through equity or debt financing when needed, we may be required to delay, limit, reduce or terminate our product development or commercialization efforts or grant rights to develop and market product candidates that we would otherwise prefer to develop and market ourselves.

A substantial portion of our future revenues may be dependent upon our agreements with OSI, Merck and Biogen Idec.

Our success will depend in significant part on our ability to attract and maintain strategic partners and strategic relationships to support the development and commercialization of our products. We currently expect that a substantial portion of our future revenues may be dependent upon our strategic partnerships with OSI Pharmaceuticals, Inc., or OSI, Merck and Biogen Idec, Inc., or Biogen Idec. Under each of these strategic partnerships, our strategic partners have significant development and commercialization responsibilities with respect to anticipated therapeutics to be developed and sold. If these strategic partners were to terminate their agreements with us, fail to meet their obligations or otherwise decrease their level of efforts, allocation of resources or other commitments under these agreements, our future revenues could be negatively impacted and the development and commercialization of our product candidates would be interrupted. In addition, if OSI, Merck or Biogen Idec do not achieve some or any of the development, regulatory and commercial milestones or if they do not achieve certain net sales thresholds, in each case, as set forth in the respective agreements, we will not fully realize the expected economic benefits of the agreements. Further, the achievement of certain of the milestones under these strategic partnership agreements will depend on factors that are outside of our control and most are not expected to be achieved for several years, if at all. Any failure to successfully maintain our strategic partnership agreements could materially and adversely affect our ability to generate revenues.

For a discussion of additional risks that we face with respect to our strategic partnership agreements, see If any of our current strategic partners fails to perform its obligations or terminates its agreement with us, the development and commercialization of the product candidates under such agreement could be delayed or terminated and our business could be substantially harmed beginning on page 22.

Unstable market and economic conditions may have serious adverse consequences on our business, financial condition and stock price.

As widely reported, global credit and financial markets have been experiencing extreme disruptions over the past several years, including severely diminished liquidity and credit availability, declines in consumer confidence, declines in economic growth, increases in unemployment rates, and uncertainty about economic stability. There can be no assurance that further deterioration in credit and financial markets and confidence in economic conditions will not occur. Our general business strategy may be adversely affected by the recent economic downturn and volatile business environment and continued unpredictable and unstable market conditions. If the current equity and credit markets deteriorate further, or do not improve, it may make any necessary debt or equity financing more difficult, more costly, and more dilutive. Failure to secure any necessary financing in a timely manner and on favorable terms could have a material adverse effect on our growth strategy, financial performance and stock price and could require us to delay or abandon clinical development plans. In addition, there is a risk that one or more of our current service providers, manufacturers and other partners may not survive these difficult economic times, which could directly affect our ability to attain our operating goals on schedule and on budget.

At December 31, 2009, we had $51.3 million of cash, cash equivalents and marketable securities consisting of cash, money market and government obligations. While as of the date of this prospectus, we are not aware of any downgrades, material losses, or other significant deterioration in the fair value of our cash equivalents or marketable securities since December 31, 2009, no assurance can be given that further deterioration in conditions of the global credit and financial markets would not negatively impact our current portfolio of cash equivalents or marketable securities or our ability to meet our financing objectives. Further dislocations in the credit market may adversely impact the value and/or liquidity of marketable securities owned by us.

There is a possibility that our stock price may decline, due in part to the volatility of the stock market and the general economic downturn.

Table of Contents

Risks Related to Our Business and Industry

Because we have a short operating history, there is a limited amount of information about us upon which you can evaluate our business and prospects.

