AVEO PHARMACEUTICALS INC
Form 424B4
March 12, 2010
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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

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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.

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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

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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.

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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

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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

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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.

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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.

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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)

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	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.

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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.

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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.

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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.

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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

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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

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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

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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

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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.

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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

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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.

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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.

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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;

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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.

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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

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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.

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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

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obtain, on terms acceptable to us, a license from such strategic partner to any of its intellectual property that may be necessary or useful for us to continue to develop and commercialize a product candidate. Any of these events could have a material adverse effect on our business, results of operations and our ability to achieve future profitability, and could cause our stock price to decline.

We may not be successful in establishing and maintaining additional strategic partnerships, which could adversely affect our ability to develop and commercialize products.

In addition to our current strategic partnerships, a part of our strategy is to enter into additional strategic partnerships in the future, including alliances with major biotechnology or pharmaceutical companies. We face significant competition in seeking appropriate strategic partners and the negotiation process is time-consuming and complex. Moreover, we may not be successful in our efforts to establish a strategic partnership or other alternative arrangements for any future product candidates and programs because our research and development pipeline may be insufficient, our product candidates and programs may be deemed to be at too early of a stage of development for collaborative effort and/or third parties may not view our product candidates and programs as having the requisite potential to demonstrate safety and efficacy. Even if we are successful in our efforts to establish new strategic partnerships, the terms that we agree upon may not be favorable to us and we may not be able to maintain such strategic partnerships if, for example, development or approval of a product candidate is delayed or sales of an approved product are disappointing. Any delay in entering into new strategic partnership agreements related to our product candidates could delay the development and commercialization of our product candidates and reduce their competitiveness even if they reach the market.

Moreover, if we fail to establish and maintain additional strategic partnerships related to our product candidates:

- the development of certain of our current or future product candidates may be terminated or delayed;
- our cash expenditures related to development of certain of our current or future product candidates would increase significantly and we may need to seek additional financing;
- we may be required to hire additional employees or otherwise develop expertise, such as sales and marketing expertise, for which we have not budgeted; and
- we will bear all of the risk related to the development of any such product candidates.

In addition, if we fail to establish and maintain additional strategic partnerships involving our Human Response Platform, we would not realize its potential as a means of identifying and validating targets for new cancer therapies in collaboration with strategic partners or of identifying biomarkers to aid in the development of our strategic partners drug candidates.

We rely on third-party manufacturers to produce our preclinical and clinical drug supplies and we intend to rely on third parties to produce commercial supplies of any approved product candidates. Any failure by a third-party manufacturer to produce supplies for us may delay or impair our ability to complete our clinical trials or commercialize our product candidates.

We have relied upon a small number of third-party manufacturers for the manufacture of our product candidates for preclinical and clinical testing purposes and intend to continue to do so in the future. For instance, we rely on one supplier for the active pharmaceutical ingredient for tivozanib. Currently, a separate contract manufacturer manufactures, packages and distributes clinical supplies of tivozanib. While we believe that our existing supplier of active pharmaceutical ingredient or an alternative supplier would be capable of continuing to produce active pharmaceutical ingredient in commercial quantities, we will need to identify a third-party manufacturer capable of providing commercial quantities of drug product. If we are unable to arrange for such a third-party manufacturing source, or fail to do so on commercially reasonable terms, we may not be able to successfully produce and market tivozanib or may be delayed in doing so.

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The process for producing AV-299 has been developed and multiple batches of drug substance have been and are continuing to be produced to support clinical trials of AV-299 through phase 2 clinical trials. Our strategic partner Merck is responsible for the continued process development and all manufacturing of AV-299, including for clinical trial and commercial use. If our strategic partner Merck does not complete process development and manufacture of AV-299 as we expect, clinical trials and any commercial production of AV-299 could be adversely affected.

As with tivozanib and AV-299, we also expect to rely upon third parties to produce materials required for the clinical and commercial production of any other product candidates. If we are unable to arrange for third-party manufacturing sources, or to do so on commercially reasonable terms, we may not be able to complete development of such other product candidates or market them.

Reliance on third-party manufacturers entails risks to which we would not be subject if we manufactured product candidates ourselves, including reliance on the third party for regulatory compliance and quality assurance, the possibility of breach of the manufacturing agreement by the third party because of factors beyond our control (including a failure to synthesize and manufacture our product candidates in accordance with our product specifications) and the possibility of termination or nonrenewal of the agreement by the third party, based on its own business priorities, at a time that is costly or damaging to us. In addition, the FDA and other regulatory authorities require that our product candidates be manufactured according to cGMP and similar foreign standards. Any failure by our third-party manufacturers to comply with cGMP or failure to scale up manufacturing processes, including any failure to deliver sufficient quantities of product candidates in a timely manner, could lead to a delay in, or failure to obtain, regulatory approval of any of our product candidates. In addition, such failure could be the basis for action by the FDA to withdraw approvals for product candidates previously granted to us and for other regulatory action, including recall or seizure, fines, imposition of operating restrictions, total or partial suspension of production or injunctions.

We rely on our manufacturers to purchase from third-party suppliers the materials necessary to produce our product candidates for our clinical studies. There are a small number of suppliers for certain capital equipment and raw materials that we use to manufacture our drugs. Such suppliers may not sell these raw materials to our manufacturers at the times we need them or on commercially reasonable terms. We do not have any control over the process or timing of the acquisition of these raw materials by our manufacturers. Moreover, we currently do not have any agreements for the commercial production of these raw materials. Although we generally do not begin a clinical trial unless we believe we have a sufficient supply of a product candidate to complete the clinical trial, any significant delay in the supply of a product candidate or the raw material components thereof for an ongoing clinical trial due to the need to replace a third-party manufacturer could considerably delay completion of our clinical studies, product testing and potential regulatory approval of our product candidates. If our manufacturers or we are unable to purchase these raw materials after regulatory approval has been obtained for our product candidates, the commercial launch of our product candidates would be delayed or there would be a shortage in supply, which would impair our ability to generate revenues from the sale of our product candidates.

Although we believe the current manufacturing process for the active pharmaceutical ingredient for tivozanib is adequate to support future development and commercial demand, because of the complex nature of many of our other compounds, our manufacturers may not be able to manufacture such other compounds at a cost or in quantities or in a timely manner necessary to develop and commercialize other products. If we successfully commercialize any of our drugs, we may be required to establish or access large-scale commercial manufacturing capabilities. In addition, as our drug development pipeline increases and matures, we will have a greater need for clinical trial and commercial manufacturing capacity. We do not own or operate manufacturing facilities for the production of clinical or commercial quantities of our product candidates and we currently have no plans to build our own clinical or commercial scale manufacturing capabilities. To meet our projected needs for commercial manufacturing, third parties with whom we currently work will need to increase their scale of production or we will need to secure alternate suppliers.

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We rely on third parties to conduct preclinical and clinical trials for our product candidates, and if they do not properly and successfully perform their obligations to us, we may not be able to obtain regulatory approvals for our product candidates.

We design the clinical trials for our product candidates, but we rely on contract research organizations and other third parties to assist us in managing, monitoring and otherwise carrying out many of these trials. We compete with larger companies for the resources of these third parties.

Although we rely on these third parties to conduct many of our clinical trials, we are responsible for ensuring that each of our clinical trials is conducted in accordance with its general investigational plan and protocol. Moreover, the FDA and foreign regulatory agencies require us to comply with regulations and standards, commonly referred to as good clinical practices, for designing, conducting, monitoring, recording, analyzing, and reporting the results of clinical trials to assure that the data and results are credible and accurate and that the rights, integrity and confidentiality of trial participants are protected. Our reliance on third parties that we do not control does not relieve us of these responsibilities and requirements.

The third parties on whom we rely generally may terminate their engagements with us at any time and having to enter into alternative arrangements would delay introduction of our product candidates to market.

If these third parties do not successfully carry out their duties under their agreements with us, if the quality or accuracy of the data they obtain is compromised due to their failure to adhere to our clinical trial protocols or regulatory requirements, or if they otherwise fail to comply with clinical trial protocols or meet expected deadlines, our clinical trials may not meet regulatory requirements. If our clinical trials do not meet regulatory requirements or if these third parties need to be replaced, our preclinical development activities or clinical trials may be extended, delayed, suspended or terminated. If any of these events occur, we may not be able to obtain regulatory approval of our product candidates.

Risks Related to Our Intellectual Property Rights

We could be unsuccessful in obtaining adequate patent protection for one or more of our product candidates.

The following is a list of patents issued and granted to date to us and the number of patent applications filed by us that are currently pending with respect to our lead programs and technologies:

tivozanib and related technologies
- U.S. patents: 4 issued; 2 pending; expirations ranging from 2018 to 2029
- European patents: 3 granted; none pending; expirations ranging from 2018 to 2023
- Canadian patents: none granted; 1 pending; expiration 2022
- Australian patents: 1 granted; none pending; expiration 2022
- International application: 1 pending; expiration 2029

our antibody product pipeline and related technologies
- U.S. patents: 3 issued; 3 pending; expirations ranging from 2027 to 2029
- European patents: none granted; 2 pending; expirations 2027
- International application: 2 pending; expiration 2029

various facets of our technology platform
- U.S. patents: 4 issued; 2 pending; expirations ranging from 2020 to 2025
- European patents: 1 granted; 3 pending; expirations ranging from 2022 to 2026
- Australian patents: 2 granted; 2 pending; expirations ranging from 2022 to 2026

We cannot be certain that patents will be issued or granted with respect to applications that are currently pending, or that issued or granted patents will not later be found to be invalid and/or unenforceable. The patent position of biotechnology and pharmaceutical companies is generally uncertain because it involves complex legal and factual considerations. The standards applied by the United States Patent and Trademark Office and foreign patent offices in granting patents are not always applied uniformly or predictably. For example, there is no

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uniform worldwide policy regarding patentable subject matter or the scope of claims allowable in biotechnology and pharmaceutical patents. Consequently, patents may not issue from our pending patent applications. As such, we do not know the degree of future protection that we will have on our proprietary products and technology. The scope of patent protection that the U.S. Patent and Trademark Office will grant around the antibodies in our antibody product pipeline is uncertain. It is possible that the U.S. Patent and Trademark Office will not allow broad antibody claims that cover closely related antibodies as well as the specific antibody. Upon receipt of FDA approval, competitors would be free to market antibodies almost identical to ours, thereby decreasing our market share.

Issued patents covering one or more of our products could be found invalid or unenforceable if challenged in court.

If we or one of our corporate partners were to initiate legal proceedings against a third party to enforce a patent covering one of our products, the defendant could counterclaim that our patent is invalid and/or unenforceable. In patent litigation in the United States, defendant counterclaims alleging invalidity and/or unenforceability are commonplace. Grounds for a validity challenge could be an alleged failure to meet any of several statutory requirements, for example, lack of novelty, obviousness or non-enablement. Grounds for an unenforceability assertion could be an allegation that someone connected with prosecution of the patent withheld relevant information from the U.S. Patent and Trademark Office, or made a misleading statement, during prosecution. Although we have conducted due diligence on patents we have exclusively in-licensed, and we believe that we have conducted our patent prosecution in accordance with the duty of candor and in good faith, the outcome following legal assertions of invalidity and unenforceability during patent litigation is unpredictable. With respect to the validity question, for example, we cannot be certain that there is no invalidating prior art, of which we and the patent examiner were unaware during prosecution. If a defendant were to prevail on a legal assertion of invalidity and/or unenforceability, we would lose at least part, and perhaps all, of the patent protection on one of our products or certain aspects of our Human Response Platform. Such a loss of patent protection could have a material adverse impact on our business.

Claims that our platform technologies, our products or the sale or use of our products infringe the patent rights of third parties could result in costly litigation or could require substantial time and money to resolve, even if litigation is avoided.

We cannot guarantee that our platform technologies, our products, or the use of our products, do not infringe third party patents. Third parties might allege that we are infringing their patent rights or that we have misappropriated their trade secrets. Such third parties might resort to litigation against us. The basis of such litigation could be existing patents or patents that issue in the future.

It is also possible that we failed to identify relevant patents or applications. For example, applications filed before November 29, 2000 and certain applications filed after that date that will not be filed outside the United States remain confidential until patents issue. Patent applications in the United States and elsewhere are published approximately 18 months after the earliest filing, which is referred to as the priority date. Therefore, patent applications covering our products or platform technology could have been filed by others without our knowledge. Additionally, pending patent applications which have been published can, subject to certain limitations, be later amended in a manner that could cover our platform technologies, our products or the use of our products.

With regard to tivozanib, we are aware of a third party United States patent, and corresponding foreign counterparts, that contain broad claims related to the use of an organic compound that, among other things, inhibits VEGF binding to one of the VEGF receptors. Additionally, tivozanib falls within the scope of certain pending patent applications that have broad generic disclosure and disclosure of certain compounds possessing structural similarities to tivozanib. Although we believe it is unlikely that such applications will lead to issued claims that would cover tivozanib and still be valid in view of the prior art, patent prosecution is inherently unpredictable. We are also aware of third party United States patents that contain broad claims related to the use of a tyrosine kinase inhibitor in combination with a DNA damaging agent such as chemotherapy or radiation and we have received written notice from the owners of such patents indicating that they believe we may need a

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license from them in order to avoid infringing their patents. With regard to AV-299, we are aware of two separate families of United States patents, United States patent applications and foreign counterparts, with each of the two families being owned by a different third party, that contain broad claims related to anti-HGF antibodies having certain binding properties and their use. We are also aware of a United States patent that contains claims related to a method of treating a tumor by administering an agent that blocks the ability of HGF to promote angiogenesis in the tumor. With regard to AV-203, we are aware of a third party United States patent that contains broad claims relating to anti-ErbB3 antibodies. Based on our analyses, if any of the above third party patents were asserted against us, we do not believe our proposed products or activities would be found to infringe any valid claim of these patents. If we were to challenge the validity of any issued United States patent in court, we would need to overcome a statutory presumption of validity that attaches to every United States patent. This means that in order to prevail, we would have to present clear and convincing evidence as to the invalidity of the patent s claims. There is no assurance that a court would find in our favor on questions of infringement or validity.

In order to avoid or settle potential claims with respect to any of the patent rights described above or any other patent rights of third parties, we may choose or be required to seek a license from a third party and be required to pay license fees or royalties or both. These licenses may not be available on acceptable terms, or at all. Even if we or our future strategic partners were able to obtain a license, the rights may be nonexclusive, which could result in our competitors gaining access to the same intellectual property. Ultimately, we could be prevented from commercializing a product, or be forced to cease some aspect of our business operations, if, as a result of actual or threatened patent infringement claims, we are unable to enter into licenses on acceptable terms. This could harm our business significantly.

Defending against claims of patent infringement or misappropriation of trade secrets could be costly and time consuming, regardless of the outcome. Thus, even if we were to ultimately prevail, or to settle at an early stage, such litigation could burden us with substantial unanticipated costs. In addition, litigation or threatened litigation could result in significant demands on the time and attention of our management team, distracting them from the pursuit of other company business.

Unfavorable outcomes in intellectual property litigation could limit our research and development activities and/or our ability to commercialize certain products.

If third parties successfully assert intellectual property rights against us, we might be barred from using certain aspects of our technology platform, or barred from developing and commercializing certain products. Prohibitions against using certain technologies, or prohibitions against commercializing certain products, could be imposed by a court or by a settlement agreement between us and a plaintiff. In addition, if we are unsuccessful in defending against allegations of patent infringement or misappropriation of trade secrets, we may be forced to pay substantial damage awards to the plaintiff. There is inevitable uncertainty in any litigation, including intellectual property litigation. There can be no assurance that we would prevail in any intellectual property litigation, even if the case against us is weak or flawed. If litigation leads to an outcome unfavorable to us, we may be required to obtain a license from the patent owner, in order to continue our research and development programs or to market our product(s). It is possible that the necessary license will not be available to us on commercially acceptable terms, or at all. This could limit our research and development activities, our ability to commercialize certain products, or both.

Most of our competitors are larger than we are and have substantially greater resources. They are, therefore, likely to be able to sustain the costs of complex patent litigation longer than we could. In addition, the uncertainties associated with litigation could have a material adverse effect on our ability to raise the funds necessary to continue our clinical trials, continue our internal research programs, in-license needed technology, or enter into strategic partnerships that would help us bring our product candidates to market.

In addition, any future patent litigation, interference or other administrative proceedings will result in additional expense and distraction of our personnel. An adverse outcome in such litigation or proceedings may expose us or our strategic partners to loss of our proprietary position, expose us to significant liabilities, or require us to seek licenses that may not be available on commercially acceptable terms, if at all.

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Intellectual property litigation may lead to unfavorable publicity that harms our reputation and causes the market price of our common stock to decline.

During the course of any patent litigation, there could be public announcements of the results of hearings, rulings on motions, and other interim proceedings in the litigation. If securities analysts or investors regard these announcements as negative, the perceived value of our products, programs, or intellectual property could be diminished. Accordingly, the market price of our common stock may decline.

Tivozanib and certain aspects of our platform technology 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 and market share will be harmed.

We are a party to several license agreements under which certain aspects of our business depend on patents and/or patent applications owned by other companies or institutions. In particular, we hold exclusive licenses from Kyowa Hakko Kirin for tivozanib and the Dana-Farber Cancer Institute for our MaSS screen, which is a method of using our models to screen for, and identify, novel targets for new cancer drugs. We are likely to enter into additional license agreements as part of the development of our business in the future. Our licensors may not successfully prosecute certain patent applications under which we are licensed and on which our business depends. Even if patents issue from these applications, our licensors may fail to maintain these patents, may decide not to pursue litigation against third party infringers, may fail to prove infringement, or may fail to defend against counterclaims of patent invalidity or unenforceability. In addition, in spite of our best efforts, our licensors might conclude that we have materially breached our license agreements and might therefore terminate the license agreements, thereby removing our ability to obtain regulatory approval and to market products covered by these license agreements. If these in-licenses are terminated, or if the underlying patents fail to provide the intended market exclusivity, competitors would have the freedom to seek regulatory approval of, and to market, products identical to ours. This could have a material adverse effect on our competitive business position and our business prospects.

We could be unsuccessful in obtaining patent protection on one or more components of our technology platform.

We believe that an important factor in our competitive position relative to other companies in the field of targeted oncology therapeutics is our proprietary Human Response Platform. This platform is useful for identifying new targets for drug discovery, confirming that newly-identified drug targets actually play a role in cancer, testing new compounds for effectiveness as drugs, and identifying traits useful for predicting which patients will respond to which drugs. We own issued U.S. patents covering our chimeric model technology and directed complementation technology. We have exclusively licensed certain patent rights covering a method of using our inducible cancer models to identify new targets for cancer drugs. However, patent protection on other aspects of our technology platform, such as our reconstituted human breast tumor model, is still pending. There is no guarantee that any of such pending patent applications, in the United States or elsewhere, will result in issued patents, and, even if patents eventually issue, there is no certainty that the claims in the eventual patents will have adequate scope to preserve our competitive position. Third parties might invent alternative technologies that would substitute for our technology platform while being outside the scope of the patents covering our platform technology. By successfully designing around our patented technology third parties could substantially weaken our competitive position in oncology research and development.

Confidentiality agreements with employees and third parties may not prevent unauthorized disclosure of trade secrets and other proprietary information.

In addition to patents, we rely on trade secrets, technical know-how, and proprietary information concerning our business strategy in order to protect our competitive position in the field of oncology. In the course of our research and development activities and our business activities, we often rely on confidentiality agreements to protect our proprietary information. Such confidentiality agreements are used, for example, when we talk to vendors of laboratory or clinical development services or potential strategic partners. In addition, each of our employees is

required to sign a confidentiality agreement upon joining our company. We take steps to protect our proprietary information, and our confidentiality agreements are carefully drafted to protect our proprietary interests. Nevertheless, there can be no guarantee that an employee or an outside party will not make an unauthorized disclosure of our proprietary confidential information. This might happen intentionally or inadvertently. It is possible that a competitor will make use of such information, and that our competitive position will be compromised, in spite of any legal action we might take against persons making such unauthorized disclosures.

Trade secrets are difficult to protect. Although we use reasonable efforts to protect our trade secrets, our employees, consultants, contractors, or outside scientific collaborators might intentionally or inadvertently disclose our trade secret information to competitors. Enforcing a claim that a third party illegally obtained and is using any of our trade secrets is expensive and time consuming, and the outcome is unpredictable. In addition, courts outside the United States sometimes are less willing than U.S. courts to protect trade secrets. Moreover, our competitors may independently develop equivalent knowledge, methods and know-how.

Our research and development strategic partners may have rights to publish data and other information to which we have rights. In addition, we sometimes engage individuals or entities to conduct research relevant to our business. The ability of these individuals or entities to publish or otherwise publicly disclose data and other information generated during the course of their research is subject to certain contractual limitations. These contractual provisions may be insufficient or inadequate to protect our confidential information. If we do not apply for patent protection prior to such publication, or if we cannot otherwise maintain the confidentiality of our proprietary technology and other confidential information, then our ability to obtain patent protection or to protect our trade secret information may be jeopardized.

Intellectual property rights do not necessarily address all potential threats to our competitive advantage.

The degree of future protection afforded by our intellectual property rights is uncertain because intellectual property rights have limitations, and may not adequately protect our business, or permit us to maintain our competitive advantage. The following examples are illustrative:

- Others may be able to make compounds that are similar to our product candidates but that are not covered by the claims of the patents that we own or have exclusively licensed.
- We or our licensors or strategic partners might not have been the first to make the inventions covered by the issued patent or pending patent application that we own or have exclusively licensed.
- We or our licensors or strategic partners might not have been the first to file patent applications covering certain of our inventions.
- Others may independently develop similar or alternative technologies or duplicate any of our technologies without infringing our intellectual property rights.
- It is possible that our pending patent applications will not lead to issued patents.
- Issued patents that we own or have exclusively licensed may not provide us with any competitive advantages, or may be held invalid or unenforceable, as a result of legal challenges by our competitors.
- Our competitors might conduct research and development activities in countries where we do not have patent rights and then use the information learned from such activities to develop competitive products for sale in our major commercial markets.
- We may not develop additional proprietary technologies that are patentable.

The patents of others may have an adverse effect on our business.

Changes in U.S. patent law could diminish the value of patents in general, thereby impairing our ability to protect our products.

As is the case with other biopharmaceutical companies, our success is heavily dependent on intellectual property, particularly patents. Obtaining and enforcing patents in the biopharma industry involve both

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technological complexity and legal complexity. Therefore, obtaining and enforcing biopharma patents is costly, time-consuming and inherently uncertain. In addition, Congress may pass patent reform legislation. The Supreme Court has ruled on several patent cases in recent years, either narrowing the scope of patent protection available in certain circumstances or weakening the rights of patent owners in certain situations. In addition to increasing uncertainty with regard to our ability to obtain patents in the future, this combination of events has created uncertainty with respect to the value of patents, once obtained. Depending on decisions by the U.S. Congress, the federal courts, and the U.S. Patent and Trademark Office, the laws and regulations governing patents could change in unpredictable ways that would weaken our ability to obtain new patents or to enforce our existing patents and patents that we might obtain in the future.

Risks Related to This Offering and Ownership of Our Common Stock

We do not know whether a market will develop for our common stock or what the market price of our common stock will be and as a result it may be difficult for you to sell your shares of our common stock.

Before this offering, there was no public trading market for our common stock. If a market for our common stock does not develop or is not sustained, it may be difficult for you to sell your shares of common stock at an attractive price or at all. Further, an inactive market may also impair our ability to raise capital by selling shares of our common stock and may impair our ability to enter into strategic partnerships or acquire companies or products by using our shares of common stock as consideration. We cannot predict the prices at which our common stock will trade. It is possible that in one or more future periods our results of operations may be below the expectations of public market analysts and investors and, as a result of these and other factors, the price of our common stock may fall.

The market price of our common stock may be highly volatile, and you may not be able to resell your shares at or above the initial public offering price.

The trading price of our common stock is likely to be highly volatile and could be subject to wide fluctuations in price in response to various factors, many of which are beyond our control, including:

- new products, product candidates or new uses for existing products introduced or announced by our strategic partners, or our competitors, including Roche s Avastin, Pfizer s Sutent, Onyx s Nexavar, GSK s Votrient and the timing of these introductions or announcements;
- actual or anticipated results from and any delays in our clinical trials, including our phase 3 clinical trial of tivozanib, as well as results of regulatory reviews relating to the approval of our product candidates;
- the results of our efforts to discover, develop, acquire or in-license additional product candidates or products;
- disputes or other developments relating to proprietary rights, including patents, litigation matters and our ability to obtain patent protection for our technologies;
- announcements by us or our competitors of significant acquisitions, strategic partnerships, joint ventures and capital commitments;
- additions or departures of key scientific or management personnel;
- conditions or trends in the biotechnology and biopharmaceutical industries;

actual or anticipated changes in earnings estimates, development timelines or recommendations by securities analysts;

general economic and market conditions and other factors that may be unrelated to our operating performance or the operating performance of our competitors, including changes in market valuations of similar companies; and

sales of common stock by us or our stockholders in the future, as well as the overall trading volume of our common stock.

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In addition, the stock market in general and the market for biotechnology and biopharmaceutical companies in particular have experienced extreme price and volume fluctuations that have often been unrelated or disproportionate to the operating performance of those companies. These broad market and industry factors may seriously harm the market price of our common stock, regardless of our operating performance. In the past, following periods of volatility in the market, securities class-action litigation has often been instituted against companies. Such litigation, if instituted against us, could result in substantial costs and diversion of management s attention and resources, which could materially and adversely affect our business and financial condition.

Our principal stockholders and management own a significant percentage of our stock and will be able to exercise significant influence over matters subject to stockholder approval.

As of February 1, 2010, our executive officers, directors and principal stockholders, together with their respective affiliates, owned approximately 41.7% of our common stock, including shares subject to outstanding options and warrants that are exercisable within 60 days after February 1, 2010, and we expect that upon completion of this offering, that same group will continue to hold at least 29.5% of our outstanding common stock. Accordingly, even after this offering, these stockholders will be able to exert a significant degree of influence over our management and affairs and over matters requiring stockholder approval, including the election of our board of directors and approval of significant corporate transactions. This concentration of ownership could have the effect of delaying or preventing a change in our control or otherwise discouraging a potential acquirer from attempting to obtain control of us, which in turn could have a material and adverse effect on the fair market value of our common stock.

A significant portion of our total outstanding shares may be sold into the public market in the near future, which could cause the market price of our common stock to drop significantly, even if our business is doing well.

Sales of a substantial number of shares of our common stock in the public market could occur at any time after the expiration of the lock-up agreements described in the Underwriting section of this prospectus. These sales, or the market perception that the holders of a large number of shares intend to sell shares, could reduce the market price of our common stock. After this offering, we will have 29,644,831 shares of common stock outstanding based on the number of shares outstanding as of February 1, 2010. This includes the 9,000,000 shares that we are selling in this offering, which may be resold in the public market immediately. The remaining 20,644,831 shares, or 69.6% of our outstanding shares after this offering, are currently restricted as a result of securities laws or lock-up agreements but will be able to be sold, subject to any applicable volume limitations under federal securities laws with respect to affiliate sales, in the near future as set forth below.

Number of Shares and % of Total Outstanding	Date Available for Sale into Public Market
16,250 shares, or .05%	On the date of this prospectus
88,934 shares, or .30%	90 days after the date of this prospectus
20,539,647 shares, or 69.29%	180 days after the date of this prospectus, subject to extension in specified instances, due to lock-up agreements between the holders of these shares and the underwriters. However, the representatives of the underwriters can waive the provisions of these lock-up agreements and allow these stockholders to sell their shares at any time.

In addition, as of February 1, 2010, there were 728,800 shares of convertible preferred stock convertible into 182,200 shares of common stock subject to outstanding warrants, 3,248,207 shares of common stock subject to outstanding options, an additional 398,611 shares of common stock reserved for future issuance under our employee benefit plans and an aggregate of 2,125,000 additional shares of common stock that will be available for future grant under our 2010 stock incentive plan and 2010 employee stock purchase plan upon the closing of this offering. The shares of common stock underlying these securities, including the shares underlying grants that may be made in the future under our employee benefit plans, will become eligible for sale in the public market to the extent permitted by any applicable vesting requirements, the lock-up agreements and Rules 144 and 701

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under the Securities Act of 1933, as amended. Moreover, after this offering, holders of an aggregate of 18,937,663 shares of our common stock and holders of warrants to purchase 25,000 shares of our common stock will have rights, subject to some conditions, to require us to file registration statements covering their shares or to include their shares in registration statements that we may file for ourselves or other stockholders. If such holders, by exercising their registration rights, cause a large number of securities to be registered and sold into the public market, these sales could have an adverse effect on the market price for our common stock. We also intend to register all shares of common stock that we may issue under our employee benefit plans. Once we register these shares, they can be freely sold in the public market upon issuance, subject to the lock-up agreements and the restrictions imposed on our affiliates under Rule 144.

You will incur immediate and substantial dilution as a result of this offering.