Our operations began in October 2001 and we have only a limited operating history upon which you can evaluate our business and prospects. In addition, as an early stage company, we have limited experience and have not yet demonstrated an ability to successfully overcome many of the risks and uncertainties frequently encountered by companies in new and rapidly evolving fields, particularly in the biopharmaceutical area. For example, to execute our business plan, we will need to successfully:

- execute product development activities;
- obtain required regulatory approvals for the development and commercialization of our product candidates;
- build and maintain a strong intellectual property portfolio;
- build and maintain robust sales, distribution and marketing capabilities;
- gain market acceptance for our products;
- develop and maintain successful strategic relationships; and
- manage our spending as costs and expenses increase due to clinical trials, regulatory approvals and commercialization.

If we are unsuccessful in accomplishing these objectives, we may not be able to develop product candidates, raise capital, expand our business or continue our operations.

We face substantial competition, which may result in others discovering, developing or commercializing products before, or more successfully, than we do.

Our future success depends on our ability to demonstrate and maintain a competitive advantage with respect to the design, development and commercialization of product candidates. Our objective is to design, develop and commercialize new products with superior efficacy, convenience, tolerability and safety. We expect any product candidate that we commercialize with our strategic partners or on our own will compete with existing, market-leading products. For example, we anticipate that tivozanib, if approved for the treatment of advanced RCC, would compete with angiogenesis inhibitors and mTOR inhibitors that are currently approved for the treatment of advanced RCC, such as Avastin, marketed by Roche Laboratories, Inc., Nexavar, marketed by Onyx Pharmaceuticals, Inc. and Bayer HealthCare AG, Sutent, marketed by Pfizer Inc., Votrient, marketed by GlaxoSmithKline plc, Torisel, marketed by Pfizer, and Afinitor, marketed by Novartis Pharmaceuticals Corporation, and other therapies in development.

Many of our potential competitors have substantially greater financial, technical and personnel resources than we have. In addition, many of these competitors have significantly greater commercial infrastructures than we have. We will not be able to compete successfully unless we successfully:

- design and develop products that are superior to other products in the market;

attract qualified scientific, medical, sales and marketing and commercial personnel;

obtain patent and/or other proprietary protection for our processes and product candidates;

obtain required regulatory approvals; and

collaborate with others in the design, development and commercialization of new products.

Established competitors may invest heavily to quickly discover and develop novel compounds that could make our product candidates obsolete. In addition, any new product that competes with an approved product must demonstrate compelling advantages in efficacy, convenience, tolerability and safety in order to overcome

Table of Contents

price competition and to be commercially successful. If we are not able to compete effectively against our current and future competitors, our business will not grow and our financial condition and operations will suffer.

If we fail to attract and keep senior management and key scientific personnel, we may be unable to successfully develop our product candidates, conduct our clinical trials and commercialize our product candidates.

Our success depends in part on our continued ability to attract, retain and motivate highly qualified management, clinical and scientific personnel. We are highly dependent upon our senior management, particularly Tuan Ha-Ngoc, our Chief Executive Officer, Elan Ezickson, our Chief Business Officer, David Johnston, our Chief Financial Officer, William Slichenmyer, our Chief Medical Officer, and Jeno Gyuris, our Senior Vice President, Head of Research, as well as other senior scientists on our management team. Although none of these individuals has informed us to date that he intends to retire or resign in the near future, the loss of services of any of these individuals or one or more of our other members of senior management could delay or prevent the successful development of our product pipeline, completion of our planned clinical trials or the commercialization of our product candidates. We do not carry key person insurance covering any members of our senior management. Although we have entered into an employment agreement and a severance and change in control agreement with Tuan Ha-Ngoc, and severance and change in control agreements with each of Elan Ezickson, David Johnston, William Slichenmyer and Jeno Gyuris, these agreements do not provide for a fixed term of service.

Although we have not historically experienced unique difficulties attracting and retaining qualified employees, we could experience such problems in the future. For example, competition for qualified personnel in the biotechnology and pharmaceuticals field is intense. We will need to hire additional personnel as we expand our clinical development and commercial activities. We may not be able to attract and retain quality personnel on acceptable terms.

Our employees may engage in misconduct or other improper activities, including noncompliance with regulatory standards and requirements and insider trading.