If you purchase common stock in this offering, you will incur immediate and substantial dilution of $6.96 per share, representing the difference between the initial public offering price of $9.00 per share and our pro forma net tangible book value per share after giving effect to this offering and the conversion of all outstanding shares of our convertible preferred stock upon the closing of this offering. Based upon our shares outstanding on December 31, 2009, purchasers of shares of our common stock in this offering will have contributed 32.2% of the aggregate investment made by all purchasers of our capital stock to date based on the initial public offering price of $9.00 per share, but will own only 30.4% of the outstanding shares of our common stock immediately after the offering. Moreover, we issued warrants and options in the past to acquire common stock at prices significantly below the initial public offering price. As of February 1, 2010, there were 728,800 shares of convertible preferred stock subject to outstanding warrants with a weighted average exercise price of $2.38 per share (such warrants will be converted into warrants for 182,200 shares of common stock with a weighted average exercise price of $9.52 per share upon the consummation of this offering) and 3,248,207 shares of common stock subject to outstanding options with a weighted average exercise price of $4.56 per share. To the extent that these outstanding warrants or options are ultimately exercised, you will incur further dilution. In addition, an aggregate of 2,125,000 additional shares of common stock will be available under our 2010 stock incentive plan and 2010 employee stock purchase plan upon the closing of this offering. To the extent that any of these shares are granted as awards under the plans, you will incur further dilution.

Failure to achieve and maintain effective internal controls in accordance with Section 404 of the Sarbanes-Oxley Act could have a material adverse effect on our ability to produce accurate financial statements and on our stock price.

Pursuant to Section 404 of the Sarbanes-Oxley Act of 2002, we will be required to furnish a report by our management on our internal control over financial reporting. We have not been subject to these requirements in the past. The internal control report must contain (a) a statement of management s responsibility for establishing and maintaining adequate internal control over financial reporting, (b) a statement identifying the framework used by management to conduct the required evaluation of the effectiveness of our internal control over financial reporting, (c) management s assessment of the effectiveness of our internal control over financial reporting as of the end of our most recent fiscal year, including a statement as to whether or not internal control over financial reporting is effective, and (d) a statement that our independent registered public accounting firm has issued an attestation report on internal control over financial reporting.

To achieve compliance with Section 404 within the prescribed period, we will be engaged in a process to document and evaluate our internal control over financial reporting, which is both costly and challenging. In this regard, we will need to dedicate internal resources, engage outside consultants and adopt a detailed work plan to (a) assess and document the adequacy of internal control over financial reporting, (b) take steps to improve control processes where appropriate, (c) validate through testing that controls are functioning as documented, and (d) implement a continuous reporting and improvement process for internal control over financial reporting. Despite our efforts, we can provide no assurance as to our, or our independent registered public accounting firm s, conclusions with respect to the effectiveness of our internal control over financial reporting under Section 404. There is a risk that neither we nor our independent registered public accounting firm will be able to

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conclude within the prescribed timeframe that our internal control over financial reporting is effective as required by Section 404. This could result in an adverse reaction in the financial markets due to a loss of confidence in the reliability of our financial statements.

We do not expect to pay any cash dividends for the foreseeable future. Investors in this offering may never obtain a return on their investment.

You should not rely on an investment in our common stock to provide dividend income. We do not anticipate that we will pay any cash dividends to holders of our common stock in the foreseeable future. Instead, we plan to retain any earnings to maintain and expand our existing operations. In addition, our ability to pay cash dividends is currently prohibited by the terms of one of our debt financing arrangements, and any future debt financing arrangement may contain terms prohibiting or limiting the amount of dividends that may be declared or paid on our common stock. Accordingly, investors must rely on sales of their common stock after price appreciation, which may never occur, as the only way to realize any return on their investment. As a result, investors seeking cash dividends should not purchase our common stock.

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

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

Provisions in our certificate of incorporation, our by-laws or Delaware law might discourage, delay or prevent a change in control of our company or changes in our management and, therefore, depress the trading price of our common stock.

Provisions of our certificate of incorporation, our by-laws or Delaware law may have the effect of deterring unsolicited takeovers or delaying or preventing a change in control of our company or changes in our management, including transactions in which our stockholders might otherwise receive a premium for their shares over then current market prices. In addition, these provisions may limit the ability of stockholders to approve transactions that they may deem to be in their best interest. These provisions include:

- advance notice requirements for stockholder proposals and nominations;
- the inability of stockholders to act by written consent or to call special meetings;
- the ability of our board of directors to make, alter or repeal our by-laws; and
- the ability of our board of directors to designate the terms of and issue new series of preferred stock without stockholder approval, which could be used to institute a rights plan, or a poison pill, that would work to dilute the stock ownership of a potential hostile acquirer, likely preventing acquisitions that have not been approved by our board of directors.

In addition, Section 203 of the Delaware General Corporation Law prohibits a publicly-held Delaware corporation from engaging in a business combination with an interested stockholder, generally a person which together with its affiliates owns, or within the last three years has owned, 15% of our voting stock, for a period of three years after the date of the transaction in which the person became an interested stockholder, unless the business combination is approved in a prescribed manner.

The existence of the foregoing provisions and anti-takeover measures could limit the price that investors might be willing to pay in the future for shares of our common stock. They could also deter potential acquirers of our company, thereby reducing the likelihood that you could receive a premium for your common stock in an acquisition.

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CAUTIONARY NOTE REGARDING FORWARD-LOOKING STATEMENTS

This prospectus contains forward-looking statements that involve substantial risks and uncertainties. All statements, other than statements of historical facts, contained in this prospectus, including statements regarding our strategy, future operations, future financial position, future revenues, projected costs, prospects, plans and objectives of management, are forward-looking statements. The words anticipate, believe, estimate, expect, intend, may, plan, predict, project, target, potential, will, would, could, should, continue, con terms or other similar expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words.

The forward-looking statements in this prospectus include, among other things, statements about:

- our plans to develop and commercialize tivozanib and AV-299;
- our ongoing and planned preclinical studies and clinical trials;
- the potential benefits of strategic partnership agreements and our ability to enter into selective strategic partnership arrangements;
- the timing of and our ability to obtain and maintain regulatory approvals for our product candidates;
- the rate and degree of market acceptance and clinical utility of our products;
- our plans to leverage our Human Response Platform to discover and develop product candidates;
- our ability to quickly and efficiently identify and develop product candidates;
- our commercialization, marketing and manufacturing capabilities and strategy;
- our intellectual property position;
- our estimates regarding expenses, future revenues, capital requirements and needs for additional financing; and
- other risks and uncertainties, including those listed under the caption Risk Factors.

We may not actually achieve the plans, intentions or expectations disclosed in our forward-looking statements, and you should not place undue reliance on our forward-looking statements. Actual results or events could differ materially from the plans, intentions and expectations disclosed in the forward-looking statements we make. We have included important factors in the cautionary statements included in this prospectus, particularly in the Risk Factors section, that we believe could cause actual results or events to differ materially from the forward-looking statements that we make. Our forward-looking statements do not reflect the potential impact of any future acquisitions, mergers, dispositions, joint ventures or investments we may make.

You should read this prospectus and the documents that we reference in this prospectus and have filed as exhibits to the registration statement of which this prospectus is a part completely and with the understanding that our actual future results may be materially different from what we

expect.

The forward-looking statements in this prospectus represent our views as of the date of this prospectus. We anticipate that subsequent events and developments will cause our views to change. However, while we may elect to update these forward-looking statements at some point in the future, we have no current intention of doing so except to the extent required by applicable law. You should, therefore, not rely on these forward-looking statements as representing our views as of any date subsequent to the date of this prospectus.

This prospectus also contains estimates and other statistical data made by independent parties and by us relating to market size and growth and other data about our industry. This data involves a number of assumptions and limitations, and you are cautioned not to give undue weight to such estimates. We have not independently verified the statistical and other industry data generated by independent parties and contained in this prospectus. In addition, projections, assumptions and estimates of our future performance and the future performance of the industries in which we operate are necessarily subject to a high degree of uncertainty and risk.

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USE OF PROCEEDS

We estimate that the net proceeds from our issuance and sale of 9,000,000 shares of common stock in this offering will be approximately $72.6 million, based on the initial public offering price of $9.00 per share, after deducting underwriting discounts and commissions and estimated offering expenses payable by us.

If the underwriters exercise their over-allotment option in full, we estimate that the net proceeds from this offering will be approximately $83.9 million, based on the initial public offering price of $9.00 per share, 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.

This expected use of net proceeds from this offering represents our intentions based upon our current plans and business conditions. The amounts and timing of our actual expenditures depend on numerous factors, including the ongoing status of and results from clinical trials and other studies, as well as any strategic partnerships that we may enter into with third parties for our product candidates and any unforeseen cash needs. As a result, our management will retain broad discretion over the allocation of the net proceeds from this offering.

Pending use of the proceeds from this offering, we intend to invest the proceeds in a variety of capital preservation investments, including short-term, investment-grade and interest-bearing instruments.

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DIVIDEND POLICY

We have never declared or paid cash dividends on our capital stock and our ability to pay cash dividends is currently prohibited by the terms of one of our debt financing arrangements. We currently intend to retain all of our future earnings, if any, to finance the growth and development of our business. We do not intend to pay cash dividends to our stockholders in the foreseeable future.

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INDUSTRY AND MARKET DATA

We obtained the industry, market and competitive position data in this prospectus from our own internal estimates and research as well as from industry and general publications and research surveys and studies conducted by third parties. While we believe that each of these studies and publications is reliable, we have not independently verified market and industry data from third-party sources. While we believe our internal company research is reliable and the market definitions we use are appropriate, neither such research nor these definitions have been verified by any independent source.

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CAPITALIZATION

The following table sets forth our capitalization as of December 31, 2009:

- on an actual basis;
- on a pro forma basis to give effect to the conversion of all of our outstanding convertible preferred stock into common stock upon the closing of this offering; and
- on a pro forma as adjusted basis to give further effect to the 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 and the receipt by us of the proceeds of such sale.

You should read this table together with our consolidated financial statements and the related notes appearing at the end of this prospectus, the sections entitled Selected Consolidated Financial Data and Management s Discussion and Analysis of Financial Condition and Results of Operations and other financial information contained in this prospectus.

	As of December 31, 2009 (unaudited)		
	Actual	Pro Forma	Pro Forma As Adjusted
	(in thousands, except per share data)		
Cash, cash equivalents, and marketable securities	$ 51,301	$ 51,301	$ 123,881
Current portion of loans payable	7,467	7,467	7,467
Loans payable, net of current portion	12,278	12,278	12,278
Warrants to purchase convertible preferred stock	1,459		
Series A convertible preferred stock, $.001 par value: 12,448,000 shares authorized; 12,428,198 shares issued and outstanding, actual; no shares authorized, issued or outstanding, pro forma and pro forma adjusted	15,560		
Series B convertible preferred stock, $.001 par value: 27,215,385 shares authorized; 26,906,354 shares issued and outstanding actual; no shares authorized, issued or outstanding, pro forma and pro forma adjusted	43,723		
Series C convertible preferred stock, $.001 par value: 4,166,668 shares authorized, issued and outstanding, actual; no shares authorized, issued or outstanding, pro forma and pro forma adjusted	11,583		
Series D convertible preferred stock, $.001 par value: 21,794,310 shares authorized; 21,165,510 shares issued and outstanding, actual; no shares authorized, issued or outstanding, pro forma and pro forma adjusted	52,914		
Series E convertible preferred stock, $.001 par value: 15,000,000 shares authorized; 11,250,000 shares issued and outstanding, actual; no shares authorized, issued or outstanding, pro forma and pro forma adjusted	32,925		

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	As of December 31, 2009 (unaudited)		
	Actual	Pro Forma	Pro Forma As Adjusted
	(in thousands, except per share data)		
Common stock, $.001 par value: 25,500,000 and 100,000,000 shares authorized actual and pro forma; 1,640,714 shares issued and outstanding, actual; 20,619,869 shares issued and outstanding, pro forma; and 29,619,869 shares issued and outstanding, pro forma as adjusted	2	21	30
Additional paid-in capital	7,432	165,577	238,148
Accumulated other comprehensive income			
Accumulated deficit	(177,725)	(177,725)	(177,725)
Total stockholders deficit	$ (170,291)	$ (12,127)	$ 60,453
Total capitalization	$ 151	$ 151	$ 72,731

The table above does not include:

3,275,906 shares of common stock issuable upon exercise of stock options outstanding as of December 31, 2009 at a weighted average exercise price of $4.56 per share;

728,800 shares of convertible preferred stock issuable upon the exercise of warrants outstanding as of December 31, 2009 at a weighted average exercise price of $2.38 per share (such warrants will be converted into warrants to purchase 182,200 shares of common stock upon the consummation of this offering); and

an aggregate of 395,876 shares of common stock reserved for future issuance under our stock incentive plans as of December 31, 2009 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.

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DILUTION

If you invest in our common stock in this offering, your ownership interest will be diluted immediately to the extent of the difference between the initial public offering price per share of our common stock and the net tangible book value per share of our common stock after this offering.

Our historical net tangible book value (deficit) as of December 31, 2009 was $(170.3) million or $(103.79) per share of our common stock. Our historical net tangible book value (deficit) per share represents the amount of our total tangible assets less total liabilities, divided by the number of shares of common stock outstanding.

Our pro forma net tangible book value (deficit) as of December 31, 2009 was $(12.1) million or $(0.59) per share of our common stock. Pro forma net tangible book value (deficit) per share represents the amount of our total tangible assets less total liabilities, divided by the total number of shares of common stock outstanding after giving effect to 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.

After giving effect to the issuance and sale by us of 9,000,000 shares of common stock in this offering at the initial public offering price of $9.00 per share, less underwriting discounts and commissions and estimated offering expenses payable by us, our pro forma as adjusted net tangible book value as of December 31, 2009 would have been $60.5 million, or $2.04 per share. This represents an immediate increase in pro forma net tangible book value per share of $2.63 to existing stockholders and immediate dilution of $6.96 in pro forma net tangible book value per share to new investors purchasing common stock in this offering. Dilution per share to new investors is determined by subtracting pro forma as adjusted net tangible book value per share after this offering from the initial public offering price per share paid by new investors. The following table illustrates this dilution on a per share basis:

Initial public offering price per share of common stock		$ 9.00
Pro forma net tangible book value per share as of December 31, 2009	$ (0.59)	
Increase per share attributable to new investors	2.63	
Pro forma as adjusted net tangible book value per share after this offering		$ 2.04
Dilution per share to new investors		$ 6.96

If the underwriters exercise their over-allotment option, the pro forma as adjusted net tangible book value will increase to $2.32 per share, representing an immediate increase to existing stockholders of $2.91 per share and an immediate dilution of $6.68 per share to new investors. If any shares are issued upon exercise of outstanding options or warrants, you will experience further dilution.

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The following table summarizes, as of December 31, 2009, the number of shares purchased or to be purchased from us after giving effect to 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, the total consideration paid or to be paid to us and the average price per share paid or to be paid to us by existing stockholders and by new investors purchasing shares of our common stock in this offering at the initial public offering price of $9.00 per share, before deducting underwriting discounts and commissions and estimated offering expenses payable by us. As the table below shows, new investors purchasing shares of our common stock in this offering will pay an average price per share substantially higher than our existing stockholders paid.

	Shares Purchased		Total Consideration		Average Price per Share
	Number	Percentage	Amount	Percentage	
Existing stockholders	20,619,869	69.6%	$ 170,218,278	67.8%	$ 8.26
New investors	9,000,000	30.4%	$ 81,000,000	32.2%	$ 9.00
Total	29,619,869	100%	$ 251,218,278	100%	$ 8.48

The number of shares purchased from us by existing stockholders is based on 20,619,869 shares of common stock outstanding as of December 31, 2009 after giving effect to the conversion of all outstanding shares of our convertible preferred stock into common stock upon the closing of this offering and excludes:

- 3,275,906 shares of common stock issuable upon exercise of stock options outstanding as of December 31, 2009 at a weighted average exercise price of $4.56 per share;
- 728,800 shares of convertible preferred stock issuable upon the exercise of warrants outstanding as of December 31, 2009 at a weighted average exercise price of $2.38 per share (such warrants will be converted into warrants to purchase 182,200 shares of common stock at a weighted average exercise price of $9.52 per share upon the consummation of this offering); and
- an aggregate of 395,876 shares of common stock reserved for future issuance under our stock incentive plans as of December 31, 2009 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.

If all our outstanding stock options and outstanding warrants had been exercised as of December 31, 2009, assuming the treasury stock method, our pro forma net tangible book value as of December 31, 2009 would have been approximately $(12.1) million or $(0.55) per share of our common stock, and the pro forma net tangible book value after giving effect to this offering would have been $1.94 per share, representing dilution in our pro forma net tangible book value per share to new investors of $7.06.

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SELECTED CONSOLIDATED FINANCIAL DATA

You should read the following selected consolidated financial data together with our financial statements, the related notes appearing at the end of this prospectus and the Management s Discussion and Analysis of Financial Condition and Results of Operations section of this prospectus.

We derived the annual consolidated financial data from our audited financial statements, the last three years of which are included elsewhere in this prospectus. We derived the summary statement of operations data for the years ended December 31, 2005 and 2006 and the balance sheet data as of December 31, 2005, 2006 and 2007 from our audited financial statements not 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. Pro forma basic and diluted net loss per common share have been calculated assuming the conversion of all outstanding shares of convertible preferred stock into shares of common stock.

	Years Ended December 31,				
	2005	2006	2007	2008	2009
	(in thousands, except per share data)				
Statement of operations data:					
Revenue	$ 6,213	$ 7,783	$ 11,034	$ 19,660	$ 20,719
Operating expenses:					
Research and development	17,758	26,845	29,248	41,821	51,792
General and administrative	4,783	5,161	6,502	9,164	10,120
Total operating expenses	22,541	32,006	35,750	50,985	61,912
Loss from operations	(16,328)	(24,223)	(24,716)	(31,325)	(41,193)
Other income and expense:					
Other income, net	7			18	(333)
Loss on loan extinguishment				(248)	
Interest expense	(635)	(1,591)	(2,437)	(2,086)	(2,811)
Interest income	859	909	2,171	1,168	144
Other income (expense), net	231	(682)	(266)	(1,148)	(3,000)
Net loss before taxes	(16,097)	(24,905)	(24,982)	(32,473)	(44,193)
Tax benefit					100
Net loss	$ (16,097)	$ (24,905)	$ (24,982)	$ (32,473)	(44,093)
Net loss per share applicable to common stockholders-basic and diluted	$ (12.35)	$ (18.73)	$ (17.89)	$ (21.08)	$ (27.43)
Weighted average number of common shares used in net loss per share calculation basic and diluted	1,303	1,330	1,396	1,541	1,607
Pro forma net loss per share basic and diluted (unaudited)					$ (2.23)
Shares used in computing pro forma net loss per share basic and diluted (unaudited)					19,768

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	As of December 31,				
	2005	2006	2007	2008	2009
			(in thousands)		
Balance sheet data:					
Cash, cash equivalents, and marketable securities	$ 25,991	$ 16,748	$ 61,742	$ 32,364	$ 51,301
Working capital	17,087	3,674	42,542	16,073	18,789
Total assets	33,074	22,448	67,654	40,087	59,844
Loans payable, including current portion	7,076	19,365	15,078	21,055	19,745
Preferred stock warrant liability		727	905	1,211	1,459
Convertible preferred stock	66,223	66,223	123,720	123,720	156,705
Accumulated deficit	(51,323)	(76,176)	(101,158)	(133,631)	(177,725)
Total stockholders deficit	(49,817)	(74,547)	(98,458)	(128,688)	(170,291)

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MANAGEMENT S DISCUSSION AND ANALYSIS OF

FINANCIAL CONDITION AND RESULTS OF OPERATIONS

You should read the following discussion and analysis of our financial condition and results of operations together with our financial statements and the related notes appearing at the end of this prospectus. Some of the information contained in this discussion and analysis or set forth elsewhere in this prospectus, including information with respect to our plans and strategy for our business and related financing, includes forward-looking statements that involve risks and uncertainties. You should read the Risk Factors section of this prospectus for a discussion of important factors that could cause actual results to differ materially from the results described in or implied by the forward-looking statements contained in the following discussion and analysis.

Overview

We are a biopharmaceutical company focused on discovering, developing and commercializing novel cancer therapeutics. Our product candidates are directed against important mechanisms 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. We have completed a successful 272-patient phase 2 clinical trial of tivozanib in patients with advanced renal cell cancer, or RCC, and initiated patient screening for a phase 3 clinical trial of tivozanib in patients with advanced RCC in December 2009, in which we plan to enroll 500 patients. We commenced enrollment of patients in the phase 3 clinical trial in February 2010. We are also conducting phase 1b clinical trials of tivozanib in RCC, breast, lung and colorectal cancer. We have completed a phase 1 clinical trial of our next most advanced product candidate, AV-299, and expect AV-299 to enter a phase 2 clinical trial for non-small cell lung cancer in the first half of 2010. We are also developing a pipeline of earlier stage novel antibodies which are designed to target mechanisms which we believe to be important in cancer. Our drug discovery and development activities are supported by our novel proprietary cancer modeling platform, which we refer to as our Human Response Platform. Our Human Response Platform is based on a unique method of building genetically-engineered preclinical models of human cancer, which are intended to more accurately reflect human disease.

We have devoted substantially all of our resources to our drug discovery efforts comprising research and development, conducting clinical trials for our product candidates, protecting our intellectual property and the general and administrative support of these operations. We have generated no revenue from product sales and, through December 31, 2009, have principally funded our operations through:

- $91.5 million of non-dilutive capital in the form of license fees, milestone payments and research and development funding received from our strategic partners; and
- $169.6 million of funding from the sale of convertible preferred stock to all of our investors, including $77.5 million of equity sales to our strategic partners.

We have never been profitable and, as of December 31, 2009, we had an accumulated deficit of $177.7 million. We incurred net losses of approximately $25.0 million, $32.5 million and $44.1 million in the years ended December 31, 2007, 2008 and 2009, respectively. We expect to incur significant and increasing operating losses for the foreseeable future as we advance our product candidates from discovery through preclinical studies and clinical trials to seek regulatory approval and eventual commercialization. We will need additional financing to support our operating activities. 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 will seek to fund our operations through public or private equity or debt financings or other sources, such as strategic partnerships. Adequate additional funding may not be available to us on acceptable terms, or at all. We expect that research and development expenses will increase along with

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general and administrative costs, as we grow and operate as a public company. We will need to generate significant revenues to achieve profitability and we may never do so.

Financial Obligations Related to the License and Development of Tivozanib

In December 2006, we entered into a license agreement with Kirin Brewery Co. Ltd. (now Kyowa Hakko Kirin) under which we obtained an exclusive license to research, develop, manufacture and commercialize tivozanib (f/k/a KRN951), pharmaceutical compositions thereof and associated biomarkers. Our exclusive license covers all territories in the world, except for Asia. Kyowa Hakko Kirin has retained rights to tivozanib in Asia. Under the license agreement, we obtained exclusive rights in our territory under certain Kyowa Hakko Kirin patents, patent applications and know-how related to tivozanib, to research, develop, make, have made, use, import, offer for sale, and sell tivozanib for the diagnosis, prevention and treatment of any and all human diseases and conditions.

Upon entering into the license agreement with Kyowa Hakko Kirin, we made a one-time cash payment in the amount of $5.0 million. We will be required to make a $10.0 milestone payment to Kyowa Hakko Kirin in connection with our phase 3 clinical trial of tivozanib, which we expect to pay in the first quarter of 2010. In addition, we may be required to make up to an aggregate of $50.0 million in additional milestone payments upon the achievement of specified regulatory milestones. We are also required to pay tiered royalty payments on net sales we make of tivozanib in our territory. The royalty rates under the agreement range from the low to mid teens as a percentage of our net sales of tivozanib. In the event we sublicense the rights licensed to us under the license agreement, we are required to pay Kyowa Hakko Kirin a specified percentage of any amounts we receive from any third party sublicensees, other than amounts we receive in respect of research and development funding or equity investments, subject to certain limitations.

Strategic Partnerships

OSI Pharmaceuticals

In September 2007, we entered into a collaboration and license agreement with OSI Pharmaceuticals, Inc., or OSI. 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 are currently working with OSI on the development of proprietary target-driven tumor models for use in target validation, drug screening and biomarker identification to support OSI s drug discovery and development activities. The research program portion of our strategic partnership began in October 2007 and will expire at the end of June 2011 unless the agreement is terminated earlier by either party. Under the terms of our agreement, OSI may, but has no obligation to, elect to obtain exclusive rights, with the right to grant sublicenses, under 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 agreement. 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. In July 2009, we expanded our strategic partnership with OSI and we granted OSI a non-exclusive license to use our proprietary bioinformatics platform, and non-exclusive, perpetual licenses to use bioinformatics data and to use a proprietary gene index related to a specific target pathway. Further, as part of our expanded strategic partnership, we granted OSI an option to receive non-exclusive perpetual rights to certain elements of our Human Response Platform and our bioinformatics platform, including the right to obtain certain of our tumor models and tumor archives. If OSI elects to exercise this additional option and we transfer the relevant technology to OSI, OSI will be required to pay us license expansion fees equal to, in the aggregate, $25 million.

In September 2007, OSI paid us an up-front payment of $7.5 million, which was recorded in deferred revenue and is being amortized over our period of substantial involvement which is now determined to be through July 2011. OSI also paid us $2.5 million for the first year of research program funding, which was recorded in deferred revenue and was recognized as revenue over the performance period and, thereafter, made sponsored research payments of $625,000 per quarter through July 2009. In addition, OSI purchased 1,833,334

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shares of series C convertible preferred stock, at a per share price of $3.00, resulting in gross proceeds to us of $5.5 million. We determined that the price paid of $3.00 per share by OSI represents a premium of $0.50 over the price per share for shares of our series D convertible preferred stock sold in April 2007; accordingly, we will recognize the premium of $917,000 as additional license revenue on a straight-line basis over the period of substantial involvement.

In July 2009 under the amended agreement, OSI paid us an up-front payment of $5.0 million, which was recorded in deferred revenue and will be amortized over our remaining period of substantial involvement. OSI also agreed to fund research costs through June 30, 2011. In addition, OSI purchased 3,750,000 shares of series E convertible preferred stock at a per share price of $4.00, resulting in gross proceeds to us of $15.0 million. We determined that the price of $4.00 per share paid by OSI represents a premium of $1.04 per share over the fair value of the series E convertible preferred stock of $2.96 as calculated by us in our retrospective stock valuation; accordingly, we will recognize the premium of $3.9 million as additional license revenue on a straight-line basis over the period of substantial involvement.

Under the new agreement, if all applicable milestones are achieved, payments for the successful achievement of discovery, development and commercialization milestones under the agreement could total, in the aggregate, over $94.0 million for each target and its associated products.

Under these agreements, we received cash payments related to upfront license fees, milestone payments, research and development funding, and sales of equity of $26.5 million, $2.0 million and $15.5 million, and recorded revenue of $9.8 million, $6.1 million and $1.1 million, for the years ended December 31, 2009, 2008 and 2007, respectively.

Biogen Idec

In March 2009, we entered into an exclusive option and license agreement with Biogen Idec International GmbH, a subsidiary of Biogen Idec Inc., which we collectively refer to herein as 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. 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 this phase 2 clinical trial and deliver to Biogen Idec a detailed data package containing the results thereof, Biogen Idec may elect to obtain (1) a co-exclusive (with us), worldwide license, including the right to grant sublicenses, under our relevant intellectual property to develop and manufacture ErbB3 antibody products, and (2) an exclusive license, including the right to grant sublicenses, 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 retain the exclusive right to commercialize ErbB3 antibody products in the United States, Canada and Mexico.

Under the terms of the agreement, Biogen Idec paid us an upfront cash payment of $5.0 million in March 2009, which will be amortized over our period of substantial involvement once determined. In addition, Biogen Idec purchased 7,500,000 shares of series E convertible preferred stock at a per share price of $4.00, resulting in gross proceeds to us of $30.0 million. We determined that the price of $4.00 paid by Biogen Idec includes a premium of $1.09 per share over the fair value of the series E convertible preferred stock of $2.91 as calculated by us in our retrospective stock valuation; accordingly, we will recognize the premium of $8.2 million as revenue on a straight-line basis over the period of substantial involvement. In June 2009, we received a $5.0 million milestone payment for achievement of the first pre-clinical discovery milestone under the agreement. We could also receive (i) a $5 million milestone payment related to the selection of a development candidate as well as another $5 million near-term pre-clinical discovery and development milestone payment, and (ii) if Biogen Idec exercises its option to obtain exclusive rights to commercialize ErbB3 antibody products in its territory, an option exercise fee and regulatory milestone payments of $50.0 million in the aggregate. Since the $5.0 million milestone payment received in June 2009 is a near term milestone and not considered to be substantive and at risk, the revenue is being amortized as additional license revenue over our period of substantial involvement. We expect to select a

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development candidate in the first quarter of 2010, and once a development candidate has been selected we will begin amortizing all license revenue under this agreement over the projected twenty-year patent life of the candidate.

Under this agreement, we received cash payments related to upfront license fees, milestone payments and sales of equity of $40.0 million for the year ended December 31, 2009. We have not yet recorded any revenue under this agreement as the period of substantial involvement had not yet been determined as of December 31, 2009.