We are exposed to the risk of employee fraud or other misconduct. Misconduct by employees could include intentional failures to comply with FDA regulations, to provide accurate information to the FDA, to comply with manufacturing standards we have established, to comply with federal and state health-care fraud and abuse laws and regulations, to report financial information or data accurately or to disclose unauthorized activities to us. In particular, sales, marketing and business arrangements in the healthcare industry are subject to extensive laws and regulations intended to prevent fraud, kickbacks, self-dealing and other abusive practices. These laws and regulations may restrict or prohibit a wide range of pricing, discounting, marketing and promotion, sales commission, customer incentive programs and other business arrangements. Employee misconduct could also involve the improper use of information obtained in the course of clinical trials, which could result in regulatory sanctions and serious harm to our reputation. We have adopted a Code of Business Conduct and Ethics, but it is not always possible to identify and deter employee misconduct, and the precautions we take to detect and prevent this activity may not be effective in controlling unknown or unmanaged risks or losses or in protecting us from governmental investigations or other actions or lawsuits stemming from a failure to be in compliance with such laws or regulations. If any such actions are instituted against us, and we are not successful in defending ourselves or asserting our rights, those actions could have a significant impact on our business, including the imposition of significant fines or other sanctions.

In addition, during the course of our operations, our directors, executives and employees may have access to material, nonpublic information regarding our business, our results of operations or potential transactions we are considering. Despite the adoption of an Insider Trading Policy, we may not be able to prevent a director, executive or employee from trading in our common stock on the basis of, or while having access to, material, nonpublic information. If a director, executive or employee was to be investigated, or an action was to be brought against a director, executive or employee for insider trading, it could have a negative impact on our reputation and our stock price. Such a claim, with or without merit, could also result in substantial expenditures of time and money, and divert attention of our management team from other tasks important to the success of our business.

Table of Contents

We may encounter difficulties in managing our growth and expanding our operations successfully.

As we seek to advance our product candidates through clinical trials, we will need to expand our development, regulatory, manufacturing, marketing and sales capabilities or contract with third parties to provide these capabilities for us. As our operations expand, we expect that we will need to manage additional relationships with various strategic partners, suppliers and other third parties. Future growth will impose significant added responsibilities on members of management. Our future financial performance and our ability to commercialize our product candidates and to compete effectively will depend, in part, on our ability to manage any future growth effectively. To that end, we must be able to manage our development efforts and clinical trials effectively and hire, train and integrate additional management, administrative and sales and marketing personnel. We may not be able to accomplish these tasks, and our failure to accomplish any of them could prevent us from successfully growing our company.

If product liability lawsuits are brought against us, we may incur substantial liabilities and may be required to limit commercialization of our product candidates.

We face an inherent risk of product liability as a result of the clinical testing of our product candidates and will face an even greater risk if we commercialize any products. For example, we may be sued if any product we develop allegedly causes injury or is found to be otherwise unsuitable during product testing, manufacturing, marketing or sale. Any such product liability claims may include allegations of defects in manufacturing, defects in design, a failure to warn of dangers inherent in the product, negligence, strict liability, and a breach of warranties. Claims could also be asserted under state consumer protection acts. If we cannot successfully defend ourselves against product liability claims, we may incur substantial liabilities or be required to limit commercialization of our product candidates. Even successful defense would require significant financial and management resources. Regardless of the merits or eventual outcome, liability claims may result in:

decreased demand for our product candidates or products that we may develop;

injury to our reputation;

withdrawal of clinical trial participants;

costs to defend the related litigation;

a diversion of management s time and our resources;

substantial monetary awards to trial participants or patients;

product recalls, withdrawals or labeling, marketing or promotional restrictions;

loss of revenue;

the inability to commercialize our product candidates; and

a decline in our stock price.

Our inability to obtain and retain sufficient product liability insurance at an acceptable cost to protect against potential product liability claims could prevent or inhibit the commercialization of products we develop. We currently carry product liability insurance covering our clinical studies in the amount of $10 million in the aggregate. Although we maintain such insurance, any claim that may be brought against us could result in a court judgment or settlement in an amount that is not covered, in whole or in part, by our insurance or that is in excess of the limits of our insurance coverage. Our insurance policies also have various exclusions, and we may be subject to a product liability claim for which we have no coverage. We will have to pay any amounts awarded by a court or negotiated in a settlement that exceed our coverage limitations or that are not covered by our insurance, and we may not have, or be able to obtain, sufficient capital to pay such amounts.

Table of Contents

We may incur significant costs complying with environmental laws and regulations, and failure to comply with these laws and regulations could expose us to significant liabilities.

We use hazardous chemicals and radioactive and biological materials in certain aspects of our business and are subject to a variety of federal, state and local laws and regulations governing the use, generation, manufacture, distribution, storage, handling, treatment and disposal of these materials. Although we believe our safety procedures for handling and disposing of these materials and waste products comply with these laws and regulations, we cannot eliminate the risk of accidental injury or contamination from the use, manufacture, distribution, storage, handling, treatment or disposal of hazardous materials. In the event of contamination or injury, or failure to comply with environmental, occupational health and safety and export control laws and regulations, we could be held liable for any resulting damages and any such liability could exceed our assets and resources. We do not maintain insurance for any environmental liability or toxic tort claims that may be asserted against us.

Risks Related to Commercialization of Our Product Candidates

We have no sales, marketing or distribution experience and we will have to invest significant resources to develop those capabilities.

We have no sales, marketing or distribution experience. To develop internal sales, distribution and marketing capabilities, we will have to invest significant amounts of financial and management resources, some of which will be committed prior to any confirmation that tivozanib will be approved. For product candidates such as tivozanib where we decide to perform sales, marketing and distribution functions ourselves, we could face a number of additional risks, including:

- we may not be able to attract and build an effective marketing or sales force;
- the cost of establishing a marketing or sales force may not be justifiable in light of the revenues generated by any particular product; and
- our direct sales and marketing efforts may not be successful.

Outside of the United States, where appropriate, we may elect in the future to utilize strategic partners or contract sales forces to assist in the commercialization of tivozanib and future products, if approved. We may have limited or no control over the sales, marketing and distribution activities of these third parties. Our future revenues may depend heavily on the success of the efforts of these third parties.

Our commercial success depends upon attaining significant market acceptance of our product candidates, if approved, including tivozanib and AV-299, among physicians, patients, health care payors and, in the cancer market, acceptance by the major operators of cancer clinics.

Even if tivozanib, AV-299 or any other product candidate that we may develop or acquire in the future obtains regulatory approval, the product may not gain market acceptance among physicians, health care payors, patients and the medical community. Market acceptance of any products for which we receive approval depends on a number of factors, including:

- the efficacy and safety of tivozanib, as demonstrated in clinical trials;
- the clinical indications for which the drug is approved;
- acceptance by physicians, major operators of cancer clinics and patients of the drug as a safe and effective treatment;

the results obtained in our phase 3 clinical trial of tivozanib for the treatment of advanced clear cell RCC and the extent to which the results demonstrate that treatment with tivozanib represents a clinically meaningful improvement in care as compared to other available VEGF inhibitors;

the potential and perceived advantages of tivozanib over alternative treatments, including, for example, Avastin, Nexavar, Sutent or Votrient;

Table of Contents

the cost of treatment in relation to alternative treatments;

the availability of adequate reimbursement and pricing by third parties and government authorities;

the continued projected growth of oncology drug markets;

relative convenience and ease of administration;

the prevalence and severity of adverse side effects; and

the effectiveness of our sales and marketing efforts.

If our approved drugs fail to achieve market acceptance, we would not be able to generate significant revenue.