Schering-Plough (now Merck)

In March 2007, we entered into an agreement with Schering-Plough Corporation, or Schering-Plough (now Merck & Co., Inc., or Merck), through its subsidiary Schering Corporation, acting through its Schering-Plough Research Institute division, under which we granted Merck exclusive, worldwide rights to develop and commercialize all of our monoclonal antibody antagonists of hepatocyte growth factor, or HGF, including AV-299, for therapeutic and prophylactic use in humans and for veterinary use. We also granted Merck an exclusive, worldwide license to related biomarkers for diagnostic use. Merck has the right to grant sublicenses under the foregoing licensed rights. We have primary responsibility for certain U.S.-related development activities through 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 clinical trial. We also 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.

Under the agreement, Merck paid us an up-front payment of $7.5 million in May 2007, which is being amortized over our period of substantial involvement, or through completion of the first proof-of-concept trial which is estimated for this purpose to be to be the first half of 2012. In addition, Merck purchased 4,000,000 shares of series D convertible preferred stock, at a per share price of $2.50, resulting in gross proceeds to us of $10.0 million. The amount paid for the series D convertible preferred stock represented fair value as it was the same as the amounts paid by unrelated investors in March and April 2007. Milestone payments for the successful development and commercialization of AV-299, if all approvals in multiple indications and all sales milestones are achieved, could total, in the aggregate, $464.0 million. Upon commercialization, we are eligible to receive tiered royalty payments on Merck s net sales of AV-299, which range from low double digits to high teens as a percentage of net sales. Under this agreement, we received cash payments related to upfront license fees, milestone payments, research and development funding and sales of equity of $10.6 million, $9.5 million and $25.8 million, and recorded revenue of $10.9 million, $13.3 million and $6.6 million, for the years ended December 31, 2009, 2008 and 2007, respectively.

Merck

In November 2003, we entered into a license and collaboration agreement with Merck to discover and validate oncology targets. During the research program portion of the collaboration, which concluded in November 2006, we used our proprietary cancer models to identify and subsequently validate essential tumor maintenance genes suitable as targets for small molecule drug development. During the research program, Merck exercised its option with respect to, and we granted Merck an exclusive, worldwide license, with the right to grant sublicenses, to six molecular targets, and associated data, discovered and validated by us under the research collaboration, to develop, manufacture and commercialize small molecule products directed to such targets for therapeutic use. In conjunction with the exclusive license granted to Merck, we granted Merck non-exclusive licenses, with the right to grant sublicenses, to (1) develop, manufacture and commercialize products and compounds directed at certain targets for diagnostic use, and (2) develop, manufacture and use biological products directed at certain targets solely for the research or development of products for therapeutic and/or diagnostic use. Merck is solely responsible for drug discovery, clinical development and commercialization of the products directed to the six collaboration targets it selected.

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If all development and regulatory milestones are reached with respect to each of the six targets, potential additional milestone payments could total, in the aggregate, $249.0 million. We are also eligible to receive tiered royalties from Merck based on the sales of products that are directed to or use the collaboration targets selected by Merck.

In August 2005, we entered into a second license and research collaboration agreement with Merck relating to the use of our Human Response Platform. Over the course of the collaborative research program, which has concluded, we received approximately $4.5 million in research funding. If all development and regulatory milestones under the agreement are achieved, potential milestone payments could total, in the aggregate, $4.9 million.

In connection with these agreements, Merck purchased an aggregate of 2,333,334 shares of series C convertible preferred stock, at a per share price of $3.00, resulting in gross proceeds to us of approximately $7.0 million.

Revenue earned under all Merck agreements was $3.2 million and $7.8 million for the years ended December 31, 2007 and 2006, respectively, for a total of $21.8 million earned under these agreements. No revenue was earned after 2007.

Financial Operations Overview

Revenue

To date, we have not generated any revenue from product sales. All of our revenue to date has been derived from license fees, milestone payments, and research and development payments received from our strategic partners.

In the future, we may generate revenue from a combination of product sales, license fees, milestone payments and research and development payments in connection with strategic partnerships, and royalties resulting from the sales of products developed under licenses of our intellectual property. We expect that any revenue we generate will fluctuate from quarter to quarter as a result of the timing and amount of license fees, research and development reimbursements, milestone and other payments received under our strategic partnerships, and the amount and timing of payments that we receive upon the sale of our products, to the extent any are successfully commercialized. We do not expect to generate revenue from product sales until 2013 at the earliest. If we or our strategic partners fail to complete the development of our drug candidates in a timely manner or obtain regulatory approval for them, our ability to generate future revenue, and our results of operations and financial position, would be materially adversely affected.

Research and Development Expenses

Research and development expense consists of expenses incurred in connection with the discovery and development of our product candidates. These expenses consist primarily of:

- employee-related expenses, which include salaries and benefits;
- expenses incurred under agreements with contract research organizations, investigative sites and consultants that conduct our clinical trials and a substantial portion of our preclinical studies;
- the cost of acquiring and manufacturing clinical trial materials;
- facilities, depreciation and other allocated expenses, which include direct and allocated expenses for rent and maintenance of facilities and equipment, and depreciation of fixed assets;
- license fees for and milestone payments related to in-licensed products and technology;

stock-based compensation expense to employees and non-employees; and

costs associated with non-clinical activities and regulatory approvals.

We expense research and development costs as incurred.

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Conducting a significant amount of research and development is central to our business model. Product candidates in late stages of clinical development generally have higher development costs than those in earlier stages of clinical development, primarily due to the increased size and duration of late stage clinical trials. We plan to increase our research and development expenses for the foreseeable future as we seek to complete development of our most advanced product candidate, tivozanib, and to further advance our earlier-stage research and development projects.

Prior to January 1, 2006, we did not record our internal research and development costs or our personnel and personnel-related costs on a project-by-project basis. Prior to 2006, our research resources were shared among all of our programs. Since January 1, 2006, we have tracked external development expenses and personnel expense on a program-by-program basis and have allocated common expenses, such as scientific consultants and lab supplies, to each program based on the personnel resources allocated to each program. Facilities, depreciation, stock-based compensation, research and development management and research and development support services are not allocated and are considered overhead. Below is a summary of our research and development expenses for the years ended December 31, 2007, 2008 and 2009:

	Years Ended December 31,		
	2007	2008	2009
		(in thousands)	
Tivozanib	$ 5,810	$ 14,231	$ 23,399
AV-299	4,101	5,671	6,498
AV-203 program		992	1,763
Platform collaborations	2,025	2,836	2,960
Antibody pipeline	4,660	5,176	5,523
Other research and development	5,010	3,437	2,358
Overhead	7,642	9,478	9,291
Total research and development expenses	$ 29,248	$ 41,821	$ 51,792

Tivozanib

We have completed a phase 2 clinical trial and in December 2009 initiated a phase 3 clinical trial for tivozanib in advanced RCC. We are also conducting phase 1b clinical trials of tivozanib in various combinations and dosing regimens in advanced RCC and additional solid tumor indications. Future research and development costs for the tivozanib program are not reasonably certain because such costs are dependent on a number of variables, including the cost and design of any additional clinical trials including additional trials in combination with other drugs, the timing of the regulatory process, and the success of the phase 3 clinical trial. Our current estimate for the cost of the phase 3 clinical trial program, including the cost of the comparator drug, Nexavar, is approximately $67.0 million. Additionally, we will be required to pay a $10.0 million milestone to Kyowa Hakko Kirin in connection with our phase 3 clinical trial of tivozanib, which we expect to pay in the first quarter of 2010. We may also be required to make up to an aggregate of $50.0 million in additional milestone payments to Kyowa Hakko Kirin upon the achievement of specified regulatory milestones. Further, we are required to pay tiered royalty payments on net sales we make of tivozanib in our territory, which range from the low to mid teens as a percentage of net sales. In the event we sublicense the rights licensed to us under the license agreement, we are required to pay Kyowa Hakko Kirin a specified percentage of any amounts we receive from any third party sublicensees, other than amounts we receive in respect of research and development funding or equity investments, subject to certain limitations.

AV-299

We have entered into a license agreement related to AV-299 with Schering-Plough (now Merck) and under the terms of the exclusive worldwide research, development and license agreement, we are responsible for leading the clinical development of AV-299 through completion of the first phase 2 proof-of-concept trial. All

expenses related to development are reimbursed by Merck in accordance with an agreed-upon budget. We record revenue and expenses on a gross basis under this arrangement. All future costs of this program are expected to be fully funded by Merck. We have completed a phase 1 clinical trial of AV-299 and expect to commence a phase 2 clinical trial of AV-299 in 2010.

AV-203 Program

Our AV-203 program is focused on identifying inhibitors of ErbB3 and is currently in preclinical development. We have granted Biogen Idec an exclusive option to co-develop (with us) and commercialize our ErbB3-targeted antibodies for the potential treatment and diagnosis of cancer and other diseases outside of the United States, Canada and Mexico. Due to the unpredictable nature of preclinical and clinical development and given the early stage of this program, we are unable to estimate with any certainty the costs we will incur in the future development of any candidate identified from this program. We expect to select a development candidate and commence manufacturing of this candidate in 2010 in preparation for preclinical and human clinical trials.

Platform Collaborations

We perform research services for third parties using our Human Response Platform. The related expenses, including personnel and related expenses, are captured as a cost of our various agreements with such third parties. Expenses incurred under our existing agreement with OSI are fully supported by the revenue from that agreement.

Antibody Pipeline

We expect that the expenses related to our antibody pipeline will continue to increase as we seek to identify additional targets for preclinical research and additional personnel are added to these projects. Future research and development costs for our antibody pipeline are not reasonably certain because such costs are dependent on a number of variables, including the success of preclinical studies on these antibodies and the identification of other potential candidates across multiple oncology indications.

The process of conducting preclinical studies and clinical trials necessary to obtain FDA approval for each of our product candidates is costly and time consuming. The probability of success for each product candidate and clinical trial may be affected by a variety of factors, including, among others, the quality of the product candidate s early clinical data, investment in the program, competition, manufacturing capabilities and commercial viability.

At this time, we cannot reasonably estimate or know the nature, specific timing and estimated costs of the efforts that will be necessary to complete the remainder of the development of our product candidates, or the period, if any, in which material net cash inflows may commence from our product candidates. This is due to the numerous risks and uncertainties associated with developing drugs, including the uncertainty of:

- the progress and results of our clinical trials;
- the scope, progress, results and costs of preclinical development, laboratory testing and clinical trials for any other product candidate;
- the costs, timing and outcome of regulatory review of our product candidates;
- our ability to establish and maintain strategic partnerships and the terms and success of those strategic partnerships, if any, including the timing and amount of payments that we might receive from potential strategic partners;
- the emergence of competing technologies and products and other adverse market developments; and

the costs of preparing, filing and prosecuting patent applications and maintaining, enforcing and defending intellectual property-related claims.

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As a result of the uncertainties discussed above, we are unable to determine the duration and completion costs of current or future clinical stages of our product candidates or when, or to what extent, we will generate revenues from the commercialization and sale of any of our product candidates. Development timelines, probability of success and development costs vary widely. We anticipate that we will make determinations as to which additional programs to pursue and how much funding to direct to each program on an ongoing basis in response to the scientific and clinical success of each product candidate, as well as ongoing assessment of the product candidate s commercial potential. We plan to develop additional product candidates internally which will increase significantly our research and development expenses in future periods. We will need to raise additional capital in the future in order to complete the development and commercialization of tivozanib and to fund the development of our other product candidates.

Other Research and Development

Other research and development includes expenses related to AV-412, a product candidate for which we have decided not to pursue further development, and certain funding related to our Human Response Platform which is not specifically related to a particular product candidate or a specific strategic partnership. AV-412 was the subject of a license agreement with Mitsubishi Pharma Corporation. We terminated the license agreement with Mitsubishi Pharma effective January 26, 2010. The costs to wind down this program are expected to be minimal.

General and Administrative Expenses

General and administrative expenses consist principally of salaries and related costs for personnel in executive, finance, business development, marketing, information technology, legal and human resources functions. Other general and administrative expenses include facility costs not otherwise included in research and development expenses, patent filing, prosecution and defense costs and professional fees for legal, consulting, auditing and tax services.

We anticipate that our general and administrative expenses will increase for, among others, the following reasons:

- we expect to incur increased general and administrative expenses to support our research and development activities, which we expect to expand as we continue the development of our product candidates;
- we may also begin to incur expenses related to the sales and marketing of our product candidates in anticipation of commercial launch before we receive regulatory approval of a product candidate; and
- we expect our general and administrative expenses to increase as a result of increased payroll, expanded infrastructure and higher consulting, legal, accounting and investor relations costs, and director and officer insurance premiums associated with being a public company.

Interest Income and Interest Expense

Interest income consists of interest earned on our cash and cash equivalents and marketable securities. The primary objective of our investment policy is capital preservation.

Interest expense consists primarily of interest, amortization of debt discount, and amortization of deferred financing costs associated with our loans payable.

Critical Accounting Policies and Significant Judgments and Estimates

Our discussion and analysis of our financial condition and results of operations are based on our consolidated financial statements, which have been prepared in accordance with accounting principles generally

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accepted in the United States. The preparation of these financial statements requires us to make estimates and judgments that affect the reported amounts of assets, liabilities, revenues and expenses and the disclosure of contingent assets and liabilities in our financial statements. On an ongoing basis, we evaluate our estimates and judgments, including those related to accrued expenses and stock-based compensation. We base our estimates on historical experience, known trends and events and various other factors that are believed to be reasonable under the circumstances, the results of which form the basis for making judgments about the carrying values of assets and liabilities that are not readily apparent from other sources. Actual results may differ from these estimates under different assumptions or conditions.

Our significant accounting policies are described in more detail in Note 2 of the notes to our consolidated financial statements appearing elsewhere in this prospectus. We believe the following accounting policies to be most critical to the judgments and estimates used in the preparation of our consolidated financial statements.

Revenue Recognition

Our revenues are generated primarily through collaborative research, development and commercialization agreements. The terms of these agreements typically include payment to us of one or more of the following: non-refundable, up-front license fees; funding of research and/or development efforts; milestone payments; and royalties on future product sales.

When evaluating multiple element arrangements, we consider whether the components of the arrangement represent separate units of accounting. This evaluation requires subjective determinations and requires management to make judgments about the fair value of the individual elements and whether such elements are separable from the other aspects of the contractual relationship.

We typically receive upfront, nonrefundable payments when licensing our intellectual property in conjunction with a research and development agreement. We believe that these payments generally are not separable from the activity of providing research and development services because the license does not have stand-alone value separate from the research and development services that we provide under our agreements. Accordingly, we account for these elements as one unit of accounting and recognize upfront, nonrefundable payments as revenue on a straight-line basis over our contractual or estimated performance period, which is typically the term of our research and development obligations. If we cannot reasonably estimate when our performance obligation ends, then revenue is deferred until we can reasonably estimate when the performance obligation ends. The periods over which revenue should be recognized are subject to estimates by management and may change over the course of the strategic partnership agreement. Such a change could have a material impact on the amount of revenue we record in future periods.

Our strategic partnership agreements may also contain milestone payments. Revenues from milestones, if they are nonrefundable and considered substantive, are recognized upon successful accomplishment of the milestones. If not considered substantive, milestones are initially deferred and recognized over the remaining performance obligation.

We receive payments and reimbursements for development activities undertaken by us for the benefit of our strategic partners and present them on a gross basis when we are acting as the principal in the arrangement, so long as there is persuasive evidence of an arrangement, the fee is fixed or determinable, and collection of the related receivable is reasonably assured.

We have not received any royalty revenues to date.

Accrued Clinical Expenses

As part of the process of preparing our financial statements, we are required to estimate our accrued expenses. This process involves reviewing open contracts and purchase orders, communicating with our applicable personnel to identify services that have been performed on our behalf and estimating the level of service performed and the associated cost incurred for the service when we have not yet been invoiced or

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otherwise notified of actual cost. The majority of our service providers invoice us monthly in arrears for services performed. We make estimates of our accrued expenses as of each balance sheet date in our financial statements based on facts and circumstances known to us at that time. We periodically confirm the accuracy of our estimates with the service providers and make adjustments if necessary. Examples of estimated accrued clinical expenses include:

- fees paid to contract research organizations in connection with clinical studies;
- fees paid to investigative sites in connection with clinical studies;
- fees paid to contract manufacturers in connection with the production of clinical trial materials; and
- fees paid to vendors in connection with the preclinical development activities.

We base our expenses related to clinical studies on our estimates of the services received and efforts expended pursuant to contracts with multiple research institutions and contract research organizations that conduct and manage clinical studies on our behalf. The financial terms of these agreements are subject to negotiation, vary from contract to contract and may result in uneven payment flows. Payments under some of these contracts depend on factors such as the successful enrollment of patients and the completion of clinical trial milestones. In accruing service fees, we estimate the time period over which services will be performed and the level of effort to be expended in each period. If the actual timing of the performance of services or the level of effort varies from our estimate, we adjust the accrual accordingly. Although we do not expect our estimates to be materially different from amounts actually incurred, our understanding of the status and timing of services performed relative to the actual status and timing of services performed may vary and may result in us reporting amounts that are too high or too low in any particular period. Based on our level of clinical trial expenses as of December 31, 2009, if our estimates are too high or too low by 5%, this may result in an adjustment to our accrued clinical trial expenses in future periods of approximately $231,000.

Stock-Based Compensation

Effective January 1, 2006, we adopted the fair value recognition provisions of Financial Accounting Standards Board Accounting Standards Codification, or ASC, 718 Accounting for Stock Based Compensation (formerly Statement of Financial Accounting Standards No. 123(R), Share-Based Payments), which we refer to as ASC 718, using the modified prospective transition method. The modified prospective transition method applies the provisions of ASC 718 to new awards and to awards modified, repurchased or cancelled after the adoption date. Additionally, compensation cost for the portion of the awards for which the requisite service has not been rendered that are outstanding as of the adoption date is recognized in the Statement of Operations over the remaining service period after the adoption date based on the award s original estimate of fair value. All stock-based awards granted to non-employees are accounted for at their fair value in accordance with ASC 718, and ASC 505, Accounting for Equity Instruments that are Issued to Other Than Employees for Acquiring, or in Conjunction with Selling, Goods or Services, under which compensation expense is generally recognized over the vesting period of the award. Determining the amount of stock-based compensation to be recorded requires us to develop estimates of fair values of stock options as of the grant date. Calculating the fair value of stock-based awards requires that we make highly subjective assumptions. We use the Black-Scholes option pricing model to value our stock option awards. Our expected stock price volatility is based on an average of several peer companies. For purposes of identifying peer companies, we considered characteristics such as industry, length of trading history, similar vesting terms and in-the-money option status. For periods prior to 2009, we used an average of several peer companies with the characteristics described above to calculate our expected term given our limited history. For 2009, due to lack of available quarterly data for these peer companies, we elected to use the simplified method for plain vanilla options to estimate the expected term of the stock option grants. Under this approach, the weighted-average expected life is presumed to be the average of the vesting term and the contractual term of the option. We utilize a dividend yield of zero based on the fact that we have never paid cash dividends and have no present intention to pay cash dividends. The risk-free interest rate used for each grant is based on the U.S. Treasury yield curve in effect at the time of grant for instruments with a similar expected life.

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The fair value of stock options was estimated at the grant date using the following assumptions:

	Years Ended December 31,		
	2007	2008	2009
Volatility	68.16%	68.70%	70.35%-72.04%
Expected Term (in years)	5.58	5.61	5.50-6.25
Risk-Free Interest Rates	3.49%-5.03%	1.55%-3.34%	1.98%-3.04%
Dividend Yield			

We recognized stock based compensation expense of approximately $788,000, $2.3 million and $2.4 million for the years ended December 31, 2007, 2008, and 2009, respectively, in accordance with ASC 718. As of December 31, 2009, we had $4.4 million in total unrecognized compensation expense, net of related forfeiture estimates which we expect to recognize over a weighted-average period of approximately 2.3 years.

Upon the adoption of ASC 718, we were also required to estimate the level of forfeitures expected to occur and record compensation expense only for those awards that we ultimately expect will vest. We performed a historical analysis of option awards that were forfeited prior to vesting and recorded total stock option expense that reflected this estimated forfeiture rate.

We have historically granted stock options at exercise prices not less than the fair market value of our common stock as determined by our board of directors, with input from management. Our board of directors has historically determined the estimated fair value of our common stock on the date of grant based on a number of objective and subjective factors, including external market conditions affecting the biotechnology industry sector, the prices at which we sold shares of convertible preferred stock, the superior rights and preferences of securities senior to our common stock at the time of each grant, the results of operations, financial position, status of our research and development efforts, our stage of development and business strategy and the likelihood of achieving a liquidity event such as an initial public offering, or IPO, or sale of our company.

The following table presents the grant dates and related exercise prices of stock options granted to employees since December 18, 2008:

Date	Number of Shares Subject to Options Granted	Exercise Price	Reassessed Fair Value of Common Stock Per Share at Date of Grant	Intrinsic Value at Date of Grant
December 18, 2008	2,500	$ 6.88	$ 7.12	$ 0.24
January 30, 2009	114,437	$ 8.00	$ 8.60	$ 0.60
April 1, 2009	145,526	$ 8.48	$ 9.28	$ 0.80
June 16, 2009	94,300	$ 8.72	$ 10.04	$ 1.32
July 17, 2009	10,000	$ 8.72	$ 10.04	$ 1.32
October 8, 2009	208,025	$ 9.64	$ 10.40	$ 0.76
December 17, 2009	18,887	$ 11.32	N/A	N/A
February 2, 2010	398,182	$ 12.24	N/A	N/A
Total	991,857			

The exercise price for stock options granted above was set by our board of directors based upon our valuation models. Our valuation models used the Market Approach and the Probability Weighted Expected Return Method as outlined in the AICPA Technical Practice Aid, *Valuation of Privately-Held-Company Equity Securities Issued as Compensation*, or Practice Aid. The exercise prices for stock options granted on December 18, 2008, January 30, 2009, April 1, 2009, June 16, 2009, July 17, 2009, October 8, 2009, December 17, 2009 and February 2, 2010 were determined by the results of our contemporaneous valuations completed in November 2008, January 2009, March 2009, June 2009, September 2009, December 2009 and January 2010, respectively. These valuations considered the following scenarios for achieving shareholder liquidity:

an IPO;

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sale of the company at an equity value greater than the aggregate liquidation preference of the preferred stock; and

sale of the company at an equity value equal to or less than the aggregate liquidation preference of the preferred stock.

In connection with the preparation of the consolidated financial statements for the year ended December 31, 2009 and in preparing for an IPO, we reexamined the contemporaneous valuations of our common stock during the period November 2008 to September 2009. In connection with that reexamination, we prepared retrospective valuation reports of the fair value of our common stock for financial reporting purposes as of November 28, 2008, January 15, 2009, March 20, 2009, June 1, 2009 and September 25, 2009. We believe that the valuation methodologies used in the retrospective valuations and the contemporaneous valuations are reasonable and consistent with the Practice Aid. We also believe that the preparation of the retrospective valuations was necessary due to the fact that the timeframe and probability for a potential IPO had accelerated significantly since the time of our initial contemporaneous valuations.

In the IPO scenario for our retrospective and contemporaneous valuations, on November 28, 2008 and January 15, 2009, we applied the guideline transactions method under the market approach as provided in the Practice Aid and for the subsequent valuations, we applied the guideline public company method under the market approach as provided in the Practice Aid due to the very limited number of biotechnology company IPOs in 2008 and 2009. Our selection of guideline companies included companies deemed comparable because of their disease focus (oncology), stage of clinical trials, and size.

In the sale above liquidation preference scenario for each of our retrospective and contemporaneous valuations, we applied the guideline transactions method under the market approach as provided in the Practice Aid. Our selection of guideline transactions took into account the timing of the transactions and the characteristics of the acquired companies. We selected target companies which were deemed comparable because of their disease focus (oncology), stage of clinical trials, and size.

In the liquidation scenario for each of our retrospective and contemporaneous valuations, we assumed a sale or liquidation of the company at an equity value equal to the aggregate liquidation preference of our preferred stock.

Future values for each scenario are converted to present value by applying a discount rate estimated using a size-adjusted capital asset pricing model, or CAPM. As described in the Practice Aid, the CAPM takes into account risk-free rates, an equity risk premium, the betas of selected public guideline companies and a risk premium for size. The estimated discount rate includes a premium for company-specific risk as well.

In our application of CAPM, on each of the valuation dates disclosed, we assumed a risk-free rate of 3.17% to 4.56% based on long-term U.S. Treasuries, a supply-side equity-risk premium of 5.0% to 6.2% based on Ibbotson s *SBBI Valuation Yearbook* and *PPC s Guide to Business Valuation*, a beta of 1.27 to 1.71 based on historical trading data for our guideline public companies and a risk premium for size of 2.71% to 5.82% based on Ibbotson s *SBBI Valuation Yearbook* and company-specific risk of 5.5% to 10.0%. Changes in the risk-free rate, the equity-risk premium and beta reflect changes in market conditions. Market volatility in late 2008 and early 2009 corresponded to a decline in guideline public company betas. Changes in the risk premium for size reflect changes in the value of the company relative to the categories of size reported by Ibbotson. The company-specific risk premium reflects the significant overall business risk associated with our pre-commercial stage of development prior to the IPO and also includes our:

dependence on the success of our lead drug candidate, tivozanib, which is in phase 3 development;

short operating history and history of operating losses since inception;

need for substantial additional financing to achieve our goals; and

dependence on a limited number of collaboration partners.

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In our retrospective valuations for the period from November 2008 to September 2009 and our contemporaneous valuations for December 2009 and January 2010, we estimated the following probabilities and future sale and IPO dates:

Appraisal Date	11/28/08	1/15/09	3/20/09	6/1/09	9/25/09	12/17/09	2/2/10
Exercise price per share of options	$ 6.88	$ 8.00	$ 8.48	$ 8.72	$ 9.64	$ 11.32	$ 12.24
Reassessed fair value of common stock per share at date of grant	$ 7.12	$ 8.60	$ 9.28	$ 10.04	$ 10.40	N/A	N/A
Probabilities							
IPO in Q1 2010	20%	25%	35%	40%	25%	35%	35%
IPO in Q2 2010					25%	35%	35%
Sale above liquidation preference	70%	70%	60%	55%	45%	25%	25%
Sale below liquidation preference	10%	5%	5%	5%	5%	5%	5%
Future sale date	12/31/09	12/31/10	12/31/10	9/30/11	9/30/11	9/30/11	9/30/11
1st IPO date	12/31/09	12/31/09	3/31/10	3/31/10	3/31/10	3/31/10	3/31/10
2nd IPO date					6/30/10	6/30/10	6/30/10
Discount rate	24%	24%	24%	24%	24%	24%	24%

The estimated fair market value of our common stock at each valuation date is equal to the sum of the probability weighted present values for each scenario.

We have incorporated the fair values calculated in the retrospective valuations into the Black-Scholes option pricing model when calculating the stock-based compensation expense to be recognized for the stock options granted during the period November 2008 to September 2009. The retrospective valuations generated per share fair values of common stock of $7.12, $8.60, $9.28, $10.04 and $10.40, respectively, at November 2008 and January, March, June and September 2009, respectively. This resulted in intrinsic values of $0.24, $0.60, $0.80, $1.32 and $0.76 per share, respectively, at each grant date.

The retrospective fair values of our common stock increased throughout 2009 thereby reducing the difference between the fair value of our common stock and the estimated IPO price range. The increases were caused by business and scientific milestones, financing transactions and the proximity to a potential IPO. The retrospective fair value of our common stock underlying options to purchase 2,500 shares granted on December 18, 2008 was determined to be $7.12 per share. The fair value of the common stock on that date took into account changes in the following factors:

- initiation of a phase 1 clinical trial for AV-299, for which the first patient dosed triggered a $3.0 million milestone payment from Merck; and
- because of the unfavorable conditions in the public markets, we deemed the probability of an IPO to be low, or 20%.

The retrospective fair value of our common stock underlying options to purchase 114,437 shares granted on January 30, 2009 was determined to be $8.60 per share. The increase in value from the November 2008 valuation was primarily due to the following:

- we received a term sheet for the Biogen Idec agreement for ErbB3 that included a proposed $30.0 million investment in new series E convertible preferred stock which would be priced at a premium to our other series of convertible preferred stock;
- the expected proceeds from the Biogen Idec agreement would improve our position for funding future cash needs;
- due to our progress, including continued progress of our phase 2 clinical trial of tivozanib showing a favorable safety profile in patients with advanced RCC, we deemed that the probability of an IPO increased to 25% and the probability of a sale below the

liquidation preference decreased to 5%; and

the timeline for a sale above the liquidation preference was extended due to expected timing of enrollment of our phase 3 clinical trial of tivozanib.

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The retrospective fair value of our common stock underlying options to purchase 145,526 shares granted on April 1, 2009 was determined to be $9.28 per share. The increase in value from the January 2009 valuation was primarily due to the following:

- execution of the agreement with Biogen Idec, which included a $30.0 million investment in series E convertible preferred stock at $4.00 per share and a $5.0 million upfront payment;
- we initiated a phase 1b/2a clinical trial of tivozanib as monotherapy for the treatment of non-small cell lung cancer; and
- due to our progress, including continued progress of our phase 2 clinical trial of tivozanib showing a favorable safety profile in patients with advanced RCC, we deemed that the probability of an IPO increased to 35%, although the assumed timing was adjusted to March 31, 2010 due to our assessment of current market conditions.