Reimbursement may be limited or unavailable in certain market segments for our product candidates, which could make it difficult for us to sell our products profitably.

Market acceptance and sales of our product candidates will depend significantly on the availability of adequate coverage and reimbursement from third-party payors for any of our product candidates and may be affected by existing and future health care reform measures. Government authorities and third-party payors, such as private health insurers and health maintenance organizations, decide which drugs they will pay for and establish reimbursement levels. Reimbursement by a third-party payor may depend upon a number of factors, including the third-party payor s determination that use of a product is:

a covered benefit under its health plan;

safe, effective and medically necessary;

appropriate for the specific patient;

cost-effective; and

neither experimental nor investigational.

Obtaining coverage and reimbursement approval for a product from a government or other third party payor is a time consuming and costly process that could require us to provide supporting scientific, clinical and cost-effectiveness data for the use of our products to the payor. We may not be able to provide data sufficient to gain acceptance with respect to coverage and reimbursement. We cannot be sure that coverage or adequate reimbursement will be available for any of our product candidates. Also, we cannot be sure that reimbursement amounts will not reduce the demand for, or the price of, our products. If reimbursement is not available or is available only to limited levels, we may not be able to commercialize certain of our products.

In both the United States and certain foreign jurisdictions, there have been a number of legislative and regulatory changes to the health care system that could impact our ability to sell our products profitably. In particular, the Medicare Modernization Act of 2003 revised the payment methodology for many products under Medicare. This has resulted in lower rates of reimbursement. There have been numerous other federal and state initiatives designed to reduce payment for pharmaceuticals.

As a result of legislative proposals and the trend towards managed health care in the United States, third-party payors are increasingly attempting to contain health care costs by limiting both coverage and the level of reimbursement of new drugs. They may also refuse to provide any coverage of approved products for medical indications other than those for which the FDA has granted market approvals. As a result, significant uncertainty exists as to whether and how much third-party payors will reimburse patients for their use of newly approved drugs, which in turn will put pressure on the pricing of drugs. We expect to experience pricing pressures in connection with the sale of our products due to the trend toward managed health care, the increasing influence of health maintenance organizations, additional legislative proposals, as well as country, regional, or local healthcare budget limitations.

Table of Contents

Governments may impose price controls, which may adversely affect our future profitability.

We intend to seek approval to market our future products in both the United States and in foreign jurisdictions. If we obtain approval in one or more foreign jurisdictions, we will be subject to rules and regulations in those jurisdictions relating to our product. In some foreign countries, particularly in the European Union, the pricing of prescription pharmaceuticals and biologics is subject to governmental control. In these countries, pricing negotiations with governmental authorities can take considerable time after the receipt of marketing approval for a product candidate. If reimbursement of our future products is unavailable or limited in scope or amount, or if pricing is set at unsatisfactory levels, we may be unable to achieve or sustain profitability.

Healthcare reform measures, if implemented, could hinder or prevent our commercial success.

There have been, and likely will continue to be, legislative and regulatory proposals at the federal and state levels directed at broadening the availability of healthcare and containing or lowering the cost of healthcare. We cannot predict the initiatives that may be adopted in the future. The continuing efforts of the government, insurance companies, managed care organizations and other payors of healthcare services to contain or reduce costs of healthcare may adversely affect:

- the demand for any drug products for which we may obtain regulatory approval;
- our ability to set a price that we believe is fair for our products;
- our ability to generate revenues and achieve or maintain profitability;
- the level of taxes that we are required to pay; and
- the availability of capital.

Risks Related to Our Dependence on Third Parties

If any of our current strategic partners fails to perform its obligations or terminates its agreement with us, the development and commercialization of the product candidates under such agreement could be delayed or terminated and our business could be substantially harmed.

We currently have strategic partnerships in place relating to certain of our product candidates and technologies as follows:

- We have a collaboration agreement with Merck related to the development and commercialization of AV-299, our monoclonal antibody antagonist of hepatocyte growth factor, or HGF. Pursuant to the agreement, we have primary responsibility for certain U.S.-related development activities through completion of the first phase 2 clinical trial for AV-299 designed to demonstrate achievement of a primary efficacy endpoint in humans as established by the parties, which we refer to as a proof-of-concept trial. Merck will be responsible for clinical development of AV-299 after completion of the first proof-of-concept trial. We are currently leading the clinical development of AV-299, which includes conducting multiple phase 1 clinical trials and preparing to conduct a phase 2 clinical trial, and we are using our Human Response Platform to conduct translational research to guide the clinical development of AV-299. Merck is responsible for all costs related to the clinical development of AV-299 and clinical and commercial manufacturing, subject to an agreed-upon budget.

- We have entered into a strategic partnership with OSI, primarily focused on the identification and validation of genes and targets involved in the processes of epithelial-mesenchymal transition or mesenchymal-epithelial transition in cancer. Key elements of our

strategic partnership with OSI include: (1) identifying and validating a pre-agreed number of oncology targets for drug discovery, development and commercialization by OSI, (2) generating target-driven *in vivo* mouse tumor models for use in drug screening and biomarker validation to support OSI s drug discovery and translational research activities, and (3) applying our Human Response Platform to identify genetic profiles that correlate with drug response to compounds in certain of OSI s small molecule drug discovery

Table of Contents

programs. We are required to devote, and OSI is required to fund, a mutually agreed minimum number of individuals to the research program each year. Under the terms of our agreement, OSI may, but has no obligation to, elect to obtain exclusive rights to certain aspects of our intellectual property to research, develop, make, sell and import drug products and associated diagnostics directed to a specified number of targets identified and/or validated under the strategic partnership. OSI has sole responsibility and is required to use commercially reasonable efforts to develop and commercialize drugs and associated diagnostics directed to the targets to which it has obtained rights.

We have entered into an exclusive option and license agreement with Biogen Idec regarding the development and commercialization of our ErbB3-targeted antibodies for the potential treatment and diagnosis of cancer and other diseases outside of the United States, Canada and Mexico. Under the agreement, we are responsible for developing ErbB3 antibodies through completion of the first phase 2 clinical trial designed in a manner that, if successful, will generate data sufficient to support advancement to a phase 3 clinical trial. Within a specified time period after we complete the phase 2 clinical trial and deliver to Biogen Idec a detailed data package containing the results of the trial, Biogen Idec may elect to obtain (1) a co-exclusive (with us) worldwide license under our relevant intellectual property to develop and manufacture ErbB3 antibody products, and (2) an exclusive license under our relevant intellectual property to commercialize ErbB3 antibody products in all countries in the world other than the United States, Canada and Mexico. We will retain an exclusive right to commercialize ErbB3 antibody products in the United States, Canada and Mexico. Until completion of the first phase 2 clinical trial, we are solely responsible for the research, development, and manufacture of ErbB3 antibody(ies) pursuant to a written work plan meeting specific pre-agreed guidelines. We are solely responsible for all expenses incurred through completion of the first phase 2 clinical trial. If Biogen Idec exercises its option to obtain exclusive commercialization rights to ErbB3 products in its territory, then we will be solely responsible, subject to a mutually agreed development plan, budget and the oversight of a joint development committee, for the global development of ErbB3 antibody products, except that Biogen Idec will be solely responsible for ErbB3 antibody product development activities that relate solely to the Biogen Idec territory. We and Biogen Idec will share global development costs (including manufacturing costs to support development) for ErbB3 antibody products equally, except that Biogen Idec will be solely responsible for all development costs associated solely with the development of ErbB3 antibody products for its territory, and we will be solely responsible for all development costs associated solely with the development of ErbB3 antibody products for the United States, Canada and Mexico.