The retrospective fair value of our common stock underlying options to purchase 94,300 shares granted on June 16, 2009 was determined to be $10.04 per share. The increase in value from the March 2009 valuation was primarily due to the following:

- in May 2009, we announced additional data from our phase 2 clinical trial of tivozanib, which demonstrated an overall median progression-free survival of patients of 11.8 months and a favorable safety profile in patients with advanced RCC;
- due to our progress with respect to tivozanib, including the data noted above, we deemed that the probability of an IPO increased to 40%; and
- the timeline for a sale above the liquidation preference was extended to September 30, 2011, which is closer to the date we anticipate that data will become available from our phase 3 clinical trial of tivozanib.

The retrospective fair value of our common stock underlying options to purchase 208,025 shares granted on October 8, 2009 was determined to be $10.40 per share. The increase in value from the June 2009 valuation was primarily due to the following:

- execution of an agreement with OSI which included a $15.0 million investment in Series E convertible preferred stock at $4.00 per share and a $5.0 million upfront payment;
- our plans to commence the phase 3 clinical trial of tivozanib; and
- due to our progress and plans to commence a phase 3 clinical trial of tivozanib, we deemed that the probability of an IPO increased to 50%, with a 25% probability of an IPO being completed in the first quarter of 2010 and a 25% probability of an IPO being completed in the second quarter of 2010.

The fair value of our common stock underlying options to purchase 18,887 shares granted on December 17, 2009 was determined to be $11.32 per share. The increase in value from the October 2009 valuation was primarily due to the following:

- initiation of the phase 3 clinical trial of tivozanib; and

due to our progress and initiation of the phase 3 clinical trial of tivozanib, we deemed that the probability of an IPO increased to 70%, with a 35% probability of an IPO being completed in the first quarter of 2010 and a 35% probability of an IPO being completed in the second quarter of 2010.

The fair value of our common stock underlying options to purchase 398,182 shares granted on February 2, 2010 was determined to be $12.24 per share. The increase in value from the December valuation was primarily due to a reduction in the period of time before the expected completion of an IPO.

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On February 9, 2010, we and the underwriters determined a preliminary range for the initial public offering price. The midpoint of the range was $14.00 per share as compared to $12.24 per share, which was based on management s contemporaneous valuation prepared on January 22, 2010, of the estimated fair value of our common stock. The $12.24 was used on February 2, 2010, the date of our most recent grant of stock options. This estimated fair value represents a discount of approximately 12.6% from the midpoint of the range and an increase of 8% from the estimated fair value of our common stock on December 17, 2009. We note that, as is typical in initial public offerings, the preliminary range was not derived using a formal determination of fair value, but was determined based upon discussions between us and the underwriters. Among the factors considered in setting the preliminary range were prevailing market conditions and estimates of our business potential. In addition to this difference in purpose and methodology, we believe that the difference in value reflected between the midpoint of the preliminary range and management s determination of the estimated fair value of our common stock on January 22, 2010 was primarily the result of the following factors:

- The contemporaneous valuation we prepared on January 22, 2010 contained multiple scenarios including two IPO scenarios with an aggregate probability of 70% and two sale scenarios. If we had considered only a single scenario with 100% probability and that assumed that the IPO will be completed as of March 31, 2010, the contemporaneous valuation would have resulted in a fair value determination of $14.48 per share.

- On February 2, 2010, Ironwood Pharmaceuticals completed their initial public offering, which we believe demonstrates a significant improvement in the market for initial public offerings in the U.S. in the biopharmaceutical industry. We note, however, that Ironwood s initial public offering was completed at $11.25 per share, or a 25% discount from the midpoint of their filing range.

- Our February 2010 discussions with the underwriters took into account our and the underwriters perceptions of significantly increased optimism regarding the market for initial public offerings, and confirmed our and our underwriters expectations that we would complete our initial public offering by the end of the first quarter of 2010. As noted above, our January 22, 2010 contemporaneous valuation included a scenario with a 35% probability that the IPO would not be completed until the end of the second quarter of 2010.

- History has shown that it is reasonable to expect that the completion of an initial public offering will increase the value of stock as a result of the significant increase in the liquidity and ability to trade/sell such securities. However, it is not possible to measure such increase in value with precision or certainty.

Based on the $14.00 midpoint of the preliminary range, the intrinsic value of the options granted on February 2, 2010, the last date we granted stock options, was approximately $701,000, all of which related to unvested options. Also based on the $14.00 midpoint of the preliminary range, the intrinsic value of outstanding options as of February 2, 2010 was $31.3 million, of which $24.3 million related to vested options and $7.0 million related to unvested options.

There are significant judgments and estimates inherent in the determination of these valuations. These judgments and estimates include assumptions regarding our future performance, the time to completing an IPO or other liquidity event, and the timing of and probability of successful completion of our clinical trials as well as determinations of the appropriate valuation methods. If we had made different assumptions, our share-based compensation expense, net loss and net loss per share could have been significantly different.

Valuation models require the input of highly subjective assumptions. Because our common stock has characteristics significantly different from that of publicly traded common stock and because changes in the subjective input assumptions can materially affect the fair value estimate, in management s opinion, the existing models do not necessarily provide a reliable, single measure of the fair value of our common stock. The foregoing valuation methodologies are not the only valuation methodologies available and will not be used to value our common stock once this offering is complete. We cannot make assurances as to any particular valuation for our stock. Accordingly, investors are cautioned not to place undue reliance on the foregoing valuation methodologies as an indicator of future stock prices.

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Results of Operations

Comparison of Years Ended December 31, 2008 and 2009

	Years Ended December 31,		Increase/	
	2008	2009	(decrease)	%
	(in thousands)			
Revenue	$ 19,660	$ 20,719	$ 1,059	5%
Operating expenses:				
Research and development	41,820	51,792	9,972	24%
General and administrative	9,165	10,120	955	10%
Total operating expenses	50,985	61,912	10,927	21%
Loss from operations	(31,325)	(41,193)	(9,868)	32%
Other income (expense), net	18	(333)	(351)	(1950)%
Loss on loan extinguishment	(248)		248	(100)%
Interest income	1,168	144	(1,024)	(88)%
Interest expense	(2,086)	(2,811)	(725)	35%
Loss before taxes	(32,473)	(44,193)	(11,720)	36%
Taxes		100	100	
Net loss	$ (32,473)	$ (44,093)	$ (11,620)	36%

Revenue	Years Ended December 31, 2008	2009	Increase/ (decrease)	%
	(in thousands)			
Strategic Partner:				
Schering-Plough (Merck)	$ 13,349	$ 10,853	$ (2,496)	(19)%
OSI Pharmaceuticals	6,144	9,788	3,644	59%
Kyowa Hakko Kirin		78	78	
Eli Lilly	167		(167)	(100)%
	$ 19,660	$ 20,719	$ 1,059	5%

Revenue. Revenue for the year ended December 31, 2009 was $20.7 million compared to $19.7 million for the year ended December 31, 2008, an increase of approximately $1.1 million or 5%. Revenue for the year ended December 31, 2008 included a $3.0 million milestone payment from Schering-Plough (now Merck) for the first human dosed in the phase 1 clinical trial of AV-299. There was no corresponding milestone in 2009. Excluding the $3.0 million milestone payment in 2008, revenue for the year ended December 31, 2009 increased $4.1 million over the same period in 2008. The increase was attributable to an increase in amortization of deferred revenue associated with the amended OSI agreement in the amount of $2.4 million; an increase in research revenue earned under the OSI agreement of $1.3 million; additional research and development revenue of $1.0 million earned under the agreement with Schering-Plough (now Merck); and a $0.1 million reimbursement by Kyowa Hakko Kirin for our supply of tivozanib to Kyowa Hakko Kirin to be used in a phase 1 clinical trial which Kyowa Hakko Kirin is conducting in Japan. These increases were offset by a decrease of $0.5 million in amortization of deferred revenue under the agreement with Schering-Plough (now Merck) due to a change in the estimated period of our substantial involvement and $0.2 million in revenue from Eli Lilly and Company pursuant to our agreement with Eli Lilly and Company which ended in 2008.

Research and Development. Research and development expense for the year ended December 31, 2009 was $51.8 million compared to $41.8 million for the year ended December 31, 2008, an increase of $10.0 million or 24%. The increase was primarily attributable to a $3.0 million purchase of Nexavar, the comparator drug

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which will be used in our phase 3 clinical trial of tivozanib; an increase in clinical trial costs of $2.1 million resulting primarily from costs for the phase 3 clinical trial of tivozanib offset by a reduction in costs of the phase 2 clinical trial for tivozanib as it winds down; an increase in spending for toxicology supporting tivozanib of $1.4 million; a $1.4 million increase in salaries and benefits mainly due to an increase in personnel primarily supporting development activities for tivozanib and our antibody pipeline; a $1.0 million increase in contract manufacturing for tivozanib to support an increasing number of trials, including our phase 3 clinical trial; a $0.8 million increase in costs related to AV-299 which are reimbursed by Merck but recorded on a gross basis; a $0.5 million increase in outsourced services primarily supporting research activities for the antibody pipeline; a $0.4 million increase in lab supplies and mice; a $0.4 million increase in stock-based compensation for employees and nonemployees; and a $0.2 million increase in facility expenses as result of our lease in September 2008 of an additional 7,407 square foot of space. These increases were offset by a decrease in licensing costs of $0.8 million as a result of a license of a third party drug discovery technology in 2008 which was fully expensed in 2008; and a $0.3 million decrease in contract manufacturing costs for the AV-412 program which has been discontinued.

Included in research and development expense were stock-based compensation charges of $1.2 million and $0.8 million for the years ended December 31, 2009 and 2008, respectively.

General and Administrative. General and administrative expense for the year ended December 31, 2009 was $10.1 million compared to $9.2 million for the year ended December 31, 2008, an increase of $1.0 million or 10%. The increase was primarily a result of $0.8 million in salaries and benefits mainly due to an increase in personnel needed to support increased research and development; a $0.2 million increase in consulting associated with finance and marketing; a $0.1 million increase in patent expenses related to AV-299 which are reimbursed by Merck but are recorded on a gross basis; a $0.1 million increase in legal expenses primarily related to the support of our phase 3 clinical trial of tivozanib; and a $0.1 million increase in public relations expense. Such increases were partially offset by a $0.4 million decrease in stock-based compensation expense. The decrease in stock-based compensation expense results from a $0.8 million share-based expense for a stock issuance in 2008 to a former consultant and an entity affiliated with a board member after a warrant held by such entity expired unexercised.

Included in general and administrative expense were stock-based compensation charges of $1.1 million and $1.5 million for the years ended December 31, 2009 and 2008, respectively. Stock-based compensation charges for 2008 included a $0.8 million share-based expense for a stock issuance in 2008 to a former consultant and an entity affiliated with a board member after a warrant held by such entity expired unexercised.

Other Income (Expense), Net. Other income (expense), net for the year ended December 31, 2009 was ($0.3 million) compared to $18,000 for the year ended December 31, 2008, a decrease of $0.4 million. The decrease was largely a result of a charge for the increase in the value of warrants to purchase preferred stock resulting from an increase in value of the underlying stock.

Loss on Loan Extinguishment. Loss on loan extinguishment in 2008 resulted from the repayment of an existing loan upon entering into a new loan agreement. Under the guidance for Debtor s Accounting for a Modification or Exchange of Debt Instruments, the repayment was considered an extinguishment of debt and the remaining loan discount and prepaid loan fees of $0.2 million were recorded as a loss on loan extinguishment.

Interest Income. Interest income for the year ended December 31, 2009 was $0.1 million compared to $1.2 million for the year ended December 31, 2008, a decrease of $1.0 million or 88%. Although the average cash balances were higher for the year ended December 31, 2009, interest rates decreased to only slightly above 0% in 2009 causing the significant decrease in interest income.

Interest Expense. Interest expense for the year ended December 31, 2009 was $2.8 million compared to $2.1 million for the year ended December 31, 2008, an increase of $0.7 million or 35%. The increase was due to an increase in the average loan balance in 2009 due to a drawdown of $10.0 million in September 2008 which was outstanding for the full period of 2009.

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Comparison of Years Ended December 31, 2007 and 2008

	Years Ended December 31,		Increase/	
	2007	2008	(decrease)	%
	(in thousands)			
Revenue	$ 11,034	$ 19,660	$ 8,626	78%
Operating expenses:				
Research and development	29,248	41,820	12,572	43%
General and administrative	6,502	9,165	2,663	41%
Total operating expenses	35,750	50,985	15,235	43%
Loss from operations	(24,716)	(31,325)	(6,609)	27%
Other income, net		18	18	
Loss on loan extinguishment		(248)	(248)	
Interest income	2,171	1,168	(1,003)	(46)%
Interest expense	(2,437)	(2,086)	351	(14)%
Net loss	$ (24,982)	$ (32,473)	$ (7,491)	30%

Revenue	Years Ended December 31, 2007	2008	Increase/ (decrease)	%
		(in thousands)		
Strategic Partner:				
Schering-Plough (Merck)	$ 6,624	$ 13,349	$ 6,725	102%
OSI Pharmaceuticals	1,083	6,144	5,061	467%
Merck	3,244		(3,244)	(100)%
Eli Lilly and Company	83	167	84	101%
	$ 11,034	$ 19,660	$ 8,626	78%

Revenue. Revenue for the year ended December 31, 2008 was $19.7 million compared to $11.0 million for the year ended December 31, 2007, an increase of $8.6 million, or 78%. The increase resulted from a $6.7 million increase in revenue from Schering-Plough (now Merck) consisting of a $3.0 million milestone for the start of the phase 1 clinical trial for AV-299; a $2.6 million increase in research and development funding; and a $1.1 million increase in revenue related to the amortization of upfront licensing fees and milestones. We entered into the agreement with Schering-Plough (now Merck) in March 2007, therefore 2008 represents a full year of funding. Additionally, OSI revenue increased by $5.1 million, consisting of a $2.8 million increase in research funding and a $2.3 million increase in amortization of upfront licensing fees and milestones. The OSI agreement was signed in September 2007, therefore 2008 represents a full year of funding. The increases in Schering-Plough (now Merck) and OSI revenues were offset by a decrease in revenue of $3.2 million under the initial Merck agreement as the strategic partnership was completed in 2007.

Research and Development. Research and development expense for the year ended December 31, 2008 was $41.8 million compared to $29.2 million for the year ended December 31, 2007, an increase of $12.6 million, or 43%. The increase was primarily attributable to a $6.4 million increase in clinical trial expenses principally due to the phase 2 clinical trial of tivozanib, which began in October 2006 and was fully enrolled in July 2007; an increase in salaries and benefits costs of $2.4 million due primarily to an increase in personnel related to clinical development of tivozanib, our antibody pipeline and our strategic partnerships with Merck and OSI; a $1.7 million increase in lab supplies and mice due primarily to an increase in scientific personnel and support for our agreement with OSI; a $0.9 million increase in expenses related to AV-299 which are fully reimbursed by Schering-Plough (now Merck) but are recorded on a gross basis; an increase in licensing costs of $0.8 million as a result of a license of a third party drug discovery technology in 2008 which was fully expensed in 2008; and a $0.4 million increase in stock-based compensation expense.

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Included in research and development expense were stock-based compensation charges of $424,000 and $810,000 for the years ended December 31, 2007 and 2008, respectively.

General and Administrative. General and administrative expense for year ended December 31, 2008 was $9.2 million compared to $6.5 million for the year ended December 31, 2007, an increase of $2.7 million, or 41%. The increase was a result of a $1.0 million increase in salaries and benefits due primarily to an increase in personnel needed to support increased research and development; a $0.8 million expense for a stock issuance in 2008 to a former consultant and an entity affiliated with a board member, after a warrant held by such entity had expired unexercised; a $0.3 million increase in stock compensation expense; a $0.2 million increase in consulting expenses; a $0.1 million increase in recruiting expenses; a $0.1 increase in travel costs; and a $0.1 increase in facility allocation due to an increase in personnel.

Included in general and administrative expenses were stock-based compensation charges of $364,000 and $1,495,000 for the years ended December 31, 2007 and 2008, respectively. Stock-based compensation charges for the year ended December 31, 2008 included a $804,500 share-based expense for a stock issuance in 2008 to a former consultant and an entity affiliated with a board member, after a warrant held by such entity had expired unexercised as noted above.

Other Income, Net. Other income, net for 2008 represented net gains on sale of assets of $11,000 and $7,000 from the revaluation of warrants to purchase preferred stock.

Loss on Loan Extinguishment. Loss on loan extinguishment in 2008 resulted from the repayment of an existing loan upon entering into a new loan agreement. Under the guidance for Debtor s Accounting for a Modification or Exchange of Debt Instruments, the repayment was considered an extinguishment of debt and the remaining loan discount and prepaid loan fees of $248,000 were recorded as a loss on loan extinguishment.

Interest Income. Interest income for the year ended December 31, 2008 was $1.2 million compared to $2.2 million for the year ended December 31, 2007, a decrease of $1.0 million, or 46%. The decrease in interest income was a result of a decrease in interest rates from an average rate of 5.0% in 2007 to an average rate of 2.7% in 2008.

Interest Expense. Interest expense for the year ended December 31, 2008 was $2.1 million compared to $2.4 million for the year ended December 31, 2007, a decrease of approximately $0.4 million, or 14%. The decrease in interest expense was a result of a beneficial conversion charge in 2007 in the amount of $0.2 million related to a conversion option given to a financing institution which was extinguished in March 2007 upon the closing of the series D convertible preferred stock financing in which the financing institution chose not to exercise its option. The remaining $0.2 million decrease was a result of a lower principal balance under our equipment financing line with General Electric Capital Corporation.

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Liquidity and Capital Resources

We have funded our operations principally through the private placement of equity securities, revenue from strategic partnerships, debt financing and interest income. As of December 31, 2009, we have received gross proceeds of $169.6 million from the issuance of convertible preferred stock, including $52.9 million from the sale of 21,165,510 shares of series D convertible preferred stock in 2007 and $32.9 million from the sale of 11,250,000 shares of series E convertible preferred stock in 2009. As of December 31, 2009, we had received an aggregate of $91.5 million in cash from our three agreements with Merck and our agreements with OSI, Biogen Idec and Eli Lilly, and $21.0 million in funding from our debt financing with Hercules Technology Growth Capital, Inc., or Hercules, and Comerica Bank. As of December 31, 2009, we had cash, cash equivalents and short-term investments of approximately $51.3 million. Currently, our funds are invested in money market funds, U.S. Treasuries, U.S. government agencies and commercial paper. The following table sets forth the primary sources and uses of cash for each of the periods set forth below:

	Years Ended December 31,		
	2007	2008	2009
		(in thousands)	
Net cash provided by (used in) operating activities	$ (8,605)	$ (35,301)	$ (9,973)
Net cash provided by (used in) investing activities	(39,894)	28,151	3,414
Net cash provided by (used in) financing activities	52,834	6,881	31,035
Net increase (decrease) in cash and cash equivalents	$ 4,335	$ (269)	$ 24,476

During 2007, 2008 and 2009, our operating activities used cash of $8.6 million, $35.3 million and $10.0 million, respectively. The use of cash in all periods primarily resulted from our net losses adjusted for non-cash items and changes in operating assets and liabilities. The cash used in operations in 2007 was due primarily to our net loss adjusted for non-cash items and an increase in deferred revenue related to upfront license payments and near term milestones of $17.5 million from our strategic partners OSI and Schering-Plough (now Merck) offset by payment of a $5.0 million license fee to Kyowa Hakko Kirin accrued in 2006. The increase in cash used for the year ended 2008 resulted from an increase in research and development activities. The decrease in cash used for 2009 was primarily the result of an increase in deferred revenue of $22.0 million related to upfront license payments, near term milestones and equity premiums from our agreements with Biogen and OSI completed in 2009 and an increase in accounts payable and accrued expenses of $7.6 million primarily related to our phase 2 clinical trial of tivozanib and costs in preparation for our phase 3 clinical trial of tivozanib offset by an increase in our net loss.

During 2007, 2008 and 2009, our investing activities provided (used) cash of $(39.9) million, $28.2 million and $3.4 million, respectively. The cash provided by investing activities for the years ended 2008 and 2009 was due primarily to the net result of maturities and sales of marketable securities. These maturities were offset partially by purchases of property and equipment of $1.4 million and $1.7 million, respectively. The use of cash for the year ended 2007 was primarily the net result of the purchase of marketable securities and the purchases of property and equipment of $0.4 million.

During 2007, 2008 and 2009, our financing activities provided $52.8 million, $6.9 million and $31.0 million, respectively. The cash provided by financing activities in 2007 was due to the sale and issuance of 1,833,334 shares of series C convertible preferred stock and 21,165,510 shares of series D convertible preferred stock, for total net proceeds of $57.4 million, offset partially by principal payments on loans payable in the amount of $4.6 million. The cash provided in 2008 was a result of the issuance of loans payable of $20.8 million partially offset by extinguishment of the previous loan of $10.1 million and principal payments on loans payable of $3.8 million. The cash provided by financing activities in 2009 was due to the sale and issuance of 11,250,000 shares of series E convertible preferred stock, for total net proceeds of $32.9 million, offset partially by the principal payments on loans payable of $2.0 million.

Credit Facilities. On March 29, 2006, we entered into a $15.0 million financing agreement with Hercules for general corporate purposes. On May 15, 2008, we repaid the remaining principal of $10.1 million due on this

loan and entered into a new $21.0 million financing agreement with Hercules and Comerica Bank. The full amount of the new loan was drawn down in 2008. In May 2009, we triggered a provision allowing a six month extension to the original twelve month interest only period. The new loan is now repayable over 48 months beginning June 2008, with the first 18 payments representing interest only. The remaining principal and associated interest is due and payable in equal monthly installments based upon a 30-month amortization schedule. The loan also calls for a deferred charge of 5.95% to be paid upon maturity. The deferred charge of $1.3 million has been recorded as a loan discount and is being amortized to interest expense over the term of the loan using the effective interest rate method. We recorded a long-term liability for the full amount of the charge since the payment of such amount is not contingent on any future event. Interest is payable at a fixed interest rate of 9.75%. The loan is secured by a lien on all of our assets, except for intellectual property and the capital equipment securing our equipment and refinancing lines of credit. As of December 31, 2009, the principal balance outstanding was $20.4 million. We began making principal payments in December 2009 with a final loan maturity in May 2012.

In November 2003, we entered into a $7.5 million financing agreement with General Electric Capital Corporation for an equipment capital expenditure line which we refer to as the equipment line and a refinancing line of existing equipment debt which we refer to as the refinancing line. Borrowings under the equipment line are repayable over 54 months, the first six of which are interest only at fixed interest rates ranging from 8.39% to 10.11%, with a 10% end-of-term balloon payment (guaranteed purchase option). The refinancing line has been fully paid. The equipment line is secured by an interest in the specific financed assets. Under the equipment line, there is a requirement to maintain minimum unrestricted cash equal to the greater of $12.0 million or nine months cash burn. In the event we violate the minimum cash requirement, we must provide a letter of credit or security deposit equal to 70% of the outstanding balance under the equipment line. The aggregate principal outstanding under the equipment line and the refinancing line at December 31, 2009 was approximately $101,900. There is no remaining ability to borrow under the equipment line.

Operating Capital Requirements. Assuming we successfully complete clinical trials and obtain requisite regulatory approvals, we anticipate commercializing our first product in 2013 at the earliest. Therefore, we anticipate that we will continue to generate significant losses for the next several years as we incur expenses to complete our clinical trial programs for tivozanib, build commercial capabilities, develop our antibody pipeline and expand our corporate infrastructure. 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 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.

If our available cash and cash equivalents are insufficient to satisfy our liquidity requirements, or if we develop additional opportunities to do so, we may seek to sell additional equity or debt securities or obtain a credit facility. The sale of additional equity and debt securities may result in additional dilution to our

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shareholders. If we raise additional funds through the issuance of debt securities or preferred stock, these securities could have rights senior to those of our common stock and could contain covenants that would restrict our operations. We may require additional capital beyond our currently forecasted amounts. Any such required additional capital may not be available on reasonable terms, if at all. If we were unable to obtain additional financing, we may be required to reduce the scope of, delay or eliminate some or all of our planned research, development and commercialization activities, which could harm our business.

Because of the numerous risks and uncertainties associated with research, development and commercialization of pharmaceutical products, we are unable to estimate the exact amounts of our working capital requirements. Our future funding requirements will depend on many factors, including, but not limited to:

- 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.

Contractual Obligations and Commitments. The following table summarizes our contractual obligations at December 31, 2009:

	Total	Less than 1 Year	1 to 3 Years	4 to 5 Years	After 5 Years
			(in thousands)		
Short and long-term debt (including interest)	$ 24,356	$ 9,605	$ 14,751	$	$
Operating lease obligations	9,683	2,365	4,742	2,576	
Kirin License Agreement[1]	10,000	10,000			
Supply Agreement[2]	5,227	5,227			
Other License Agreements[3]	2,125	1,225	850	50	
Total contractual cash obligations	$ 51,391	$ 28,422	$ 20,343	$ 2,626	$

(1) We will be required to make a $10.0 million milestone payment to Kyowa Hakko Kirin in connection with our phase 3 clinical trial of tivozanib, which we expect to pay in the first quarter of 2010. In addition, we may be required to make up to an aggregate of $50.0 million in additional milestone payments upon the achievement of specified regulatory milestones. We are also required to pay tiered royalty payments on net sales we make of tivozanib in our territory, which range from the low to mid teens as a percentage of net sales.

(2) We have a supply arrangement with a third party for the supply of the comparator drug, Nexavar, which will be used in our phase 3 clinical trial of tivozanib. Pursuant to an open purchase order, we are committed to make a $5.2 million payment in the first quarter of 2010. We may be required to make additional payments of $5.9 million under this agreement for additional supply of Nexavar if the trial is completed as planned.

(3) As discussed in Note 7 to our consolidated financial statements, we have executed license agreements for patented technology and other technology related to research projects, including technology to humanize

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AV-299 and other antibody product candidates. The license agreements required us to pay nonrefundable license fees upon execution, and in certain cases, require milestone payments upon the achievement of defined development goals. The license agreements also require us to pay annual maintenance payments totaling a maximum of $475,000 per year. We have included maintenance and milestone payments of $1.3 million and $0.8 million, respectively, in the table above, as we consider the payment of these amounts to be probable. We have not included any additional amounts as we are not able to make a reasonable estimate of the probability and timing of such payments, if any. Including amounts in the table above, these agreements call for sales and development milestones of up to $22.5 million, $6.3 million and $4.2 million per product, and single digit royalties as a percentage of sales.

Off-Balance Sheet Arrangements

We did not have during the periods presented, and we do not currently have, any off-balance sheet arrangements, as defined under SEC rules.

Tax Loss Carryforwards

As of December 31, 2009, we have net operating loss carryforwards of approximately $130.9 million to offset future federal income taxes and approximately $102.2 million to offset future state income taxes. These federal and state loss carryforwards expire at various times through 2029. We also have research and development and investment tax credit carryforwards of approximately $3.5 million to offset future federal income taxes, and approximately $2.1 million to offset future state income taxes. The federal and state tax credits expire at various times through 2029. In addition, the occurrence of certain events, including significant changes in ownership interests, may limit the amount of the net operating loss carryforwards and tax credit carryforwards available to be used in future years. At December 31 2009, we recorded a 100% valuation allowance against our deferred tax assets of approximately $72.3 million, as our management believes it is uncertain that they will be fully realized. If we determine in the future that we will be able to realize all or a portion of our net operating loss carryforwards, an adjustment to our net operating loss carryforwards would increase net income in the period in which we make such a determination.

Recently Adopted Accounting Standards

Effective January 1, 2009, we adopted new accounting guidance related to accounting for uncertainty in income taxes. This accounting standard clarifies the recognition threshold and measurement attribute for the financial statement recognition and measurement of a tax position taken or expected to be taken in a tax return. This accounting standard also provides guidance on recognition, classification, interest and penalties, accounting in interim periods, disclosure and transition. We have not identified any material uncertain tax positions for which reserves would be required and the adoption of this accounting standard did not have an effect on its consolidated financial statements.

In April 2009, the FASB issued FASB Staff Position FAS 107-1 and APB No. 28-1, Interim Disclosures About Fair Value of Financial Instruments (codified within ASC 825), which expands the fair value disclosures required for financial instruments to interim reporting periods for publicly traded companies, including disclosure of the significant assumptions used to estimate the fair value of financial instruments. We adopted this guidance effective June 15, 2009. The adoption did not impact our financial position or results of operations.

In May 2009, the FASB established general standards of accounting for and disclosures of events that occur after the balance sheet date but before financial statements are issued or are available to be issued. It requires the disclosure of the date through which an entity has evaluated subsequent events and the basis for selecting that date, that is, whether that date represents the date the financial statements were issued or were available to be issued. Our adoption of this standard had no material impact on its financial position, results of operations and cash flows.

In June 2009, the FASB issued ASC 105, Generally Accepted Accounting Principles, which established the FASB Accounting Standards Codification as the sole source of authoritative generally accepted accounting

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principles. Pursuant to the provisions of ASC 105, we have updated references to Generally Accepted Accounting Principles, or GAAP, in our financial statements issued for the period ended December 31, 2009. The adoption of ASC 105 did not impact our financial position or results of operations.

In August 2009, the FASB issued Accounting Standards Update No. 2009-05, Measuring Liabilities at Fair Value , or ASU 2009-05. ASU 2009-05 amends Accounting Standards Codification Topic 820, Fair Value Measurements. Specifically, ASU 2009-05 provides clarification that in circumstances in which a quoted price in an active market for the identical liability is not available, a reporting entity is required to measure fair value using one or more of the following methods: (1) a valuation technique that uses (a) the quoted price of the identical liability when traded as an asset or (b) quoted prices for similar liabilities or similar liabilities when traded as assets and/or (2) a valuation technique that is consistent with the principles of Topic 820 of the Codification (e.g. an income approach or market approach). ASU 2009-05 also clarifies that when estimating the fair value of a liability, a reporting entity is not required to adjust to include inputs relating to the existence of transfer restrictions on that liability. The adoption of this standard did not have an impact on the our financial position or results of operations.

In October 2009, the FASB issued ASC Update No. 2009-13, Revenue Recognition (Topic 605): Multiple-Deliverable Revenue Arrangements. The consensus in Update No. 2009-13 supersedes certain guidance in Topic 605 (formerly EITF Issue No. 00-21, Multiple-Element Arrangements) and requires an entity to allocate arrangement consideration at the inception of an arrangement to all of its deliverables based on their relative selling prices. The consensus eliminates the use of the residual method of allocation and requires the use of the relative-selling-price method in all circumstances in which an entity recognizes revenue for an arrangement with multiple deliverables subject to ASC 605-25. We are required to adopt Update No. 2009-13 as of January 1, 2011 and are in the process of determining the impact that the adoption of Update No. 2009-13 will have on our future results of operations or financial position.

Quantitative and Qualitative Disclosures About Market Risks

We are exposed to market risk related to changes in interest rates. As of December 31, 2008 and December 31, 2009, we had cash and cash equivalents and marketable securities of $32.4 million and $51.3 million, respectively, consisting of money market funds, U.S. Treasuries, U.S. Agencies, and commercial paper. Our primary exposure to market risk is interest rate sensitivity, which is affected by changes in the general level of U.S. interest rates, particularly because our investments are in short-term marketable securities. Our marketable securities are subject to interest rate risk and will fall in value if market interest rates increase. Due to the short-term duration of our investment portfolio and the low risk profile of our investments, an immediate 10% change in interest rates would not have a material effect on the fair market value of our portfolio. We have the ability to hold our marketable securities until maturity, and therefore we would not expect our operating results or cash flows to be affected to any significant degree by the effect of a change in market interest rates on our investments. We do not currently have any auction rate securities.

We contract with contract research organizations and investigational sites globally. We may be subject to fluctuations in foreign currency rates in connection with these agreements. We do not hedge our foreign currency exchange rate risk.

Our long-term debt and our equipment line obligations bear interest at fixed rates. As a result, we have limited exposure to changes in interest rates.

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BUSINESS

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 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

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Kyowa Hakko Kirin. For further discussion of this agreement, please see 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.

Our Human Response Platform was originally based on a method of building germ line transgenic models of human cancer, which are models that contain genetic alterations in every cell of the animal, and a method of using such models to screen for new targets, which we refer to as the MaSS screen, developed at the Dana-Farber Cancer Institute, or DFCI. We exclusively licensed these models and the MaSS screen from DFCI when we were founded. We subsequently developed and patented an improved chimeric version of the model system, in which the original genetic modifications are present in some, but not all, of the cells of the animal, as well as an additional technology which we refer to as directed complementation, which allows us to engineer tumors whose growth depends on a particular gene of interest. Under our agreement with DFCI, we have exclusive, worldwide rights under DFCI patents and patent applications relating to the licensed tumor model system and the MaSS screen; the right to grant sublicenses; and sole ownership rights to any improvements made solely by our employees to the cancer model technology licensed from DFCI. We have fulfilled certain milestone payment obligations to DFCI. We will have no royalty obligation to DFCI based on sales of products discovered, designed, developed or tested using the licensed technology.

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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, or FGF, receptors.

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. We are seeking to develop tivozanib, our triple VEGF receptor inhibitor, in multiple cancer types. The first indication we are pursuing in our development strategy is advanced RCC, a significant market opportunity for which we believe we can build a focused commercial capability through a targeted specialty sales force. Based on discussions with the U.S. Food and Drug Administration, or the FDA, and the European Medicines Agency, or the EMEA, we have designed a single, global phase 3 clinical trial to demonstrate the efficacy and safety of tivozanib in patients with advanced RCC who have not been treated with any other VEGF directed therapy. If successful, this phase 3 clinical trial, which we refer to as our TIVO-1 study, together with results from our completed phase 2 clinical trial, will form the basis for registration applications to be submitted to the U.S. and European regulatory agencies for tivozanib s approval in advanced RCC. In addition, we are conducting earlier-stage clinical trials of tivozanib in combination with other anti-cancer drugs in breast cancer and colorectal cancer.

Develop and commercialize our clinical product candidate, AV-299, in collaboration with Merck. The first antibody program developed utilizing our Human Response Platform is our anti-HGF program, AV-299. We completed a phase 1 clinical trial of AV-299 in 2009 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 a strategic partnership with Schering-Plough (now Merck) for the development of AV-299, under which Merck funds all development and manufacturing expenses, subject to an agreed-upon budget. In addition, Merck is required to pay us development milestones and royalties on the sale of AV-299. Pursuant to that agreement, we are currently leading the clinical development of AV-299, which includes conducting multiple phase 1 clinical trials and preparing for the conduct of a phase 2 clinical trial, and for conducting ongoing research utilizing our Human Response Platform, all at Merck s expense. Merck is responsible for conducting clinical development of AV-299 after phase 2 and for commercializing AV-299 on a worldwide basis. Under the 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.

Build capabilities that will allow us to effectively commercialize our products. We have worldwide rights outside of Asia to develop and commercialize our lead product candidate, tivozanib, and retain an option to co-promote AV-299 in certain oncology indications in the United States. In our strategic partnership with Biogen Idec, we retain all rights to commercialize products resulting from our ErbB3 antibody program in the United States, Canada and Mexico. We intend to build a targeted, specialty sales force in the United States to effectively support the commercialization of these and future oncology products. 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 other 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. We believe that our Human Response Platform provides us a competitive advantage in discovering and developing novel oncology drugs by identifying biomarkers that can facilitate more efficient drug development. We have preclinical antibody discovery programs underway focusing on important cancer targets, including ErbB3, the

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Notch receptors, RON and the FGF receptors, all targets that we have tested in our Human Response Platform. We believe these programs provide us with future product opportunities which we can develop internally, or which can serve as the basis for future strategic partnerships. We also believe that our Human Response Platform can provide us with a competitive advantage in assessing potential in-licensing candidates by allowing us to identify the most promising targets and product candidates from among the many cancer drugs in development.

Establish strategic partnerships to accelerate and maximize the potential of our products and technology while preserving significant commercial rights. In addition to our current arrangements with Biogen Idec and Merck, we intend to continue to establish strategic partnerships where we can accelerate the development or maximize the value of our product candidates by leveraging the scientific, clinical development, manufacturing, commercialization and/or financial strengths of leading biotechnology and pharmaceutical companies while still preserving significant commercial rights. For example, we may seek a partner for tivozanib outside of the United States in addition to our current partner Kyowa Hakko Kirin, which currently holds exclusive rights to tivozanib in Asia. We also intend to establish additional strategic partnerships, as we have done with Merck and OSI, in which we utilize our Human Response Platform to (i) identify and validate targets for new cancer therapies in collaboration with the strategic partners and (ii) identify biomarkers to aid the development of our strategic partners drug candidates.

Product Pipeline

We are seeking to develop multiple new drugs that target important mechanisms known or believed to be involved in cancer. These drugs include our lead drug candidate, tivozanib, a small molecule oral cancer drug, designed to prevent tumor growth by inhibiting angiogenesis, as well as monoclonal antibodies against HGF and ErbB3. We also are developing a pipeline of earlier stage novel antibodies which are designed to target mechanisms which we believe to be important in cancer. Our drug discovery and development activities are supported by our Human Response Platform.

The chart below summarizes our current product candidates and their stages of development and planned development.

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Tivozanib: Triple VEGF Receptor Inhibitor

VEGF Pathway Inhibitors in Tumor Angiogenesis

The formation of new blood vessels, known as angiogenesis, is required to support certain important natural processes such as embryonic development, reproduction and wound healing. Angiogenesis also plays an important role in cancer progression and the spread of tumors within the body, or metastasis. Tumors cannot grow beyond a small size in the absence of the formation of new blood vessels. Tumors use these vessels to obtain oxygen and nutrients, both of which are required to sustain tumor growth, and to remove toxic waste products that result from rapid metabolism. In addition, new vessels in the tumor provide a way for tumor cells to enter the circulation and to spread to other organs.

Cancer cells and associated tumor tissue secrete a variety of protein activators, or growth factors, that bind to receptors and promote angiogenesis. Growth factors that bind to specific receptors are known as ligands for those receptors. Vascular endothelial growth factor, or VEGF, stimulates angiogenesis and is required for the maintenance of new blood vessels. Most tumors produce various forms of VEGF and other ligands which bind to the three VEGF receptors, VEGFR1, 2 and 3. The VEGF receptors are found predominantly on the surface of normal vascular endothelial cells. The secretion of these ligands attracts normal endothelial cells to the tumor site where they are stimulated to proliferate and form new blood vessels that feed the tumor.

Each of the three VEGF receptors has been shown to play a role in angiogenesis. Drugs designed to inhibit the VEGF pathway may be directed either to one or more ligands of the receptors, or to the VEGF receptors themselves. Because there are multiple ligands that can bind to the three VEGF receptors and stimulate angiogenesis, products such as Avastin which block only one of these ligands may result in an incomplete blockade of the VEGF pathway. Similarly, receptor-targeted drugs which fail to effectively block all three of the VEGF receptors may also result in incomplete blockade of the VEGF pathway.

Because essentially all solid tumors require angiogenesis to progress beyond microscopic size, anti-angiogenesis drugs have demonstrated benefit in a wide variety of tumor types. Current therapies targeting the VEGF pathway have been approved in many tumor types, including colon, lung, breast, kidney, liver and brain cancers. In many of these tumors, other than kidney, liver and brain cancer, VEGF pathway inhibitors have demonstrated meaningful efficacy only when given in combination with other drugs; therefore, the opportunity for VEGF pathway inhibitors is most significant for those agents, such as Avastin, which can be safely combined with other anti-cancer agents.

We believe that the optimal approach to inhibiting the VEGF pathway is through an oral drug that potently and selectively inhibits all three VEGF receptors. We believe that drugs, such as Avastin, which bind to only one of the ligands for the VEGF receptors may not achieve optimal inhibition of the VEGF pathway. Moreover, each of the currently approved VEGF receptor inhibitors can cause significant side effects when administered alone, and studies have shown that it is extremely challenging to administer these drugs in combination with other anti-cancer agents due to overlapping toxicities. Each of the currently available VEGF receptor inhibitors have one or more drawbacks, including: (i) a lack of adequate potency, which necessitates high dosage levels in order to sufficiently block all three VEGF receptors, (ii) a lack of selectivity, which can cause side effects due to unintended impact on other receptors, referred to as off-target toxicities, and (iii) short duration of inhibition, which may necessitate dosing more than once per day and may not ensure continuous inhibition of the VEGF pathway.

Despite the various challenges encountered with the approved VEGF receptor inhibitors, sales of VEGF pathway inhibitor drugs exceeded $6 billion worldwide in 2008, based on 2008 annual reports made publicly available by companies marketing such drugs. According to EvaluatePharma® consensus forecasts from equity research analysts, drugs targeting angiogenesis are projected to have sales of more than $14 billion by 2014. Currently approved VEGF pathway inhibitors include Avastin, an antibody which blocks only one of the ligands for the VEGF receptors, and Nexavar, Sutent and Votrient (pazopanib), each of which are small molecule drugs which target the VEGF receptors, but also bind to a number of other targets, with varying potency.

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We believe there is a significant unmet need for a new oral VEGF pathway inhibitor which more completely blocks the activities of all three VEGF receptors, which is more tolerable and can be more easily combined with other currently available cancer drugs and which can maintain continuous inhibition of the pathway with a convenient dosing regimen.

Potential Advantages of Tivozanib

The potential advantages of tivozanib include a unique potency and selectivity profile, which we believe is the basis for the favorable efficacy and safety profile observed in the clinical trials of tivozanib to date. We believe that this favorable efficacy and safety profile may allow tivozanib to be successfully used as a monotherapy and to be more readily combined with other anti-cancer agents. Coupled with a convenient dosing regimen, we believe these advantages may differentiate tivozanib from existing marketed VEGF receptor inhibitors and allow tivozanib to fulfill an unmet need in the anti-angiogenesis market.

Potency. Based on published data of marketed products or compounds in clinical development that target the VEGF pathway, we believe tivozanib is the most potent inhibitor of all three VEGF receptors. Due to its high potency, tivozanib is administered at a dose of only 1.5 mg per day. In contrast, the daily dose of the other approved VEGF receptor inhibitors ranges from 50 mg per day to 800 mg per day. Because tivozanib s high potency allows it to be administered at a very low dose, patients who take tivozanib have less drug circulating in their body and therefore less potential for off-target toxicity. This may also contribute to the favorable safety profile that has been observed to date in clinical trials of tivozanib.

Selectivity. Tivozanib more potently inhibits the VEGF receptors than it does any other targets in the body. This selectivity for the VEGF receptors has the potential to confer two important advantages:

Tolerability. Many of the existing drugs which act by inhibiting the VEGF pathway also inhibit receptors in other pathways, which can cause side effects, or off-target toxicities. Sutent, Nexavar and Votrient, all relatively non-selective VEGF inhibitors, more potently inhibit other targets than they do the VEGF receptors. For example, Sutent and Votrient more potently inhibit the receptor known as c-Kit and Nexavar more potently inhibits the protein known as raf. The common toxicities for Sutent and Nexavar are fatigue, rash and diarrhea, and a common toxicity for Votrient is diarrhea. Votrient has also been associated with severe, and sometimes fatal, liver toxicity. These drugs also frequently cause a number of other side effects in patients that can be very difficult for patients to tolerate, including mucositis, a painful inflammation and ulceration of the mucous membranes lining the digestive tract, stomatitis, inflammation of the mucous lining of the mouth, including the cheeks, gums, tongue, lips, throat and roof or floor of the mouth, and hand-foot syndrome, blistering, burning, swelling and tenderness on the soles of the feet and palms of the hands that can interfere with a patient s ability to walk and use his or her hands. Sutent, Nexavar and Votrient can also cause myelosuppression, which refers to a decrease in the production of blood cells, resulting in both anemia and neutropenia. Anemia is a decrease in the number of red blood cells which carry oxygen and neutropenia is a decrease in the number of certain white blood cells which fight infection.

None of these side effects are believed to be associated with inhibition of the VEGF pathway and, therefore are considered off-target toxicities. These side effects can be very difficult to manage, and result in frequent dose reductions and discontinuations, as well as a reduced quality of life for patients taking these drugs. In clinical trials, more than 30% of patients receiving Sutent, more than 20% of patients receiving Nexavar and more than 40% of patients receiving Votrient have required dose reductions or dose interruptions.

In the clinical trials of tivozanib to date, we have observed low rates of off-target toxicities, and fewer than 15% of patients have required dose reductions or dose interruptions. Clinical trials with tivozanib have shown that hypertension is by far the most common toxicity in patients, consistent with its high selectivity for the VEGF receptors. The occurrence of hypertension is largely driven by inhibition of the VEGF pathway. The occurrence of hypertension in patients is frequently interpreted as an

indication that the VEGF pathway has been substantially inhibited, and is therefore often referred to as an on-target toxicity. Hypertension associated with tivozanib can usually be managed using standard anti-hypertensive drugs.

Combinability. While the approved VEGF pathway inhibitors have demonstrated modest improvements in outcomes in the cancers they are used to treat, we believe an opportunity exists for significantly improved outcomes through the use of rational combinations of VEGF pathway inhibitors in combination with other anti-cancer therapies. Frequently, however, combining anti-cancer drugs, each of which carries with it significant levels of toxicity, can lead to very high levels of side effects which either make the combination unsafe or extremely difficult for patients to tolerate. For example, in a phase 1 clinical trial designed to test the combination of Sutent with Torisel, another drug approved to treat RCC, the trial had to be halted due to high levels of toxicity of the combination. This high level of toxicity was observed even though both agents were administered at doses well below the doses used when the drugs are administered alone. Similarly, in a phase 2 clinical trial in breast cancer patients designed to test the safety and efficacy of Nexavar in combination with Xeloda (capecitabine), a drug approved for the treatment of breast cancer, although patients seemed to benefit from the combination, more than 40% of patients developed Grade 3 hand-foot syndrome, a serious skin reaction, that interfered with their ability to conduct normal activities of daily living. There is no Grade 4 hand-foot syndrome.

Because of the potency and selectivity of tivozanib, we believe that tivozanib has the potential to be more safely combined with other anti-cancer drugs, and therefore has the potential for significantly improved anti-cancer activity and better clinical outcomes. We have commenced phase 1b clinical trials testing tivozanib in combination with other anti-cancer agents in multiple cancer types, including RCC, breast and colorectal cancer. All of these trials are ongoing. For our ongoing phase 1b clinical trial in RCC, we are treating patients with a combination of tivozanib and Torisel, each administered at full dose, the dose administered when the drugs are used alone. The data from the clinical trial to date indicate that the combination has been well-tolerated and resulted in tumor shrinkage in 12 out of 16 of the patients treated. Similarly, in our ongoing phase 1b trial in patients with colorectal and other gastrointestinal cancers, we are treating patients with a combination of tivozanib and FOLFOX6, a standard chemotherapy regimen, each administered at full dose.

Dosing Regimen. In clinical trials, levels of tivozanib in a patient s blood have been maintained for a prolonged period following a single dose, which allows for convenient, once-a-day dosing. Tivozanib has demonstrated a half-life, meaning the time it takes for the concentration of a drug in circulation to be reduced by one-half, of approximately four days. When drugs do not sufficiently maintain blockade of the VEGF receptors throughout the course of therapy, patients can experience a rebound effect, which can worsen their condition. For this reason, it is important to maintain sufficient levels of drug in the patient throughout the course of therapy. Because tivozanib has demonstrated a long half-life, we dose tivozanib on a convenient, once-per-day schedule. Even if a patient misses an occasional dose, we expect that sufficient levels of tivozanib will remain in the body to achieve the desired therapeutic effect.

Renal Cell Cancer

Overview. We recently completed a 272-patient phase 2 clinical trial of tivozanib in advanced RCC. In this trial, the overall median progression-free survival of patients 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 a prior 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. Tivozanib was well-tolerated by patients and relatively few patients needed to discontinue or reduce their dose of tivozanib. In December 2009, we initiated a phase 3 clinical trial for tivozanib in patients with advanced clear cell RCC who have undergone a prior nephrectomy and who have not received any prior VEGF-targeted therapy. Based on the data we have received from clinical trials conducted to date, we believe that tivozanib may offer a unique therapeutic alternative for the first-line treatment of advanced RCC.

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Market Opportunity. Based on an epidemiology study performed by D. Max Parkin et al. (published in 2005 in *CA: A Cancer Journal for Clinicians)*, there were approximately 208,000 new cases of kidney cancer diagnosed in the world in 2002, and, according to the National Cancer Institute, new cases of kidney cancer have been increasing steadily for the past 65 years. The American Cancer Society reports that there will have been approximately 57,760 new cases of kidney cancer in North America in 2009. According to an epidemiology study performed by J. Ferlay (published in 2007 in the *Annals of Oncology*), 63,000 new cases were diagnosed in the European Union in 2006. As published in a 1996 review article by R. Motzer et al. in *The New England Journal of Medicine*, RCC accounts for 80-85% of all malignant kidney tumors. We estimate, based on publicly-available information, including 2008 annual reports made publicly available by companies that market drugs approved for RCC, that the current worldwide RCC market for prescription drugs is over $1 billion, with agents targeting the VEGF pathway representing over 80% of sales. The market is expected to expand significantly over the next ten years, driven by an increased incidence of RCC, an increased use of frontline therapy as more tolerable agents are developed and an increased use of later-stage therapy as more treatment options become available.

Current Diagnosis and Treatments. The diagnosis of RCC is generally made by examination of a tumor biopsy under a microscope. Evaluation of the visual appearance of the tumor cells by a pathologist allows classification of RCC into clear cell or non-clear cell types. In general, patients with clear cell type of RCC, approximately 85% of all RCC diagnoses according to a 1996 review article by R. Motzer et al. in *The New England Journal of Medicine*, tend to have a more favorable prognosis than patients with non-clear cell RCC. The initial treatment for most patients with both clear cell and non-clear cell RCC is surgical removal of the tumor, usually requiring removal of the affected kidney, or nephrectomy, if that is technically feasible. Patients who undergo a nephrectomy tend to have a better prognosis than patients who do not undergo a nephrectomy. Patients whose tumors have metastasized to other organs or whose tumors cannot be removed surgically are considered to have advanced RCC. Advanced RCC is highly resistant to chemotherapy. The standard of care for advanced RCC is treatment with one of the recently approved drugs that inhibit the VEGF pathway, including the oral drugs Sutent, Nexavar and Votrient as well as the injectable product Avastin. Although none of these drugs have been compared head-to-head in phase 3 clinical trials, Sutent, Nexavar, Votrient and Avastin have all demonstrated improvements in progression-free survival in clear cell RCC patients compared to placebo or interferon. The reported progression-free survival in the treatment arms of the phase 3 clinical trials of these drugs in patients with advanced clear cell RCC is 11.0 months for Sutent, 5.5 months for Nexavar, 9.2 months for Votrient and 10.2 months for Avastin when Avastin is given in combination with interferon. In these trials, the percent of patients who had undergone a prior nephrectomy was 91% for Sutent, 94% for Nexavar, 89% for Votrient and 100% for Avastin. Torisel and Afinitor (everolimus), drugs which target mTOR, have also been approved in RCC. In their respective phase 3 clinical trials, the reported median progression-free survival for Torisel was 5.5 months in patients with poor-prognosis RCC, and the reported median progression-free survival for Afinitor in patients who had progressed despite prior treatment with a VEGF receptor inhibitor was 4.9 months.

Despite the efficacy of the approved oral VEGF pathway inhibitors, these drugs are also associated with significant side effects such as neutropenia, fatigue, diarrhea, hand-foot syndrome, mucositis, stomatitis and abnormalities in liver function. A significant number of patients in the phase 3 clinical trials for each of these drugs required a reduction or discontinuation of their therapy due to these side effects. Although these drugs were not tested head-to-head in their respective phase 3 clinical trials, the reported frequency of dose reductions from the phase 3 clinical trials of these drugs in patients with advanced RCC is 32% for Sutent, 13% for Nexavar and 36% for Votrient. The reported frequency of dose interruptions due to adverse events in the phase 3 clinical trials of these drugs in patients with advanced RCC is 38% for Sutent, 21% for Nexavar and 42% for Votrient.

The Tivozanib Opportunity. We believe there is unmet need for an RCC therapy that demonstrates significant efficacy while having a safety profile that will allow patients to remain on drug while maintaining a good quality of life. Added potential may exist for a selective VEGF pathway inhibitor which could be combined with other anti-cancer agents having a different mechanism of action, as VEGF pathway inhibitors are often most effective when administered in combination with other anti-cancer agents.

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Clinical Trials

Phase 1 Clinical Trials. In 2007, we completed a phase 1 clinical trial of tivozanib in 41 cancer patients. Results from the phase 1 clinical trial showed that patients were able to tolerate tivozanib at a dose of 1.5 mg/day given continuously for 4 weeks followed by a 2 week rest period, and that toxicities were reversible upon stopping treatment. The primary dose-limiting toxicity identified in the phase 1 clinical trial was hypertension, which is a frequent side effect of VEGF inhibitors and is considered an on-target effect resulting from the blockage of VEGF receptors. Hypertension was treated with standard anti-hypertensive agents such as calcium channel blockers or angiotensin converting enzyme inhibitors.

In the phase 1 clinical trial, 9 of 41 patients had RCC and all 9 patients experienced clinical benefit from tivozanib. Two of these patients had a partial response, according to RECIST criteria, including one patient whose partial response lasted for over two years. The remaining seven RCC patients had stable disease lasting for at least two months. Stable disease was also observed in patients with other types of solid tumors including colorectal cancer, where 4 out of 10 patients who had progressed after prior chemotherapy demonstrated stable disease lasting for approximately six months during treatment with tivozanib. One patient with an acinar cell tumor of the pancreas that had progressed after prior treatment with gemcitabine has been receiving tivozanib for over two years and remains on treatment with stable disease. Given the promising activity observed in the phase 1 clinical trial, we decided to move forward with the development of tivozanib in multiple solid tumors, with RCC being the leading program.

Standard Response Evaluation Criteria in Solid Tumors, or RECIST, defines disease progression and tumor response based on the sum of the longest diameters of a set of target tumor lesions identified when the patient enters the trial, which we refer to as baseline. A 20% or greater increase in the sum of diameters in target lesions, or unequivocal progression in non-target lesions, or the appearance of a new lesion, is defined as disease progression. A reduction in the sum of the diameters of at least 30% as compared to baseline is defined as a partial response. A complete disappearance of target and non-target lesions, and the normalization of any tumor markers, constitutes a complete response. Both partial and complete responses must be confirmed by repeat assessments at least four weeks after the partial or complete response was first documented. Stable disease refers to patients who exhibit neither response nor disease progression. Objective response rate is typically defined as the sum of the partial and complete response rates.

Phase 2 Clinical Trial. In 2007, we began a phase 2 clinical trial of tivozanib in patients with advanced RCC. This clinical trial was conducted under an Investigational New Drug application submitted to the FDA and 272 patients were enrolled between October 2007 and July 2008 at sites in Russia, the Ukraine and India. To be eligible for the clinical trial, patients could not have received any prior VEGF-targeted therapies. Results from the phase 1 clinical trial showed that patients were able to tolerate tivozanib at a dose of 1.5 mg/day given continuously for 4 weeks followed by a 2 week rest period, but in order to minimize the rest period during which patients are off treatment, the dosing regimen for the phase 2 clinical trial was changed to 3 weeks continuous dosing followed by a 1 week rest period. The trial included patients with both clear cell RCC (83%) and non-clear cell RCC (17%). 27% of patients had not had a prior nephrectomy. Approximately 54% of patients had not received any other drug treatment for their disease, while the remainder had received one or more prior therapies, but no VEGF pathway inhibitors.

All patients received tivozanib for the first 16 weeks, at which time patients with ³25% tumor regression continued on tivozanib while patients with <25% change from baseline were randomly assigned to tivozanib or placebo in a double-blinded manner for the next 12 weeks. Patients with ≥25% increase in tumor size discontinued tivozanib treatment.

The primary endpoints of the trial were (i) the percentage of patients remaining progression-free 12 weeks following random assignment to tivozanib or placebo, (ii) objective response rate and (iii) safety. Secondary endpoints included overall progression-free survival from start of treatment and progression-free survival after random assignment to tivozanib or placebo.

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All radiology scans from the study were reviewed by a single, centralized group of independent radiologists in the United States who were blinded to treatment assignment. All laboratory tests were conducted at a central lab in the United Kingdom. Disease progression and tumor response rates were determined in accordance with the RECIST criteria. The data reported in the following paragraph with respect to the percentage of patients remaining progression-free 12 weeks following random assignment as compared to placebo is based on data from the tivozanib phase 2 clinical trial as of the cutoff date of January 31, 2009, which was after sufficient time had elapsed for all patients in the trial to reach the pre-specified primary endpoint (i.e., 12 weeks post-randomization). All other data for the phase 2 clinical trial is based on updated data from the trial on October 31, 2009. Based on preliminary data as of February 1, 2010, 55 patients remain on tivozanib therapy in this clinical trial, with 39 patients remaining on therapy for more than 1.5 years and 16 patients remaining on therapy for more than 2 years. We intend to submit updated data from the phase 2 clinical trial for presentation at an appropriate medical meeting in 2010.

A significantly higher percentage of patients on tivozanib remained progression-free 12 weeks following random assignment as compared to placebo. 55% of patients randomized to tivozanib were progression-free compared to 28% of patients randomized to placebo. This difference was statistically significant (p=0.004). As of October 31, 2009, the median progression-free survival of patients randomized to the placebo treatment arm was 5.6 months and the median progression-free survival of patients randomized to the tivozanib treatment arm was 14.3 months.

The graph below shows the probability of a patient remaining alive without tumor progression while in the tivozanib phase 2 clinical trial. The overall median progression-free survival of patients in the phase 2 clinical trial was 11.8 months. The median was calculated based on data from the phase 2 clinical trial using a standard statistical procedure known as a Kaplan-Meier analysis. In the phase 2 clinical trial, the event being measured was progression-free survival. The vertical tick marks of the graph represent points during the clinical trial at which one or more patients were removed from the data analysis either because the patient was on treatment and still responding at the time of the data cut-off or because the patient withdrew from the clinical trial due to reasons other than disease progression or because the patient was randomized to placebo.