These strategic partnerships may not be scientifically or commercially successful due to a number of important factors, including the following:

Each of our strategic partners has significant discretion in determining the efforts and resources that it will apply to their strategic partnership with us. The timing and amount of any cash payments, related royalties and milestones that we may receive under such strategic partnerships will depend on, among other things, the efforts, allocation of resources and successful development and commercialization of our product candidates by our strategic partners under their respective agreements.

Our strategic partnership agreements permit our strategic partners wide discretion in deciding which product candidates to advance through the clinical trial process. Under certain of our strategic partnerships, it is possible for the strategic partner to reject product candidates at any point in the research, development and clinical trial process, without triggering a termination of the strategic partnership agreement. In the event of any such decision, our business and prospects may be adversely affected due to our inability to progress such candidates ourselves.

Our strategic partners may develop and commercialize, either alone or with others, products that are similar to or competitive with the product candidates that are the subject of their strategic partnerships with us.

Table of Contents

Our strategic partners may change the focus of their development and commercialization efforts or pursue higher-priority programs.

Our strategic partners may enter into one or more transactions with third parties, including a merger, consolidation, reorganization, sale of substantial assets, sale of substantial stock or change in control, which could divert the attention of a strategic partner s management and adversely affect a strategic partner s ability to retain and motivate key personnel who are important to the continued development of the programs under the applicable strategic partnership with us. For example, we entered into a strategic partnership with Schering-Plough prior to its merger with Merck. We also entered into agreements with Merck prior to that merger. Although the effect of the merger on our strategic partnerships is unknown, management of the combined company could determine to reduce the efforts and resources that the combined company will apply to its strategic partnerships with us. In addition, the third-party could determine to reprioritize the strategic partner s development programs such that the strategic partner ceases to diligently pursue the development of our programs and/or cause the respective strategic partnership with us to terminate.

Our strategic partners may, under specified circumstances, terminate their strategic partnership with us on short notice and for circumstances outside of our control, which could make it difficult for us to attract new strategic partners or adversely affect how we are perceived in the scientific and financial communities. For example, Merck can terminate its agreement related to AV-299 with us upon 90 days written notice to us or in connection with an insolvency event or material breach that remains uncured for a specified cure period. OSI can terminate its agreement with us, with respect to any or all collaboration targets and all associated products, upon written notice to us and can terminate the entire agreement with us in connection with a material breach of the agreement by us that remains uncured for a specified cure period. Biogen Idec may terminate its agreement with us for convenience with respect to any product(s), by providing us with three months prior written notice, or due to a material breach of the agreement by us that is not cured within a short time period or if all of our assets are acquired by, or we merge with, another entity, and the other entity is independently developing or commercializing a product containing an ErbB3 antibody and fails to divest the ErbB3 product within a specified time period.

Our strategic partners may have the first right to maintain or defend our intellectual property rights and, although we may have the right to assume the maintenance and defense of our intellectual property rights if our strategic partners do not, our ability to do so may be compromised by our strategic partners acts or omissions.

Our strategic partners may utilize our intellectual property rights in such a way as to invite litigation that could jeopardize or invalidate our intellectual property rights or expose us to potential liability.

Our strategic partners may not comply with all applicable regulatory requirements, or fail to report safety data in accordance with all applicable regulatory requirements.

If any strategic partner were to breach or terminate its arrangements with us, or if Biogen Idec does not elect to exercise its option to participate in development of our ErbB3 antibody candidate, the development and commercialization of the affected product candidate could be delayed, curtailed or terminated because we may not have sufficient financial resources or capabilities to continue development and commercialization of the product candidate on our own.

Our strategic partners may not have sufficient resources necessary to carry the product candidate through clinical development or may not obtain the necessary regulatory approvals.

If one or more of our strategic partner fails to develop or effectively commercialize product candidates for any of the foregoing reasons, we may not be able to replace the strategic partner with another partner to develop and commercialize a product candidate under the terms of the strategic partnership. We may also be unable to

Table of Contents