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In the subset of 176 patients in the phase 2 clinical trial who had clear cell RCC and who had undergone a prior nephrectomy, both of which are inclusion criteria for our phase 3 clinical trial of tivozanib, the median progression-free survival was 14.8 months, calculated retrospectively using a Kaplan-Meier analysis, as shown in the graph below.

More than 80% of patients who received tivozanib therapy in the phase 2 clinical trial experienced some degree of tumor shrinkage while on therapy. As of October 31, 2009, 26.8% of patients with tivozanib had demonstrated an objective response, with 1 (0.4%) confirmed complete response, 56 (20.6%) confirmed partial responses, and 16 (5.9%) unconfirmed partial responses as measured by independent radiological review. In patients with clear cell RCC who had undergone a prior nephrectomy, 31.8% had an objective response as measured by independent radiological review. This includes 1 patient (0.6%) who had a confirmed complete response, 43 patients (24.4%) who had a confirmed partial response, and 12 patients (6.8%) who had an unconfirmed partial response. Per the RECIST criteria, confirmed responses are defined as responses that are confirmed by a repeat assessment that is performed at least 4 weeks after the criteria for response are first met. If the responses cannot be confirmed by a repeat assessment (due to reasons such as discontinuation from study due to toxicity or progression), then the responses are classified as unconfirmed partial or complete responses.

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The graph below shows the change in tumor size for each of the patients in the phase 2 clinical trial as of October 31, 2009. Each vertical bar in the graph represents the percent change from the time when the patient entered the clinical trial (baseline) until the maximum change was observed for that patient. The changes in tumor size are based on independent radiological assessment.

The most common treatment-related adverse events seen in our phase 2 clinical trial of tivozanib were hypertension (50%) and hoarseness of voice, or dysphonia (22%), both of which are believed to be directly related to the mechanism of VEGF pathway inhibition. Of the 272 patients enrolled in the clinical trial, as of October 31, 2009, only 10.3% required a dose reduction and only 3.7% required a dose interruption. The incidence of certain side effects commonly associated with other VEGF receptor inhibitors was notably low.

The table below illustrates drug-related adverse events seen in >5% of patients as of October 31, 2009, including the number of patients in which these drug-related adverse events were seen. Grade 1 and 2 adverse events are generally characterized as mild. Grade 3 adverse events are considered moderate, and Grade 4 adverse events are considered severe. The incidence of mucositis, stomatitis and hand-foot syndrome were less than 5%, with less than 1% Grade 3 or Grade 4 events reported.

Drug-Related Adverse Events

(seen in >5% of patients as of October 31, 2009)

	Severity				
	Grade 1	**Grade 2**	**Grade 3**	**Grade 4**	**Total**
Adverse Event	**# (%)**	**# (%)**	**# (%)**	**# (%)**	**# (%)**
Hypertension	59(21.7)	53(19.5)	21(7.7)	3(1.1)	136(50.0)
Hoarseness of Voice	55(20.2)	4(1.5)	0	0	59(21.7)
Asthenia (Muscle weakness)	7(2.6)	21(7.7)	6(2.2)	0	34(12.5)
Diarrhea	21(7.7)	8(2.9)	4(1.5)	0	33(12.1)
Fatigue	10(3.7)	8(2.9)	4(1.5)	0	22(8.1)
Dyspnoea	10(3.7)	6(2.2)	3(1.1)	0	19(7.0)
Rash	9(3.3)	5(1.8)	3(1.1)	0	17(6.3)
Cough	10(3.7)	4(1.5)	3(1.1)	0	14(5.1)

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Phase 3 Clinical Trial. Based on the results of the phase 2 clinical trial of tivozanib and following discussions we have had with the FDA and EMEA, we initiated a phase 3 clinical trial in patients with advanced RCC in December 2009. We refer to the phase 3 clinical trial as our TIVO-1 study. The TIVO-1 study is expected to enroll 500 patients at more than 90 sites in 17 countries, including in the United States, Canada, Europe, Latin America and India.

The TIVO-1 study is a randomized, controlled clinical trial of tivozanib compared to Nexavar in patients with advanced RCC who are treatment-naïve or have received no more than one prior regimen of immunotherapy or chemotherapy, and no prior VEGF-targeted therapy. Unlike in the phase 2 clinical trial of tivozanib where we permitted the enrollment of patients with both clear cell and non-clear cell RCC, and did not require that patients be nephrectomized, enrollment in the TIVO-1 study will be restricted to patients with clear cell RCC who have had a prior nephrectomy. The primary endpoint for the trial will be progression-free survival. 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. Secondary endpoints include overall survival, objective response rate, duration of response, which is a measure of the time from when a patient s tumors have shrunk until they resume their growth in size, and quality of life, as measured from questionnaires completed by the patient which provide information about symptoms and the impact of the cancer on a patient s daily life activities. Results from the TIVO-1 study, together with results from our already completed phase 2 clinical trial, will form the basis for registration applications to be submitted to the U.S. and European regulatory agencies for tivozanib s approval in advanced RCC.

Nexavar was approved in the United States in December 2005 as the first VEGF receptor inhibitor for the treatment of advanced RCC. Nexavar received marketing authorization by the European Commission in July 2006 for the treatment of patients with advanced RCC who have failed prior interferon-a or interleukin-2 based therapy or are considered unsuitable for such therapy. In the phase 3 clinical trial of Nexavar, patients with advanced clear cell RCC, 94% of whom had undergone a prior nephrectomy, treated with Nexavar had a median progression-free survival of 5.5 months and patients treated with placebo had a median progression-free survival of 2.8 months.

We chose Nexavar as the active comparator for the TIVO-1 study because Nexavar has been extensively tested in patients with advanced RCC who had received no prior drug treatment as well as advanced RCC patients who had failed prior therapy with interferon-a or interleukin-2. Because the TIVO-1 study will allow enrollment of a broad RCC population (treatment-naïve as well as previously-treated patients), we believe that Nexavar is the most appropriate active comparator for tivozanib in this patient population. Following discussions, both the FDA and EMEA indicated that Nexavar is an acceptable choice as the active comparator in the TIVO-1 study.

In the TIVO-1 study, patients will be randomized in equal numbers to treatment with tivozanib or Nexavar. Patients randomized to the tivozanib treatment arm will receive tivozanib on the same dose and schedule that was well tolerated in our phase 2 clinical trial of tivozanib. Patients randomized to the Nexavar treatment arm of the clinical trial will receive the approved dose of Nexavar, which is 400 mg twice a day. Patients randomized to the tivozanib treatment arm who have documented disease progression will be discontinued from the clinical trial. Patients randomized to the Nexavar treatment arm who have documented disease progression will be discontinued from the clinical trial and will be given the option to receive tivozanib by enrolling in a separate long-term treatment protocol. In order to meet FDA standards for assessing results in phase 3 trials, all radiology scans will be assessed by a single, centralized group of independent radiology reviewers in the United States who will be blinded to the assigned treatment. There can be no assurance that the efficacy and safety profile seen in prior clinical trials of Nexavar and of tivozanib will be reproduced in the TIVO-1 study.

In addition to the TIVO-1 study, we plan to conduct, or seek waivers from conducting, a variety of other clinical trials that would support a New Drug Application, or NDA, including a mass balance study, a food effect study, a thorough QTc study, drug-drug interaction studies, special population studies, and a pediatric study. We are also conducting additional toxicology studies in non-human primates and rodents, which will be included in our registration application.

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Tivozanib Combination Therapy

We believe tivozanib s favorable efficacy and safety profile increases its potential to be combined with other anti-cancer agents in a manner that may produce better clinical outcomes. As a result, we have a number of clinical trials underway that are designed to test tivozanib in combination with other drugs and chemotherapies in multiple solid tumor types. We are also utilizing our Human Response Platform to help identify rational drug combinations and patient populations most likely to be responsive to these combination therapies. We expect that the results of these clinical trials, together with the results of our ongoing research efforts, will help to inform our clinical development plans for tivozanib in additional indications.

Renal Cell Cancer. In 2007, we initiated a phase 1 clinical trial of tivozanib in combination with Torisel, an injectable mTOR inhibitor, in patients with advanced clear cell RCC who have failed up to one prior VEGF-targeted therapy. Torisel was approved by the FDA for the treatment of advanced RCC in 2007, and is considered a standard of care for treatment of patients with poor-prognosis RCC. Based on preclinical studies we have conducted using our Human Response Platform, we believe that the combination of tivozanib and mTOR inhibitors may have enhanced anti-tumor activity in patients with RCC.

Clinical trials have shown that Sutent cannot be used in combination with Torisel due to severe toxicities. A phase 1 clinical trial testing the combination of Sutent and Torisel was discontinued when two out of the first three patients treated in the first cohort with less than full doses of each drug (15 mg of Torisel and 25 mg of Sutent) developed serious dose-limiting toxicities.

Nexavar has also had a significant challenge combining with Torisel at full doses due to a variety of dose-limiting toxicities. The only approved VEGF pathway inhibitor that we are aware of that is currently being developed in combination with Torisel at full doses is Avastin. The preliminary data using this combination showed a high rate of tumor shrinkage in RCC. However, the combination of Avastin and Torisel requires a weekly intravenous injection, placing a high burden on the patients quality of life.

While no other oral VEGF receptor inhibitor has demonstrated that it can be safely combined with Torisel, to date, the results of our ongoing phase 1 clinical trial indicate that tivozanib may be able to be used safely in combination with Torisel at full doses. As of October 30, 2009, with a median duration of treatment of 16.8 weeks, no dose-limiting toxicities have been reported. Preliminary results of this ongoing study show tumor shrinkage in 12 out of 16 patients in all dose groups evaluated, and two partial responses as assessed by RECIST criteria, as shown in the graph below.

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Colorectal Cancer. We believe that tivozanib has the potential to significantly enhance the treatment of colorectal cancer when used in combination with standard of care chemotherapy or other targeted drugs. According to the American Cancer Society, approximately 148,000 patients will have been diagnosed with colorectal cancer, and 50,000 patients will have died from this disease, in the United States in 2009. Despite recent advances in chemotherapy, the American Cancer Society also reports that less than 10% of patients with metastatic colorectal cancer survive beyond 5 years. Therefore, there is a critical need for new and more effective treatments for colorectal cancer. Based on recent clinical trials, Avastin in combination with chemotherapy has become the standard of care for metastatic colorectal cancer. These studies have demonstrated that the VEGF pathway is important in colorectal cancer. We believe more potent inhibitors of the pathway, such as tivozanib, have the potential to improve therapy for this disease.

In 2008, we initiated a phase 1 clinical trial of tivozanib in combination with FOLFOX6, a standard chemotherapy regimen, in patients with colorectal and other gastrointestinal cancers. This clinical trial has shown that tivozanib can be safely administered at full dose (1.5 mg) in combination with full dose FOLFOX6 chemotherapy. As of February 1, 2010, 20 patients were enrolled in this trial and being treated with one of three doses of tivozanib in combination with FOLFOX6. Three of these patients have demonstrated a confirmed partial response (one patient each with pancreatic, esophageal and colorectal cancer). This clinical trial is currently enrolling patients for an expanded assessment of safety and activity in this patient population.

Building on the safety data generated to date in the Torisel combination clinical trial in RCC, we are also interested in exploring the safety and activity of tivozanib in combination with an mTOR inhibitor in colorectal cancer. A phase 1 investigator-sponsored clinical trial is being initiated with a combination of tivozanib and Afinitor, an oral mTOR inhibitor approved for the treatment of RCC. If this trial is successful, we believe that an all oral regimen comprising a VEGF pathway inhibitor and an mTOR inhibitor would be an attractive drug combination worthy of further development in colorectal cancer.

Breast Cancer. We believe that tivozanib can provide an improved therapy for women diagnosed with breast cancer. In 2009, approximately 192,000 women will have been diagnosed with invasive breast cancer, and 40,000 women will have died from breast cancer, in the United States, according to the American Cancer Society. Currently available chemotherapy and hormonal therapies have significantly enhanced the survival of women diagnosed with breast cancer; however metastatic breast cancer remains an incurable disease. Recent clinical trials with Avastin showed improved results when used in combination with paclitaxel chemotherapy in women with metastatic breast cancer. Avastin is now FDA approved for women with metastatic breast cancer. Recently presented phase 2 clinical trial data also showed that Nexavar, when combined with Xeloda, an oral chemotherapy approved in breast cancer, showed improved outcomes over Xeloda alone; however, overlapping toxicities have resulted in numerous side effects, including more than 40% of patients experiencing Grade 3 hand-foot syndrome. Based on tivozanib s favorable toxicity profile, and minimal off-target toxicities with tivozanib monotherapy in clinical trials to date, we believe that tivozanib has the potential to be safely combined with Xeloda.

In 2008, we initiated a phase 1 clinical trial of tivozanib in combination with a standard dose of paclitaxel in patients with metastatic breast cancer. As of February 1, 2010, 18 patients have been enrolled in this trial, of whom 4 patients have demonstrated a confirmed partial response. This clinical trial is currently enrolling patients at full dose of 1.5 mg of tivozanib in combination with full dose paclitaxel chemotherapy.

Non-small Cell Lung Cancer. We believe that tivozanib could also provide an improved treatment for patients with advanced non-small cell lung cancer, or NSCLC. Lung cancer is the most deadly cancer in men and women, with approximately 219,000 new cases and 159,000 deaths in the United States in 2009, according to the American Cancer Society. Chemotherapy has shown modest activity in NSCLC and advanced lung cancer remains an incurable disease. Avastin, approved by the FDA for use in NSCLC in combination with chemotherapy, and various small molecular VEGF receptor inhibitors have demonstrated modest single-agent activity in lung cancer.

In 2009, we initiated a phase 1 clinical trial of tivozanib monotherapy in patients with advanced NSCLC. This clinical trial is testing a continuous dosing regimen of tivozanib and will also provide preliminary

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indications of activity in this cancer. Demonstrating the safety of a continuous dosing regimen of tivozanib in advanced NSCLC would facilitate the development of tivozanib in combination with chemotherapy in advanced NSCLC.

AV-299: Anti Hepatocyte Growth Factor (HGF) Antibody

Through the use of our Human Response Platform, our scientists have identified the HGF/c-Met pathway as a significant driver of tumor growth. HGF is a protein that circulates in the blood and binds to and activates a receptor called c-Met. Activation of c-Met is believed to be important in normal processes in embryonic development and wound healing. Activation of c-Met, however, is also believed to trigger many activities that are involved in cancer development and metastasis. Altered HGF/c-Met signaling is observed in many tumors including bladder, lung, breast, gastric, ovarian, prostate, colorectal, head and neck, certain sarcomas and several other solid tumors and in multiple myeloma and leukemias. There are no approved therapies which target the HGF/c-Met pathway.

Less than two years after our scientists characterized the importance of the HGF/c-Met pathway, we identified our AV-299 antibody, a potent and selective inhibitor of HGF. In preclinical models, AV-299 has demonstrated an ability to inhibit the growth of many different tumors, including lung and colon tumors, glioblastomas and multiple myeloma. In preclinical studies of AV-299 we have also shown that AV-299 has additive efficacy when given in combination with other approved anti-cancer agents such as Tarceva (erlotinib), Erbitux (cetuximab) and Temodar (temozolomide). In preclinical studies conducted by us, AV-299 was more effective at inhibiting tumor growth (at the dose tested) than AMG-102 and TAK-701, the other anti-HGF antibodies currently in clinical development. Clinical trials will need to be conducted in order to determine whether the differences observed in these preclinical studies will contribute to greater efficacy in patients.

In March 2007, we entered into a collaboration agreement with Merck under which we granted Merck worldwide rights to develop and commercialize AV-299. Merck funds all development and manufacturing expenses, subject to an agreed-upon budget, and is required to pay us development milestones and royalties on the sale of AV-299. 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, and for conducting translational research to guide the clinical development of AV-299. Merck is responsible for manufacturing AV-299 for clinical and commercial use, and for global development after completion of such proof-of-concept trial and for commercialization activities. 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.

In 2008, we commenced a phase 1 clinical trial of AV-299 in patients with a variety of solid tumors to establish the safety, tolerability, pharmacokinetics, maximum tolerated dose and the recommended phase 2 clinical trial dose of AV-299 as monotherapy. The phase 1 clinical trial showed good tolerability with no dose limiting toxicities up to the highest dose tested, 20mg/kg. The most frequently observed adverse events were mild fatigue, tissue swelling, also referred to as edema, and headache. The phase 1 clinical trial also includes a cohort to test the activity of AV-299 in multiple myeloma, as well as a cohort to test the safety of combining AV-299 with Tarceva, an EGFR inhibitor.

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Eleven out of 24 patients enrolled in the phase 1 clinical trial experienced stable disease lasting for 12 weeks or more, as shown in the chart below.

We are also conducting a phase 1 clinical trial in cancer patients with liver metastases in order to evaluate the activity of AV-299 in HGF pathway activation in metatastic tumors. Additionally, a phase 1 clinical trial is also being initiated to evaluate the ability of AV-299 to cross the blood brain barrier in patients suffering from primary brain cancer.

As part of our strategic partnership with Merck, we are also using our Human Response Platform to identify tumor types and patient populations most likely to be responsive to AV-299 therapy. There are very few traditional preclinical models that are driven by HGF/c-Met. Consequently, we have utilized our proprietary technology to develop novel model systems that can be used preclinically to give insights into the best clinical settings in which to test a novel inhibitor of the pathway. We believe that these preclinical models will provide us with an advantage over other competitive programs.

We and our partner Merck are planning a phase 2 clinical trial program to test the combination of AV-299 with other rationally chosen chemotherapeutic or targeted agents in selected indications based on our preclinical studies using our Human Response Platform. Based on the observations that the EFGR and HGF/c-Met pathways are both frequently activated in many solid tumors, and that activation of the HGF/c-MET pathway appears to be a common resistance mechanism to EGFR inhibition, the first phase 2 clinical trial will test a combination of AV-299 with Iressa (gefitinib), an EGFR inhibitor, versus Iressa alone in patients with newly diagnosed non-small-cell lung cancer. This 170-patient, randomized clinical trial, which will be conducted in Asia, is expected to begin in the first half of 2010 and will study response rate and progression-free survival in patients with a high incidence of EGFR mutations.

AV-203: Anti-ErbB3 Antibody Program

Through the use of our Human Response Platform, our scientists have highlighted the importance of the ErbB3 receptor in tumor growth. ErbB3 belongs to a family of four proteins that also includes EGFR and Her2.

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Both EGFR and Her2 have been implicated in promoting the growth of significant numbers of tumors, particularly in breast and lung cancers. Drugs blocking the activity of EGFR have demonstrated clinical benefit in lung, colon and head and neck cancers while drugs targeting Her2 show clinical benefit in the treatment of Her2 overexpressing breast cancers.

ErbB3 is significantly over-expressed in many human breast, ovarian, prostate, colorectal, pancreatic, gastric, and head and neck cancers and its overexpression generally correlates with poor prognosis. It has also been implicated in resistance to certain drugs which target EGFR in lung cancer and with resistance to radiotherapy. In addition, while the anti-Her2 antibody Herceptin has been very successful in treating many breast tumors which express Her2, as many as 60% of Her2 positive patients do not respond, as reported in a 2007 Herceptin review by C.A. Hudis published in *The New England Journal of Medicine*. Because ErbB3 preferentially binds with Her2, we believe that breast cancer patients who do not respond well to anti-Her2 therapy might benefit from drug combinations with an anti-ErbB3 antibody.

Through our discovery efforts, we have identified antibodies that have been shown to be potent and selective inhibitors of ErbB3 in preclinical studies. In preclinical testing, these antibodies have significantly inhibited the growth of a number of different tumors, including breast, prostate and pancreatic cancers. In the first quarter of 2010, we intend to select a development candidate and commence manufacturing of this candidate in preparation for preclinical studies and human clinical trials. We have not yet submitted to the FDA an investigational new drug application for any product candidate under our AV-203 program.

In March 2009, we granted Biogen Idec an exclusive option to obtain rights to co-develop (with us) and commercialize 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 thereof, 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 in the United States, Canada and Mexico. We retain the 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.

Other Antibody Pipeline Programs

In addition to the HGF/c-Met pathway and ErbB3, we have utilized our Human Response Platform to identify a number of other targets that appear to be potent drivers of tumor growth. We have further evaluated the involvement of these targets in the development of human cancers using available human cancer databases. Targets with the ability to drive tumor growth in our tumor models and with frequent genetic alterations in human cancers were selected as targets for our next generation of antibody drug discovery programs. The targets we have focused on to date are the Notch receptors, FGF receptors and the RON receptor, as more fully described below.

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Notch Program. Genetic screens conducted using our Human Response Platform have demonstrated that activation of the Notch signaling pathway is a potent driver of tumor growth and confirmed its important role in tumor formation, or tumorigenesis. The Notch receptors are a family of four receptors on the surface of cells, Notch 1-4, whose activity has been shown to play important roles in normal stem cell function and in multiple aspects of tumor biology.

Notch signaling is also thought to be important for the maintenance of cancer stem cell populations in tumors. Cancer stem cells are thought to represent a distinct cell population within the tumor contributing to tumorigenesis. Cancer stem cells may cause tumor metastasis and relapse following anti-tumor treatments by regenerating the tumor tissue. Eradication of cancer stem cells may lead to increased survival in cancer patients. We intend to use our Notch specific antibodies to investigate the role of Notch signaling in the maintenance of cancer stem cells. We believe that this effort may lead to the development of a novel therapeutic regimen that specifically targets cancer stem cell populations.

The goal of our Notch drug discovery efforts is to identify specific inhibitory antibodies to Notch1, Notch2 and Notch3 that prevent ligand binding and activation of the receptors. The program has generated functional inhibitory antibodies against the Notch1 and Notch3 receptors. Our team has demonstrated proof of concept with our lead Notch1 antibody candidate in preclinical models of angiogenesis and preclinical testing is ongoing. In these preclinical models, our Notch1 antibody shows no evidence of the gastro-intestinal toxicity that has limited the clinical development of other Notch inhibitors.

We are utilizing our Human Response Platform to investigate the context in which Notch inhibition, either alone or in combination with tivozanib, would have the greatest efficacy. Because the blockade of Notch1 signaling results in a potent inhibition of angiogenesis by a mechanism which differs from VEGF inhibition, we believe that blockade of both pathways simultaneously might significantly increase the efficacy of anti-angiogenesis therapy. We are also exploring preclinical models to determine which tumors might be uniquely dependent on Notch1 function for survival as another mechanism of action for the drug. Our scientists have identified the HeyL protein as a potential biomarker that predicts that a significant subset of tumors driven by the mutant Ras oncogene may depend on Notch function. Oncogenes are genes that, when mutated, help turn normal cells into cancer cells. Specifically, high levels of HeyL in colon and pancreatic cell lines that carry a mutated form of Ras correlate with the sensitivity of these tumors to Notch pathway inhibitors. In June 2009, we were granted a U.S. patent on a method of identifying cancer tissue likely to be sensitive or resistant to treatment with an inhibitor of Notch receptor activation.

Fibroblast Growth Factor Program. Fibroblast growth factors, or FGFs, and their receptors, FGFR1-4, represent a signaling network that plays important roles in the regulation of cell growth, survival, differentiation and angiogenesis. Work in our Human Response Platform identified FGF ligands and receptors as powerful drivers of tumor growth in a variety of tumor models and implicated the activation of the pathway in tumor development. Increasing amounts of human genetic and genomic data also point to the alteration of this pathway in the development of a number of different types of human cancers.

Recently, the human Cancer Genome Sequencing project identified the FGF/FGFR pathway as the most frequently altered signaling pathway in human cancers. Similar studies demonstrated that FGF pathway activation may not only play a role in tumor development but also may be implicated in the development of drug resistance. Different tumors and tumor types exhibit varying profiles of FGF pathway alterations; therefore, targeting individual FGFR receptors may have different therapeutic applications.

Certain FGF ligands have been shown to have pro-angiogenic activity and may act synergistically with VEGF to amplify tumor angiogenesis. The upregulation of FGF pathway activity in response to anti-VEGF therapy is thought to play an important role in the development of resistance to VEGF inhibition, suggesting that the combination of FGF and VEGF pathway inhibitors may add to the benefits achievable by targeting VEGF alone.

The goal of our ongoing drug discovery efforts is to identify specific FGFR1, FGFR2, FGFR3 and FGFR4 inhibitory antibodies that prevent activation of these receptors. We will evaluate the activity of candidate antibodies in specific target-driven tumor models created using our Human Response Platform.

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RON Program. RON is a receptor closely related to c-Met which is the receptor for HGF, the target of AV-299. Similarly, the Macrophage Stimulating Protein, or MSP protein, which activates RON, is most closely related to HGF. The activation of RON signaling is believed to trigger many of the same cellular activities as activation of the HGF/c-Met pathway. Like c-Met, RON has been implicated in promoting tumor cell metastasis and invasiveness and, in one preclinical breast cancer model, RON expression in tumor cells dramatically increased their ability and propensity to metastasize to bone.

RON and c-Met are frequently co-expressed in certain tumors. Breast, bladder and colon cancer patients whose tumors have high levels of RON or c-Met have a poor prognosis and the worst prognosis has been observed in patients in which both receptors were overexpressed.

Our scientists have identified antibodies which can inhibit the growth of RON-driven tumors created through our Human Response Platform. Preclinical testing of these antibodies is ongoing.

Our Human Response Platform

Our scientific founders, Ronald A. DePinho, M.D. and Lynda Chin, M.D., both of the Harvard Medical School and the Dana Farber Cancer Institute, Tyler Jacks, Ph.D., of the Massachusetts Institute of Technology, and Raju Kucherlapati, Ph.D., of the Harvard Medical School, leaders in the field of cancer modeling and cancer genetics, believed that traditional preclinical cancer models were poorly predictive of drug responses in patients and that work from their various laboratories indicated that substantially better models of cancer could be developed. Accessing key intellectual property and insights from our founders, we have created a series of unique genetically engineered models of cancer, as well as proprietary ways of analyzing complex gene expression data to better translate such data from our models to human patient populations. These innovations help to address three key issues in cancer drug discovery and clinical development:

Target Identification and Validation: Identifying and validating which of the many candidate cancer causing genes are most important to tumor growth.

Drug Discovery: Enabling the development of tumor models driven by the target gene of interest to facilitate the evaluation of drug candidates directed against the target, and the selection of the most promising candidate.

Biomarker Identification: Enabling the identification of genetic markers, or biomarkers, which may help identify patients who are more likely to be responsive or resistant to such drugs by leveraging the naturally occurring genetic variation in our cancer models and their divergent sensitivity to anti-cancer drugs.

We believe that our platform provides unique insights into cancer biology that may provide us and our strategic partners with a competitive advantage in all phases of cancer drug discovery and development. To date, Merck, OSI and Schering-Plough (now Merck) have entered into agreements with us to utilize our Human Response Platform.

Scientific Background

Cancer is a disease caused by genetic mutations that accumulate in cells over the lifetime of an individual that can ultimately result in the unrestrained growth of the altered cells and their invasion into surrounding normal tissues. Cancer causing mutations arise at random within a cell, which then undergoes a selective process where any mutation that provides the cell with an increased ability to grow and survive is retained. It is estimated that at least a dozen different mutations are required to transform a normal cell into a cancerous one. Even within specific types of cancer that all carry certain powerful cancer causing mutations, there are multiple combinations of additional mutations present such that each individual tumor is slightly different.

During the last 20 years, many of the mutations which promote cancer in people have been identified from human tumors. These have generally fallen into two classes: oncogene activating mutations and tumor suppressor

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gene mutations. Oncogene activating mutations function to promote cell growth. By analogy to driving a car, oncogene activating mutations act much liking pushing the accelerator to the floor, giving a permanent signal to promote cell growth. Examples of these mutations include mutations in EGFR, Her2 and K-Ras. Tumor suppressor gene mutations inactivate mechanisms which turn off cell growth. Elimination of tumor suppressor gene function is analogous to cutting the brake lines in the car: mechanisms to stop the growth of the cell are gone. When a single cell collects an oncogene activating mutation and a tumor suppressor gene mutation, it is not yet transformed into a cancer cell but it is well on its way. Research has shown that introduction of these two types of mutations in many different cell types is sufficient to induce tumor formation over time. During this time, additional spontaneous mutations arise to complete the transformation of the normal cell into a full blown cancer cell capable of unlimited growth.

Limitations of Existing Cancer Models

Researchers use cancer models to help identify targets for new cancer drugs, to help screen the best drugs directed against such targets and to help identify which cancer patients are most likely to benefit from treatment with such drugs. For these reasons, cancer models which most accurately recreate the attributes of cancer in patients are important to increase the likelihood of successfully developing new safe and effective cancer drugs.

For the past several decades the standard models used by cancer researchers have been xenograft models. A xenograft model is created by adapting cells from a human tumor to grow in a petri dish. These cells are then injected under the skin of a mouse, where they grow into a tumor. Researchers can then test drugs to see if they can inhibit growth of the resulting tumors without causing unacceptable side effects.

This approach has several limitations. First, the process of adapting the human tumor cells to grow in a petri dish results in further unintended changes to the tumor cells that cause them to change in ways that do not reflect the original tumor from which they came. Second, because of the differences between human cells and mouse cells, the human cells are not able to interact in a natural way with the cells in the surrounding tissues. Finally, because there are relatively few of these xenografts models for each human tumor type, it is difficult to understand the reasons why some of these models respond to certain drugs and others do not.

Xenograft models are often poor predictors of the success of cancer drugs in human clinical trials and there is a substantial need in oncology for preclinical models that better replicate human cancer. For example, as reported in a 2006 article by K. Garber in *Journal of National Cancer Institute*, only 3.8% of patients in phase 1 clinical cancer drug trials show a significant clinical response, whereas most of these drugs have been shown to work in xenograft models in mice.

Our Human Response Platform

We were founded with the goal of developing a fundamentally new kind of cancer model designed to overcome many of the limitations of traditional xenografts models, and thereby improve the probability of success in developing new cancer drugs. We utilize these novel models to identify and validate target genes which drive tumor growth, to identify drugs which can block the function of these targets, and to identify patients who are most likely to respond favorably to treatment with such drugs. We have used these models to advance drugs in our pipeline and in collaboration with our strategic partners such as Merck, OSI, Schering-Plough (now Merck) and Biogen Idec. Our cancer models, together with the various techniques we have developed to use these models to aid in the discovery and development of new cancer drugs, are collectively referred to as our Human Response Platform. Key components of our Human Response Platform are covered by issued patents or pending patent applications.

Our Novel Approach to Modeling Human Cancer

We begin the development of our genetically-engineered tumor models by introducing a human oncogene into mouse stem cells in which we have inactivated the function of a tumor suppressor gene. As in human cancer, these are the two key elements which are necessary to begin the process of a cell becoming cancerous. The

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oncogene is introduced in a manner which allows us to control its expression we can direct in which tissue it will be expressed (e.g., breast or lung or colon), and we can turn it on by adding a simple non-toxic chemical to the animal s drinking water. We refer to this genetic engineering process as the inducible oncogene approach, as it allows the researcher to control whether or when to induce, or turn on, the oncogene.

Originally, we used this inducible oncogene approach in germ line transgenic mice, which we licensed from the Dana Farber Cancer Institute when we were founded, in which the oncogene is expressed in all of the cells of the animal. However, recognizing that in naturally occurring human tumors oncogenes are only activated in a subset of the cells of the body, we subsequently developed an alternate method which are called chimeric mice, in which the oncogene is only activated in a subset of the cells of the animal. This makes it a more realistic model than a germ line transgenic model in which the entire animal is made up of genetically modified cells.

In our patented method of making chimeric mouse models, the key starting mutations that will allow them to develop into cancerous cells are introduced directly into the stem cells. Then, we inject the stem cells into 3-day old mouse embryos, alongside normal cells, and implant the embryos into mice. When the mice are born, we turn on the expression of the oncogene. Animals do not develop tumors right away, but expression of the oncogene begins a process whereby the engineered cells begin to accumulate additional genetic alterations randomly over a period of months. Eventually, most animals develop tumors in the tissue where we have directed the oncogene to be expressed. Importantly, although the initial driving oncogene is the same in every tumor, the additional mutations which accumulate are different from animal to animal, just as would be the case in a human population.

The power and versatility of our mouse model platform is greatly enhanced by our patented method of making chimeric mouse models. Prior to our invention of this patented method, every time a different chimeric model was desired, a germ line transgenic mouse containing all the desired genetic modifications had to be produced by a lengthy process that included at least one, and often several, rounds of breeding, in order to obtain the embryonic stem cells necessary to make the desired chimeric model. For a biopharmaceutical company frequently needing to produce new chimeric models containing different mutations, producing each new chimeric model through the conventional breeding process would be prohibitively time-consuming. We addressed this problem by greatly improving the speed of chimeric model production. In our patented method, it is no longer necessary to do mouse breeding every time a new chimeric model is produced. Instead, all the desired genetic

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modifications are assembled directly in an individual mouse embryonic stem cell, which is then injected into a mouse embryo. This reduces the time required to produce each new chimeric mouse model by as much as one year. We believe that this ability to produce new chimeric models in a commercially meaningful time frame is an important advance in the state of the art.

In addition to this patented method of making new tumor models, we have also developed a model of human breast cancer in which we have applied many of these same features to genetically modified human breast tissue. This Human-in-Mouse model is created by first isolating normal human breast tissue from surgical specimens, genetically modifying it to express oncogenes and then introducing the modified tissue into specially-engineered mice. The modified breast tissue first grows into normal breast tissue, but then rapidly develops into human breast tumors while growing in the mouse breast tissue. To our knowledge this is the first and only preclinical model in which normal human breast tissue has been engineered to develop into spontaneous breast tumors in a mouse.

Advantages of Our Cancer Models

We believe that our novel cancer models have a number of unique advantages over traditional xenografts and other methods of developing cancer models used in many academic settings. First, because the tumors grow naturally in the animals, the normal interactions between tumors and the tissues around them, including blood vessels, are preserved. This is not the case in traditional xenografts, where human tumor cells are implanted into mice, and certain of the important cellular signals sent by the growing human tumor may not be recognized by the surrounding mouse cells. Second, as is the case in human cancer, the cancer cells grow alongside normal cells, whereas in many other cancer models, all of the cells of the animal contain the cancer-causing mutations. Third, because of the switch that we introduce into our models, we can turn on the cancer-causing mutations after the animals are born, replicating what is seen in many human cancers. In many other models, these mutations are on before the animals are born, and interfere with their normal embryonic development. Finally, because tumors in our model develop spontaneously after introduction of the initial cancer causing mutations, we can develop populations of tumors that exhibit differences in genetic backgrounds, again much more akin to what is seen in a population of human tumors.

Use of Our Models in Target Discovery and Validation

In a proprietary method called the MaSS screen, we turn off the inducible oncogene driving the growth of the tumors in our models. We then activate other genes in the tumor cells to see if the tumor cells grow with the driving oncogene turned off. This allows us to screen for genes capable of replacing the function of a known oncogene. Such genes are potential new targets for anti-cancer drugs. The MaSS screen technique is protected by issued patents exclusively licensed to us by the Dana-Farber Cancer Institute.

We have conducted MaSS screens in multiple tumor models we developed in different tumor types with different genetic backgrounds. These screens identified many genes important in tumor formation. The most common pathway identified in our screens has been the HGF/c-Met pathway, and this observation triggered the initiation of our program to develop antibodies against HGF (our AV-299 program). Numerous other pathways have also been identified in our screens, including ErbB3, Notch and FGF, all of which are now the basis of certain of our ongoing antibody discovery programs.

The data from all of the screens performed to date are routinely re-evaluated and compared with data coming from other sources, such as mutations identified in the human Cancer Genome Sequencing project. Many target genes originally identified in the screen are poorly understood these targets become more interesting as targets as new data about their function becomes available. This now very large data set provided the basis of our target discovery strategic partnerships with both Merck and OSI. In the case of OSI, scientists from our company and OSI have reevaluated our target data base with a goal of finding novel targets possibly involved in the transition of a tumor cell to a more aggressive phase, where the original epithelial tumor cell becomes more mesenchymal like more invasive and able to survive passage through the blood stream the so-called epithelial-mesenchymal transition.

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Use of Our Models in Drug Discovery

One of the significant challenges in drug discovery can often be identifying preclinical models that are driven by a particular target of interest. Human xenografts, for example, may be driven by multiple targets, and have many other limitations. For this reason, developing tumor models that are known to be driven by a particular target can be an important drug discovery tool for identifying the most potent drug candidates against that target.

Because the driving oncogene in our models can be turned on and off, we can turn off the oncogene and replace it with other genes of interest. For example, in the cells of a breast tumor that was originally driven by Her2, we can turn off the Her2 gene, and replace it with EGFR, another important oncogene. When we do so, the tumors that arise from those cells are no longer sensitive to drugs that inhibit Her2, but are sensitive to drugs that inhibit EGFR. These tumors provide an excellent system for studying the relative ability of different EGFR inhibitors, either antibodies or small molecules, to affect tumor growth driven by EGFR. This is a powerful preclinical model for ranking the efficacy of different compounds and an example of our patented directed complementation technique. Frequently, similar systems are not available for new targets or newly discovered mutated forms of existing targets, and, accordingly, this technology provides a convenient way of rapidly generating new drug testing systems. We have used this approach to support our antibody drug discovery and development programs.

Use of Our Models in Biomarker Identification

Because each of the tumors that develops in our models accumulates random genetic mutations independently, populations of tumors in our models exhibit a significant degree of genetic heterogeneity. Consequently, the tumors that develop in our models, like human tumor populations, typically exhibit variation in response to anti-cancer drugs. The tumors in our models have been studied extensively for genetic characteristics, providing an opportunity to correlate the genetic makeup, or genetic context, of each tumor with its relative sensitivity or resistance to a given anti-cancer drug. By understanding the genetic context of tumors that respond to particular drugs, we hope to identify genetic markers, or biomarkers, that can be measured in patients prior to treatment to select or predict which tumors, tumor subtype, or patient subsets are most likely to respond to a given anti-cancer drug. We are using this approach to identify potential biomarkers for our pipeline drugs and it will be important to demonstrate that the biomarkers we identify translate into clinical benefit in humans. We are also using this approach to assist our strategic partners, such as Merck and OSI, in the development of drugs in their pipelines.

In our tivozanib program, we have used our Human Response Platform to identify candidate biomarkers that are expected to help to predict responsiveness to tivozanib therapy. Because most traditional xenograft models are highly sensitive to VEGF pathway inhibitors (in fact, more sensitive than human tumors in patients), such models are not useful for identifying biomarkers. In contrast, because we are able to identify both responsive and resistant tumors in our models and compare the genetic makeup of the tumors, our Human Response Platform is very useful for identifying candidate biomarkers. We have an issued United States patent on a biomarker test for identifying patients likely to be sensitive or resistant to treatment with tivozanib. We also have a pending United States patent application to a second tivozanib response biomarker test. We intend to use these candidate biomarker tests in clinical trials of tivozanib.

Similar efforts to identify candidate biomarkers for our other development programs are also underway. For instance, in June 2009, we were granted a U.S. patent on a method of identifying cancer tissue likely to be sensitive or resistant to treatment with an inhibitor of Notch activation.

Competition

The biotechnology and pharmaceutical industries are highly competitive. There are many pharmaceutical companies, biotechnology companies, public and private universities, and research organizations actively engaged in the research and development of products that may be similar to our products. A number of multinational pharmaceutical companies, as well as large biotechnology companies, including Roche

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Laboratories, Inc., or Roche, Pfizer Inc., or Pfizer, Bayer HealthCare AG, or Bayer, and GlaxoSmithKline plc, or GSK, are pursuing the development or are currently marketing pharmaceuticals that target VEGF, HGF and ErbB3, or other oncology pathways on which we are focusing. It is probable that the number of companies seeking to develop products and therapies for the treatment of unmet needs in oncology will increase.

Many of our competitors, either alone or with their strategic partners, have substantially greater financial, technical and human resources than we do and significantly greater experience in the discovery and development of product candidates, obtaining FDA and other regulatory approvals of products and the commercialization of those products. Accordingly, our competitors may be more successful than we may be in obtaining approval for drugs and achieving widespread market acceptance. Our competitors drugs may be more effective, or more effectively marketed and sold, than any drug we may commercialize and may render our product candidates obsolete or non-competitive before we can recover the expenses of developing and commercializing any of our product candidates. We anticipate that we will face intense and increasing competition as new drugs enter the market and advanced technologies become available.

Tivozanib Competition

Angiogenesis inhibitors represent a rapidly growing drug category in oncology with 2008 sales in excess of $6.0 billion worldwide, based on 2008 annual reports made publicly available by companies marketing such drugs. There are currently four FDA-approved drugs in oncology which target the angiogenesis pathway. Avastin (Roche) is an infused monoclonal antibody approved in combination with other anti-cancer agents for the treatment of metastatic colorectal cancer, metastatic non-small cell lung cancer, Her2-negative metastatic breast cancer, and advanced RCC. It is also approved as a monotherapy for the treatment of glioblastoma in patients with progressive disease following prior therapy. There are three FDA-approved oral small molecule VEGF receptor inhibitors, Nexavar, marketed by Bayer and Onyx Pharmaceuticals, Inc., Sutent, marketed by Pfizer and Votrient, marketed by GSK, that are non-specific and target other receptors more potently than the VEGF receptors. Nexavar is approved as a monotherapy for advanced RCC and unresectable hepatocellular cancer; Sutent is approved as a monotherapy for advanced RCC and for gastrointestinal stromal tumors; Votrient is approved as a monotherapy for advanced RCC. Other recently approved agents for the treatment of RCC are Torisel, marketed by Pfizer and Afinitor, marketed by Novartis Pharmaceuticals Corporation, both of which inhibit mTOR.

We are aware of a number of companies that have ongoing programs to develop both small molecules and biologics to target the VEGF pathway. We believe the only other VEGF pathway inhibitor in late stage development in RCC is Pfizer s AG013736 (axitinib), which is currently in a phase 3 clinical trial for the second-line treatment of advanced RCC. Other VEGF pathway inhibitors in late stage development in other cancer types include Amgen Inc. s and Takeda Pharmaceutical Company Limited s AMG706 (motesanib), AstraZeneca plc s AZD2171 (Recentin, cediranib) and AZD6474 (Zactima, vandetanib), Boehringer Ingelheim International GmbH s BIBF-1120, Bristol-Myers Squibb Company s BMS-582664 (brivanib alaninate), Exelixis Inc. s and BMS XL-184 (BMS-907351), ImClone LLC s IMC-1121b, Onco Therapy Science Inc. s OTS-102 and Regeneron Pharmaceuticals, Inc. s and Sanofi-Aventis US LLC s aflibercept.

We believe tivozanib potentially offers several important advantages over the other VEGF pathway inhibitors on the market and in development, including stronger potency, which could lead to better efficacy, and higher selectivity to the VEGF receptors, which could lead to fewer off-target toxicities. Taken together, we believe that these properties may also create the opportunity for a full-dose combination of tivozanib and various chemotherapies and targeted agents.

AV-299 Competition

We believe the products in development targeting HGF consist of Amgen s AMG-102 (rilotumumab), currently in phase 2 clinical trials, and Takeda s TAK-701 (HuL2G7, under license from Galaxy Biotech, LLC), currently in phase 1 clinical trials.

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Other clinical stage drugs which target the HGF/c-Met pathway include Roche s MetMAb (5D5 Fab), ArQule, Inc. s / Daiichi Sankyo, Inc. s ARQ-197, MethylGene, Inc. s MGCD-265, Exelixis and GSK s XL-880 (foretinib), Pfizer s PF-2341066 and Exelixis and BMS XL-184.

AV-203 Program Competition

We believe the most direct competitors to our AV-203 program are monoclonal antibodies which specifically target the ErbB3 receptor, including Merrimack Pharmaceuticals, Inc. s and Sanofi-Aventis MM-121 and Daiichi Sankyo s and Amgen s U3-1287 / AMG-888, both of which are in phase 1 clinical development. Other clinical-stage competitors include PharmaMar s elisidepsin and Merrimack s MM-111.

Strategic Partnerships

We have entered into multiple strategic partnerships in which we have granted rights to certain aspects of our Human Response Platform and antibody products. These agreements provide us with a source of cash flow in the form of upfront payments, equity investments, research and development funding, payments upon achievement of specified milestones, and potential royalties from product sales.

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

Strategic Partner	Initial Date of Agreement	Subject Matter	Payments Received as of December 31, 2009[1]
Kyowa Hakko Kirin	December 2006	Tivozanib[2]	N/A
OSI Pharmaceuticals	September 2007	Target and Biomarker Identification	$44.0 million
Biogen Idec	March 2009	AV-203	$50.0 million[3]
Schering-Plough	March 2007	AV-299	$45.9 million
(now Merck)			
Merck	November 2003	Target Identification	$22.3 million
Merck	August 2005	Biomarker Identification	$6.5 million

(1) Includes upfront payments, equity investments, research and development funding and milestone payments.

(2) We in-licensed the rights to our lead product candidate, tivozanib, in all territories of the world, except for Asia.

(3) Includes an equity investment made prior to the initial date of the agreement.

Kyowa Hakko Kirin

In December 2006, we entered into a license agreement with Kirin Brewery Co. Ltd. (now Kyowa Hakko Kirin) under which we obtained an exclusive license to research, develop, manufacture and commercialize tivozanib (f/k/a KRN951), pharmaceutical compositions thereof and associated biomarkers. In this description, our references to tivozanib include pharmaceutical compositions thereof and associated biomarkers. Our exclusive license covers all territories in the world, except for Asia. The territory in which we are licensed is referred to as our territory. Kyowa Hakko Kirin has retained rights to tivozanib in Asia, including the People s Republic of China, India and Japan. Under the license agreement, we obtained exclusive rights in our territory under certain Kyowa Hakko Kirin patents, patent applications and know-how related to tivozanib, to research, develop, make, have made, use, import, offer for sale, and sell tivozanib for the diagnosis, prevention and treatment of any and all human diseases and conditions. We have the right to grant sublicenses under the foregoing licensed rights, subject to certain restrictions. In addition, we may, but are not obligated to, apply our

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Human Response Platform to identify optimal chemotherapy combinations, as well as additional patient populations likely to respond to tivozanib monotherapy and combination therapy. We and Kyowa Hakko Kirin each have access to and can benefit from the other party s clinical data and regulatory filings with respect to tivozanib and biomarkers identified in the conduct of activities under the license agreement.

Under the license agreement, we are obligated to use commercially reasonable efforts to develop and commercialize tivozanib in our territory, including meeting certain specified diligence goals. We also must obtain Kyowa Hakko Kirin s consent if we intend to change the initial indication for which we seek marketing approval for tivozanib to an indication other than RCC. Prior to the first anniversary of the first post-marketing approval sale of tivozanib in our territory, neither we nor any of our subsidiaries has the right to clinically develop, seek marketing approval for or commercialize any other product that also works by inhibiting the activity of the VEGF receptor.

Upon entering into the license agreement, we made a one-time cash payment in the amount of $5.0 million. In addition, we are required to make various milestone payments which could total, in the aggregate, $60.0 million, including a milestone payment in connection with the TIVO-1 study (or initiation of the first phase 3 clinical trial for tivozanib designed to support an application for marketing approval) and certain other milestone payments upon the achievement of specified regulatory milestones. We are also required to pay tiered royalty payments on net sales we make of tivozanib in our territory, which range from the low to mid teens as a percentage of net sales. The royalty rate escalates within this range based on increasing tivozanib sales. Our royalty payment obligations in a particular country in our territory begin on the date of the first commercial sale of tivozanib in that country, and end on the later of 12 years after the date of first commercial sale of tivozanib in that country or the date of the last to expire of the patents covering tivozanib that have been issued in that country. In the event we sublicense the rights licensed to us under the license agreement, we are required to pay Kyowa Hakko Kirin a specified percentage of any amounts we receive from any third party sublicensees, other than amounts we receive in respect of research and development funding or equity investments, subject to certain limitations.

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

OSI Pharmaceuticals

In September 2007, we entered into a collaboration and license agreement with OSI Pharmaceuticals, Inc., or OSI, which provides for the use of our proprietary *in vivo* models by our scientists at our facilities, 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 EMT, or mesenchymal-epithelial transition, or MET, in cancer. EMT/MET processes are of emerging significance in tumor development and disease progression. We are currently working with OSI on the development of proprietary target-driven tumor models for use in target validation, drug screening and biomarker identification to support OSI s drug discovery and development activities. The research program portion of our strategic partnership began in October 2007 and will expire at the end of June 2011 unless the agreement is terminated earlier by either party. Key elements of our strategic partnership with OSI include:

identifying and validating a pre-agreed number of oncology targets for drug discovery, development and commercialization by OSI;

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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

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 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, with the right to grant sublicenses, under 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 agreement. 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.

In connection with the July 2009 expansion of our strategic partnership with OSI, we granted OSI a non-exclusive license to access our proprietary bioinformatics platform, and non-exclusive perpetual licenses to use bioinformatics data and to use a proprietary gene index related to a specific target pathway. Further, as part of our expanded strategic partnership, we granted OSI an option to receive non-exclusive perpetual rights to certain elements of our Human Response Platform and our bioinformatics platform, including the right to obtain certain of our tumor models and tumor archives. If OSI elects to exercise this additional option and we transfer the relevant technology to OSI, OSI will be required to pay us license expansion fees equal to, in the aggregate, $25 million.

During the remainder of the research program, which will expire in June 2011, neither we nor our affiliates has the right to conduct validation or biomarker research with respect to certain pre-agreed targets that are being, or may be, pursued under our strategic partnership, or to grant any such rights to any third party. Further, during the remainder of the research program, we cannot grant any third party rights to intellectual property used in creating the tumor models and archives to which we granted OSI an option, except that we may grant rights in this intellectual property and these archives to our affiliates and to third parties in connection with the partnering of our existing drug discovery and development programs. We also retain the right to use this intellectual property and these archives for our internal research purposes, including internal use for the benefit of our existing and future third party strategic partners.

Upon entering into the initial collaboration and license agreement with OSI in September 2007, we received a one-time cash payment of $7.5 million and an equity investment in the amount of $5.5 million. In July 2009, in connection with the expanded rights we granted to OSI, we received a one-time cash payment of $5.0 million and an equity investment in the amount of $15.0 million. As of December 31, 2009, we have received approximately $8.2 million in research and development funding under the agreement, and we will continue to receive research funding to support all individuals we devote to the strategic partnership until expiration of the research program. To date, we have received milestone payments under the agreement in the amount of $2.8 million. If all applicable milestones are achieved, payments for the successful achievement of discovery, development and commercialization milestones under the agreement could total, in the aggregate, over $94.0 million for each target and its associated products. In addition, OSI is required to make payments to us upon our completion of additional deliverables under the research plan. Upon commercialization of products under the agreement, we are eligible to receive tiered royalty payments on sales of products by OSI, its affiliates and sublicensees. OSI s royalty obligations to us in a particular country begin on the date of first commercial sale of the product in that country, and end on the latest to occur of: (i) 10 years after the first commercial sale of the product, (ii) expiration of regulatory exclusivity applicable to the product (if any) and (iii) the date of expiration of the last to expire issued patent covering the product in the applicable country.

At the conclusion of the research program, we will retain rights to any targets that were included in the strategic partnership but were not selected by OSI. We have also obtained exclusive rights to certain intellectual property developed by OSI under our strategic partnership to develop and commercialize small molecule products and associated diagnostics with respect to the targets that were returned to us, and to develop and

commercialize antibody products against any target, other than the targets OSI selected for the development of antibody products. In connection with the licenses granted to us from OSI, we are required to make a one-time milestone payment upon regulatory approval and to pay a royalty on sales of each product where the regulatory approval of the product includes a claim in the product label for a targeted patient population and such claim in the product label is covered by patent rights developed under our strategic partnership.

The collaboration and license agreement will remain in effect until the expiration of both OSI s royalty obligations to us, and our royalty obligations to OSI, in each case determined on a product-by-product and country-by-country basis. OSI has the right to terminate the agreement with respect to any or all collaboration targets and all associated products. Either party has the right to terminate the agreement in connection with a material breach of the agreement by the other party that remains uncured for a specified cure period. If OSI elects to terminate the agreement due to our material breach, we will lose our rights to certain intellectual property developed under the strategic partnership, and OSI will have the right to reduce its milestone and royalty obligations to us by the amount of monetary damages suffered by OSI as a direct result of our material breach. If OSI elects to terminate the agreement with respect to one or more collaboration targets and all associated products, OSI s licenses to such targets and products will terminate and revert to us, or if we elect to terminate the agreement due to OSI s material breach of the agreement, OSI s licenses to all targets and products will terminate and revert to us, in either case subject to our continued milestone and royalty payment obligations to OSI, which we will have the right to reduce by the amount of monetary damages we suffer as a direct result of OSI s breach. In addition, if OSI elects to terminate the agreement with respect to one or more collaboration targets and associated products, for a specified time period after such termination OSI and its affiliates may not, nor may they grant third parties the right to, conduct research or development activities with respect to the terminated collaboration target(s).

Biogen Idec

In March 2009, we entered into an exclusive option and license agreement with Biogen Idec International GmbH, a subsidiary of Biogen Idec Inc., which are collectively referred to herein as 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. 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, including the right to grant sublicenses, under our relevant intellectual property to develop and manufacture ErbB3 antibody products, and (2) an exclusive license, including the right to grant sublicenses, 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 retain the exclusive right to commercialize ErbB3 antibody products in the United States, Canada and Mexico. In this description, the countries in the world other than the United States, Canada and Mexico are referred to as Biogen Idec s territory, and the United States, Canada and Mexico are referred to as our territory. If Biogen Idec exercises its exclusive option to ErbB3 antibody products, Biogen Idec will grant us (a) co-exclusive (with Biogen Idec), worldwide license under Biogen Idec s relevant intellectual property, to develop and manufacture ErbB3 antibody products anywhere in the world, and (b) an exclusive license under Biogen Idec s relevant intellectual property, 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 will share the written work plan with Biogen Idec for its review and comment, and we are required to use commercially reasonable efforts to perform the activities set forth in the work plan. 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, we will then be solely responsible, subject to a mutually agreed development plan, budget and the oversight of a joint development committee, for

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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. Further, neither party has the right to conduct development activities in its respective territory if those development activities would materially and adversely affect the development of ErbB3 antibody products in the other party s 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. If either party wishes to develop a new ErbB3 antibody product under the agreement, and the other party does not also wish to develop that product, the party that desires to conduct development activities regarding the new ErbB3 antibody product has the right to independently, and at its sole cost, develop and manufacture the new ErbB3 antibody product for commercialization solely in its territory.

We are solely responsible for, and obligated to use commercially reasonable efforts to, manufacture and supply clinical and commercial quantities of ErbB3 antibody products for the Biogen Idec territory and for the United States, Canada and Mexico. If we determine to retain a third party to manufacture and supply ErbB3 antibody products for phase 3 clinical trials and/or for commercialization in the United States, Canada and Mexico or the Biogen Idec territory, then we must first notify Biogen Idec thereof, and, subject to certain limitations, Biogen Idec may elect to become the sole supplier of ErbB3 antibody product for phase 3 clinical trials and for worldwide commercialization.

Pursuant to the agreement, commercialization efforts will be discussed and coordinated at meetings of the joint commercialization committee, comprised of our and Biogen Idec s representatives. We have the sole right, at our sole expense (including manufacturing costs), to commercialize ErbB3 antibody products in the United States, Canada and Mexico, and we are required to use commercially reasonable efforts to do so in countries in our territory where marketing approval has been obtained. Biogen Idec has the sole right, at its sole expense (including manufacturing costs) to commercialize ErbB3 antibody products in its territory, and is required to use commercially reasonable efforts to do so in countries in its territory where marketing approval has been obtained.

We have agreed that, prior to Biogen Idec s exercise of its exclusive option, or until the expiration of Biogen Idec s option right, we and our affiliates will not grant any third party rights to develop ErbB3 antibodies in our territory or in the Biogen Idec territory. We have also agreed that, during the term of the agreement, we will not grant any third party rights to develop or commercialize ErbB3 antibody products if such third party is independently developing or commercializing its own product containing an ErbB3 antibody. Prior to entering into discussions with, or granting a license or sublicense to, any third party with respect to the commercialization of ErbB3 antibody products, we are required to negotiate in good faith with Biogen Idec for a limited time period with respect to granting such rights to Biogen Idec. We have also agreed that, except pursuant to our agreement with Biogen Idec, during the term of the agreement, neither we nor our affiliates, alone or with or on behalf of any third party, will develop, manufacture or commercialize any ErbB3 antibody for therapeutic or diagnostic use in humans, or grant rights to any third party to do any of the foregoing.

Upon entering into the exclusive option and license agreement with Biogen Idec, we received a one-time cash payment in the amount of $5.0 million and an equity investment in the amount of $30.0 million. In June 2009, we received a $5.0 million milestone payment for achievement of the first pre-clinical discovery milestone under the agreement. We could also receive (i) additional near-term pre-clinical discovery and development milestone payments of $10.0 million in the aggregate, and (ii) if Biogen Idec exercises its option to obtain exclusive rights to commercialize ErbB3 antibody products in its territory, an option exercise fee and regulatory milestone payments of $50.0 million in the aggregate. If Biogen Idec exercises its exclusive option, Biogen Idec will pay us royalties on its sales of ErbB3 antibody products in the Biogen Idec territory, and we will pay Biogen Idec royalties on our sales of ErbB3 antibody products in the United States, Canada and Mexico. Biogen Idec s royalty obligations to us, and our royalty obligations to Biogen Idec, determined on a product-by-product and country-by-country basis, commence on the first commercial sale of the ErbB3 antibody product in the applicable country, and expire on the later of the date of expiration of (1) the last applicable patent covering the

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ErbB3 antibody product in the applicable country, and (2) any regulatory exclusivity applicable to the ErbB3 antibody product in that country.

If Biogen Idec fails to exercise its exclusive option to co-develop and commercialize ErbB3 antibody products, then the agreement will terminate on the date Biogen Idec s option right expires, and we will retain all of our rights to develop, manufacture and commercialize our ErbB3 antibody products. If Biogen Idec exercises its exclusive option to co-develop and commercialize ErbB3 antibody products, then, unless earlier terminated, the agreement will remain in effect until the last to expire of all royalty obligations under the agreement, or, if later, upon completion of any development activities that were pending before the expiration of all royalty obligations under the agreement.

Biogen Idec may terminate the agreement for convenience with respect to any product(s), by providing us with three months prior written notice. Either party may terminate the agreement due to a material breach of the agreement by other party that is not cured within a short period.

If Biogen Idec terminates the agreement for convenience, or if we terminate the agreement due to a material breach of the agreement by Biogen Idec, in each case prior to Biogen Idec s exercise of its exclusive option (and prior to the expiration of the option exercise period), then Biogen Idec s exclusive option will terminate.

If Biogen Idec terminates the agreement for convenience, or if we terminate the agreement due to a material breach of the agreement by Biogen Idec, in each case with respect to one or more ErbB3 antibody products after Biogen Idec s exercise of its exclusive option, then at our election, (1) Biogen Idec will lose all rights to the terminated product(s), (2) we will have the worldwide right to develop, manufacture and commercialize the terminated product(s), subject to milestone and royalty obligations to Biogen Idec in our territory and in the Biogen Idec territory, and (3) Biogen Idec will be required to transfer to us all regulatory approvals, data, promotional materials and other documents, materials and information reasonably necessary to enable us to develop, manufacture and commercialize the terminated products in the Biogen Idec territory. Further, in the case of termination by Biogen Idec for convenience, Biogen Idec will be required to continue to pay its share of all development costs with respect to the terminated product for a specified period after the effective date of termination.

If Biogen Idec terminates the agreement due to our material breach of the agreement, at Biogen Idec s election (1) if not yet exercised, Biogen Idec will be deemed to have exercised its exclusive option and will not be required to pay us the option exercise fee, (2) Biogen Idec will have no further milestone payment obligations to us, (3) we will lose all rights to the terminated product(s), (4) Biogen Idec will have the worldwide right to develop, manufacture and commercialize the terminated product(s), subject to royalty obligations to us based on worldwide net sales, and (5) we will be required to transfer to Biogen Idec all regulatory approvals, data, promotional materials and other documents, materials and information reasonably necessary to enable Biogen Idec to develop, manufacture and commercialize the terminated products in the Biogen Idec s territory.

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, Biogen Idec will have the option to either terminate the agreement or maintain the agreement. If Biogen Idec elects to terminate the agreement, then each party will have the right to develop, manufacture and commercialize ErbB3 antibody products for its respective territory, subject to reduced royalty obligations to the other party, and Biogen Idec s activities will not be subject to the oversight of the joint committee. If Biogen Idec elects to maintain the agreement, Biogen Idec will have the right to assume the key development, manufacturing, budgeting and governance rights, responsibilities, and obligations under the agreement that had previously been our rights and obligations.

Schering-Plough (now Merck)

In March 2007, we entered into an agreement (which became effective in April 2007) with Schering-Plough (now Merck), through its subsidiary Schering Corporation, acting through its Schering-Plough Research Institute division, under which we granted Merck worldwide, exclusive rights to develop and commercialize all of our

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monoclonal antibody antagonists of hepatocyte growth factor, or HGF, including AV-299, for therapeutic and prophylactic use in humans and for veterinary use. We also granted Merck an exclusive, worldwide license to related biomarkers for diagnostic use. Merck has the right to grant sublicenses under the foregoing licensed rights. 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 designed to demonstrate achievement of a primary efficacy endpoint in humans as established by the parties. Merck will be responsible for clinical development of AV-299 after completion of such proof-of-concept trial. We are currently leading the clinical development of AV-299, which includes the conduct of multiple phase 1 trials and preparation for 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.

Merck is solely responsible for all commercialization activities and expenses, subject to our right to elect to co-promote AV-299 in the United States for the first oncology indication for which Merck files for marketing approval in the United States. If the first oncology indication for which Merck files for marketing approval is not a large market oncology indication, defined as first or second-line treatment of non-small cell lung cancer, breast cancer, colon cancer or prostate cancer, then we will also have the right to co-promote AV-299 in the United States for the first large market oncology indication for which Merck files for marketing approval. Until the date that is two years after 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, neither we nor Merck has the right, alone, or in collaboration with or by granting rights to any other party, to research, develop, manufacture or commercialize another product that binds to HGF and directly inhibits or modulates the activity of HGF.

Upon entering into the license agreement with Merck, we received a one-time cash payment in the amount of $7.5 million and an equity investment in the amount of $10.0 million. As of December 31, 2009, we have received approximately $22.6 million in research and development funding under the agreement. Milestone payments for the successful development and commercialization of AV-299, if all approvals in multiple indications and all sales milestones are achieved, could total, in the aggregate, $464.0 million. Upon commercialization, we are eligible to receive tiered royalty payments on Merck s net sales of AV-299, which range from low double digits to high teens as a percentage of net sales. Merck s royalty obligations in a particular country begin on the date of first commercial sale of a product in that country, and end on the later of 10 years after the date of first commercial sale of the product in that country or the date of the last to expire of the issued patents covering the product in that country. The agreement will remain in effect until the expiration of all of Merck s royalty obligations to us, determined on a product-by-product and country-by-country basis. Merck has the right to terminate the agreement at will upon 90 days written notice to us. Either party has the right to terminate the agreement in connection with an insolvency event or a material breach of the agreement by the other party that remains uncured for a specified cure period. In the event that Merck terminates the agreement at will, or if we terminate the agreement due to Merck s material breach of the agreement or bankruptcy, worldwide rights to the development, manufacture, and commercialization of AV-299 revert back to us. If rights to AV-299 are returned to us as a result of a termination of the agreement, we will be required to make tiered royalty payments to Merck if the termination occurs after initiation of the first clinical trial for AV-299 having safety and efficacy endpoints that, if met, are sufficient to apply for regulatory approval.

Merck

Target Identification Collaboration

In November 2003, we entered into a license and collaboration agreement with Merck to discover and validate oncology targets. During the research program portion of the collaboration, which concluded in November 2006, we used our proprietary cancer models to identify and subsequently validate essential tumor maintenance genes suitable as targets for small molecule drug development. During the research program, Merck exercised its option with respect to, and we granted Merck an exclusive, worldwide license, with the right to

grant sublicenses, to six molecular targets, and associated data, discovered and validated by us under the research collaboration, to develop, manufacture and commercialize small molecule products directed to such targets for therapeutic use. In conjunction with the exclusive license granted to Merck, we granted Merck non-exclusive licenses, with the right to grant sublicenses, to (1) develop, manufacture and commercialize products and compounds directed at certain targets for diagnostic use, and (2) develop, manufacture and use biological products (antibodies, proteins, polypeptides, etc.) directed at certain targets solely for the research or development of products for therapeutic and/or diagnostic use. We also granted Merck a non-exclusive right to use data generated during the collaboration, not related to the six collaboration targets exclusively licensed by Merck, solely for Merck s and its affiliates internal research purposes. Except for the six collaboration targets selected by Merck, we retain all of our rights to targets that were explored under the research collaboration. Merck is solely responsible for drug discovery, clinical development and commercialization of the products directed to the six collaboration targets it selected.

Upon entering into the agreement with Merck, we received a $7.0 million cash up-front payment. Over the course of the three-year research program, we received approximately $6.0 million in research funding, and as of December 31, 2009, we have received milestone payments of approximately $300,000. The collaboration was expanded in April 2005, and as part of that expansion, we received a $5.0 million equity investment. We also received cash payments of $2.0 million in each of May 2005 and April 2006 in return for providing Merck with rights to advance a pre-agreed number of targets into high-throughput screening. In addition, if all development and regulatory milestones are reached with respect to each of the six targets, potential additional milestone payments could total, in the aggregate, $249.0 million. We are also eligible to receive tiered royalties from Merck based on the sales of products that are directed to or use the collaboration targets selected by Merck. Merck s royalty obligations in a particular country begin on the date of first commercial sale of a product in that country, and end on the later of 10 years after the date of first commercial sale of the product in that country or the date of the last to expire of the issued patents covering the product in that country.

Our agreement with Merck will remain in effect for the length of Merck s royalty obligation to us, determined on a product-by-product and country-by-country basis. Merck has the right to terminate the agreement at any time, in its sole discretion, upon 120 days prior written notice to us. Either party has the right to terminate the agreement in connection with a material breach of the agreement by the other party that remains uncured for a specified cure period. If Merck terminates the agreement at will, or if we terminate the agreement due to Merck s material breach of the agreement, Merck s licenses to develop, manufacture, and commercialize products directed to or using the collaboration targets will terminate, and we will be permitted to use the data generated under our collaboration to research, develop and commercialize products directed to such targets.

Biomarker Identification Collaboration

In August 2005, we entered into our second collaboration with Merck, a license and research collaboration agreement relating to the use of our Human Response Platform. The collaboration concluded in December 2007 and was focused on the 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.

Under the terms of the agreement, Merck obtained exclusive rights to all inventions and discoveries developed in the conduct of the collaborative research program that relate to Merck s proprietary cancer compounds, including gene expression patterns that correlate with a response to Merck s compounds. We and Merck jointly own the rights to all inventions and discoveries developed in the conduct of the collaborative research program that relate to control compounds (i.e. non-Merck compounds), including gene expression patterns that correlate with a response to the control compounds. Upon entering into the license and research collaboration agreement with Merck, we received a $2.0 million equity investment, and over the course of the collaborative research program we received approximately $4.5 million in research funding. If all development and regulatory milestones under the agreement are achieved, potential milestone payments could total, in the aggregate, $4.9 million.

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Either party may terminate the agreement in the event of an uncured material breach by, or a bankruptcy event of, the other party. If Merck terminates the agreement due to our material breach of the agreement, Merck s payment obligations to us will also terminate. Merck may terminate the agreement at any time for convenience by providing us with at least 120 days prior written notice, however, Merck s payment obligations to us will continue after such termination if the applicable milestone events are achieved. If the license and research collaboration agreement is not terminated as described above, the agreement will continue in effect until the expiration of all of Merck s payment obligations to us under the agreement.

Patents and Proprietary Rights

General Intellectual Property Considerations

We have been building and will seek to continue to build a strong intellectual property portfolio. In this regard, we have focused on patents, patent applications and other intellectual property covering:

tivozanib and related technologies

- U.S. patents: 4 issued; 2 pending; expirations ranging from 2018 to 2029
- European patents: 3 granted; none pending; expirations ranging from 2018 to 2023
- Canadian patents: none granted; 1 pending; expiration 2022
- Australian patents: 1 granted; none pending; expiration 2022
- International application: 1 pending; expiration 2029

our antibody product pipeline and related technologies

- U.S. patents: 3 issued; 3 pending; expirations ranging from 2027 to 2029
- European patents: none granted; 2 pending; expirations 2027
- International application: 2 pending; expiration 2029

various facets of our technology platform

- U.S. patents: 4 issued; 2 pending; expirations ranging from 2020 to 2025

- European patents: 1 granted; 3 pending; expirations ranging from 2022 to 2026

- Australian patents: 2 granted; 2 pending; expirations ranging from 2022 to 2026

We strive for multi-tiered patent protection, where possible. For example, with respect to tivozanib, we have exclusively licensed patents that cover the molecule and its therapeutic use (patent expiration 2022, with the possibility of patent term extension to 2027 in the United States), a key step in manufacturing the molecule, and a crystal form of the molecule, i.e., a polymorph with low hygroscopicity used in the clinical formulation. Complementing these in-licensed patents relating to tivozanib, is our own issued U.S. patent that covers a biomarker test for identifying human patients likely to respond to treatment with tivozanib, a pending application on a different tivozanib response biomarker test, and a pending application on a method of using tivozanib in combination with temsirolimus.

We own issued U.S. patents containing composition-of-matter claims that cover our HGF antibodies. In addition, we own pending patent applications covering our HGF antibodies, our FGFR3 antibodies, and methods of making and using those antibodies. We are prepared to file patent applications on the other antibodies in our antibody product pipeline soon after the experimental data necessary for a strong application become available.

In addition to filing and prosecuting patent applications in the United States, we file counterpart patent applications in Europe, Canada, Japan, Australia (and sometimes additional countries), in cases where we think such foreign filing is likely to be cost-effective.

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The term of individual patents depends upon the legal term of the patents in the countries in which they are obtained. In most countries in which we file, the patent term is 20 years from the earliest date of filing a non-provisional patent application. In the United States, a patent s term may be lengthened by patent term adjustment, which compensates a patentee for administrative delays by the U.S. Patent and Trademark Office in granting a patent, or may be shortened if a patent is terminally disclaimed over another patent.

The patent term of a patent that covers an FDA-approved drug may also be eligible for patent term extension, which permits patent term restoration as compensation for the patent term lost during the FDA regulatory review process. The Drug Price Competition and Patent Term Restoration Act of 1984, or the Hatch-Waxman Act, permits a patent term extension of up to five years beyond the expiration of the patent. The length of the patent term extension is related to the length of time the drug is under regulatory review. Patent extension cannot extend the remaining term of a patent beyond a total of 14 years from the date of product approval and only one patent applicable to an approved drug may be extended. Similar provisions are available in Europe and other foreign jurisdictions to extend the term of a patent that covers an approved drug. In the future, if and when our pharmaceutical products receive FDA approval, we expect to apply for patent term extensions on patents covering those products.

In addition, our patent portfolio contains a number of patents and patent applications relevant to our business. For example, we own a granted U.S. patent and pending foreign counterpart applications covering a method of making a chimeric mouse cancer model. We also own a granted U.S. patent and pending foreign counterpart patent applications covering a method of producing primary tumor material via directed complementation. We also own pending U.S. and foreign patent applications covering a mouse model that contains a human breast tumor. Furthermore, we own a granted U.S. patent and a pending international patent application covering a method of identifying cancer tissue likely to be sensitive or resistant to treatment with an inhibitor of Notch receptor activation. Besides having a portfolio of patents and pending patent applications owned by us covering our platform technology, we are exclusively licensed under Dana-Farber patents that cover germ line transgenic mouse models of cancer, and a method of using spontaneous inducible mouse tumor models to screen for, and identify, novel targets for new cancer drugs, which we refer to as our MaSS screen technology.

For some aspects of our proprietary technology, trade secret protection is more appropriate than patent protection. For example, our proprietary bioinformatics software tools and databases are protected as trade secrets. Our bioinformatics tools and databases give us the means to store, analyze, interpret and integrate the large volume of data generated from our various tumor models and from analysis of human clinical samples from clinical trials. We continually make incremental improvements in our proprietary software tools, as we tailor them to the changing needs of our research and development programs. In general, trade secret protection can accommodate this continuing evolution of our bioinformatics system better than other forms of intellectual property protection.

Many pharmaceutical companies, biotechnology companies and academic institutions are competing with us in the field of oncology and filing patent applications potentially relevant to our business. In order to contend with the inevitable possibility of third party intellectual property conflicts, we make freedom-to-operate studies an ongoing part of our business operations. With regard to tivozanib, we are aware of a third party United States patent, and corresponding foreign counterparts, that contain broad claims related to the use of an organic compound that, among other things, inhibits VEGF binding to one of the VEGF receptors. We are also aware of third party United States patents that contain broad claims related to the use of a tyrosine kinase inhibitor in combination with a DNA damaging agent such as chemotherapy or radiation and we have received written notice from the owners of such patents indicating that they believe we may need a license from them in order to avoid infringing their patents. With regard to AV-299, we are aware of two separate families of United States patents, United States patent applications and foreign counterparts, with each of the two families being owned by a different third party, that contain broad claims related to anti-HGF antibodies having certain binding properties and their use. We are aware of a United States patent that contains claims related to a method of treating a tumor by administering an agent that blocks the ability of HGF to promote angiogenesis in the tumor. With regard to AV-203, we are aware of a third party United States patent that contains broad claims relating to anti-ErbB3 antibodies. Based on our analyses, if any of the above third party patents were asserted against us, we do not

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believe our proposed products or activities would be found to infringe any valid claim of these patents. If we were to challenge the validity of any issued United States patent in court, we would need to overcome a statutory presumption of validity that attaches to every United States patent. This means that in order to prevail, we would have to present clear and convincing evidence as to the invalidity of the patent s claims. There is no assurance that a court would find in our favor on questions of infringement or validity.

From time to time, we find it necessary or prudent to obtain licenses from third party intellectual property holders. Where licenses are readily available at reasonable cost, such licenses are considered a normal cost of doing business. In other instances, however, we may use the results of freedom-to-operate studies to guide our early-stage research away from areas where we are likely to encounter obstacles in the form of third party intellectual property. For example, where a third party holds relevant intellectual property and is a direct competitor, a license might not be available on commercially reasonable terms or available at all. We strive to identify potential third party intellectual property issues in the early stages of research of our research programs, in order to minimize the cost and disruption of resolving such issues.

In spite of these efforts to avoid obstacles and disruptions arising from third party intellectual property, it is impossible to establish with certainty that our technology platform or our product programs will be free of claims by third party intellectual property holders. Even with modern databases and on-line search engines, literature searches are imperfect and may fail to identify relevant patents and published applications. Even when a third party patent is identified, we may conclude upon a thorough analysis, that we do not infringe the patent or that the patent is invalid. If the third party patent owner disagrees with our conclusion and we continue with the business activity in question, we might have patent litigation thrust upon us. Alternatively, we might decide to initiate litigation in an attempt to have a court declare the third party patent invalid or non-infringed by our activity. In either scenario, patent litigation typically is costly and time-consuming, and the outcome is uncertain. The outcome of patent litigation is subject to uncertainties that cannot be quantified in advance, for example, the credibility of expert witnesses who may disagree on technical interpretation of scientific data. Ultimately, in the case of an adverse outcome in litigation, we could be prevented from commercializing a product or using certain aspects of our technology platform as a result of patent infringement claims asserted against us. This could have a material adverse affect on our business.

To protect our competitive position, it may be necessary to enforce our patent rights through litigation against infringing third parties. Litigation to enforce our own patent rights is subject to the same uncertainties discussed above. In addition, however, litigation involving our patents carries the risk that one or more of our patents will be held invalid (in whole or in part, on a claim-by-claim basis) or held unenforceable. Such an adverse court ruling could allow third parties to commercialize our products or our platform technology, and then compete directly with us, without payment to us.

In-Licenses

Dana-Farber Cancer Institute. When forming the company in March 2002, we entered into a license agreement with Dana-Farber Cancer Institute, or DFCI. Under the agreement, we have: exclusive, worldwide rights under certain DFCI patents and patent applications relating to spontaneous, inducible mouse tumor models; the right to grant sublicenses; and sole ownership rights to any improvements made solely by our employees to the mouse model technology licensed from DFCI. We have fulfilled certain milestone payment obligations to DFCI. We will have no royalty obligation to DFCI based on sales of products discovered, designed, developed or tested using the licensed mouse tumor models. Our license from DFCI will expire on the expiration date of the last-to-expire of the underlying patents.

Kyowa Hakko Kirin. In December 2006, we entered into a license agreement with Kirin Brewery Co. Ltd. (now Kyowa Hakko Kirin) under which we obtained an exclusive license to research, develop, manufacture and commercialize tivozanib (f/k/a KRN951), pharmaceutical compositions thereof and associated biomarkers for the diagnosis, prevention and treatment of any and all human diseases and conditions. Our exclusive license covers all territories in the world, except for Asia. Kyowa Hakko Kirin has retained rights to tivozanib in Asia. Subject to certain restrictions, we have the right to grant sublicenses under the foregoing licensed rights. Under the

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Kyowa Hakko Kirin license agreement, we have obligations to make milestone, royalty and sublicensing revenue payments to Kyowa Hakko Kirin. For further discussion of this agreement, please see Strategic Partnerships Kyowa Hakko Kirin.

Other. We hold several non-exclusive licenses from other third parties that give us access to various technologies involved in building and using our technology platform and discovering and developing our antibody pipeline.

Manufacturing

We currently contract with third parties for the manufacture of our product candidates for preclinical studies and clinical trials and intend to do so in the future. We do not own or operate manufacturing facilities for the production of clinical or commercial quantities of our product candidates. We currently have no plans to build our own clinical or commercial scale manufacturing capabilities. To meet our projected needs for commercial manufacturing, third parties with whom we currently work will need to increase their scale of production or we will need to secure alternate suppliers. Although we rely on contract manufacturers, we have personnel with extensive manufacturing experience to oversee the relationships with our contract manufacturers.

One of our contract manufacturers has manufactured what we believe to be sufficient quantities of tivozanib s active pharmaceutical ingredient (or drug substance) to support the ongoing phase 1 and phase 3 clinical trials. We believe the current manufacturing process for the active pharmaceutical ingredient for tivozanib is adequate to support future development and commercial demand. In addition, currently, a separate contract manufacturer manufactures, packages and distributes clinical supplies of tivozanib. While we believe that our existing supplier of active pharmaceutical ingredient would be capable of continuing to produce active pharmaceutical ingredient in commercial quantities, we will need to identify a third party manufacturer capable of providing commercial quantities of drug product. If we are unable to arrange for such a third-party manufacturing source, or fail to do so on commercially reasonable terms, we may not be able to successfully produce and market tivozanib.

The process for producing AV-299 has been developed and multiple batches of drug substance have been and are continuing to be produced to support clinical trials of AV-299 through phase 2 clinical trials. Our strategic partner Merck is responsible for the continued process development and all manufacturing of AV-299, including for clinical trial and commercial use.

To date, our third-party manufacturers have met our manufacturing requirements. We believe that there are alternate sources of supply that can satisfy our clinical and commercial requirements, although we cannot be certain that identifying and establishing relationships with such sources, if necessary, would not result in significant delay or material additional costs.

Sales and Marketing

Due to its unique efficacy and safety profile, we believe that tivozanib could address the needs of many patients who currently are not fully satisfied with other approved treatment options in advanced RCC. If tivozanib is approved, we intend to maximize its potential value in the U.S. by demonstrating tivozanib s efficacy and favorable safety profile, with a goal of establishing tivozanib as the first-line treatment of choice for patients with advanced RCC.

We intend to build the commercial infrastructure in the United States necessary to effectively support the commercialization of tivozanib and future oncology products, if approved. The commercial infrastructure for specialty oncology products typically consists of a targeted, specialty sales force that calls on a limited and focused group of physicians supported by sales management, internal sales support, an internal marketing group and distribution support. Additional capabilities important to the oncology marketplace include the management of key accounts such as managed care organizations, group-purchasing organizations, specialty pharmacies, oncology group networks, and government accounts. Based on the number of physicians who treat RCC and the

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size of competitive sales forces, we believe that we can effectively target the relevant audience with a sales force of approximately 50-75 representatives. To develop the appropriate commercial infrastructure, 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.

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 other products.

Government Regulation

Government authorities in the United States (including federal, state and local authorities) and in other countries, extensively regulate, among other things, the manufacturing, research and clinical development, marketing, labeling and packaging, distribution, post-approval monitoring and reporting, advertising and promotion, and export and import of pharmaceutical products, such as those we are developing. The process of obtaining regulatory approvals and the subsequent compliance with appropriate federal, state, local and foreign statutes and regulations require the expenditure of substantial time and financial resources.

United States Government Regulation

In the United States, the U.S. Food and Drug Administration, or FDA, regulates drugs under the Federal Food, Drug, and Cosmetic Act, or FDCA, and related regulations. Drugs are also subject to other federal, state and local statutes and regulations. Biological products are subject to regulation by the FDA under the FDCA, the Public Health Service Act, and related regulations, and other federal, state and local statutes and regulations. Failure to comply with the applicable U.S. regulatory requirements at any time during the product development process, approval process or after approval, may subject an applicant to administrative or judicial sanctions. These sanctions could include the imposition by the FDA or an Institutional Review Board, or IRB, of a clinical hold on trials, the FDA s refusal to approve pending applications or supplements, withdrawal of an approval, warning letters, product recalls, product seizures, total or partial suspension of production or distribution, injunctions, fines, civil penalties or criminal prosecution. Any agency or judicial enforcement action could have a material adverse effect on us.

The Investigational New Drug Process

An Investigational New Drug application, or an IND, is a request for authorization from the FDA to administer an investigational drug or biological product to humans. Such authorization must be secured prior to interstate shipment (usually to clinical investigators) and administration of any new drug or biological product to humans that is not the subject of an approved New Drug Application or Biologics License Application, except under limited circumstances.

To conduct a clinical investigation with an investigational new drug or biological product, we are required to file an IND with the FDA in compliance with Title 21 of the Code of Federal Regulations (CFR), Part 312. These regulations contain the general principles underlying the IND submission and the general requirements for an IND s content and format.

The central focus of the initial IND submission is on the general investigational plan and the protocol(s) for human studies. The IND also includes results of animal studies or other human studies, as appropriate, as well as manufacturing information, analytical data and any available clinical data or literature to support the use of the investigational new drug or biological product. An IND must become effective before human clinical trials may begin. An IND will automatically become effective 30 days after receipt by the FDA, unless before that time the FDA raises concerns or questions related to the proposed clinical trials as outlined in the IND. In such a case, the IND may be placed on clinical hold and the IND sponsor and the FDA must resolve any outstanding concerns or questions before clinical trials can begin. Accordingly, submission of an IND may or may not result in the FDA allowing clinical trials to commence.

Clinical trials involve the administration of the investigational drug or biological product to patients under the supervision of qualified investigators in accordance with Good Clinical Practices, or GCPs. Clinical trials are

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conducted under protocols detailing, among other things, the objectives of the study, the parameters to be used in monitoring safety, and the efficacy criteria to be evaluated. A protocol for each clinical trial and any subsequent protocol amendments must be submitted to the FDA as part of the IND. Additionally, approval must also be obtained from each clinical site s independent IRB before the trials may be initiated. All participants in our clinical trials must provide their informed consent in writing in compliance with GCPs and the ethical principles that have their origin in the Declaration of Helsinki.

The clinical investigation of an investigational drug or biological product is generally divided into three phases. Although the phases are usually conducted sequentially, they may overlap or be combined. The three phases of an investigation are as follows:

Phase 1. Phase 1 includes the initial introduction of an investigational new drug or biological product into humans. Phase 1 clinical trials are typically closely monitored and may be conducted in patients with the target disease or condition or healthy volunteers. These studies are designed to evaluate the safety, dosage tolerance, metabolism and pharmacologic actions of the investigational drug or biological product in humans, the side effects associated with increasing doses, and if possible, to gain early evidence on effectiveness. During phase 1 clinical trials, sufficient information about the investigational drug s or biological product s pharmacokinetics and pharmacological effects may be obtained to permit the design of well-controlled and scientifically valid phase 2 clinical trials. The total number of participants included in phase 1 clinical trials varies, but is generally in the range of 20 to 80.

Phase 2. Phase 2 includes the controlled clinical trials conducted to preliminarily or further evaluate the effectiveness of the investigational drug or biological product for a particular indication(s) in patients with the disease or condition under study, to determine dosage tolerance and optimal dosage, and to identify possible adverse side effects and safety risks associated with the drug or biological product. Phase 2 clinical trials are typically well-controlled, closely monitored, and conducted in a limited patient population, usually involving no more than several hundred participants.

Phase 3. Phase 3 clinical trials are generally controlled clinical trials conducted in an expanded patient population generally at geographically dispersed clinical trial sites. They are performed after preliminary evidence suggesting effectiveness of the drug or biological product has been obtained, and are intended to further evaluate dosage, clinical effectiveness and safety, to establish the overall benefit-risk relationship of the investigational drug or biological product, and to provide an adequate basis for product approval. Phase 3 clinical trials usually involve several hundred to several thousand participants.

The FDA s primary objectives in reviewing an IND are to assure the safety and rights of patients and to help assure that the quality of the investigation will be adequate to permit an evaluation of the drug s effectiveness and safety and of the biological product s safety, purity and potency. The decision to terminate development of an investigational drug or biological product may be made by either a health authority body such as the FDA (or IRB/ethics committees), or by us for various reasons. Additionally, some trials are overseen by an independent group of qualified experts organized by the trial sponsor, known as a data safety monitoring board or committee. This group provides authorization for whether or not a trial may move forward at designated check points based on access that only the group maintains to available data from the study. Suspension or termination of development during any phase of clinical trials can occur if it is determined that the participants or patients are being exposed to an unacceptable health risk. Other reasons for suspension or termination may be made by us based on evolving business objectives and/or competitive climate.

In addition, there are requirements and industry guidelines to require the posting of ongoing clinical trials on public registries, and the disclosure of designated clinical trial results.

Assuming successful completion of all required testing in accordance with all applicable regulatory requirements, detailed investigational drug or biological product information is submitted to the FDA in the form of an NDA or Biologics License Application, or BLA, requesting approval to market the product for one or more indications.

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The NDA/BLA Approval Process

In order to obtain approval to market a drug or biological product in the United States, a marketing application must be submitted to the FDA that provides data establishing the safety and effectiveness of the drug product for the proposed indication, and the safety, purity and potency of the biological product for its intended indication. The application includes all relevant data available from pertinent preclinical and clinical trials, including negative or ambiguous results as well as positive findings, together with detailed information relating to the product s chemistry, manufacturing, controls and proposed labeling, among other things. Data can come from company-sponsored clinical trials intended to test the safety and effectiveness of a use of a product, or from a number of alternative sources, including studies initiated by investigators. To support marketing approval, the data submitted must be sufficient in quality and quantity to establish the safety and effectiveness of the investigational drug product and the safety, purity and potency of the biological product to the satisfaction of the FDA.

The steps required before an investigational drug or biological product may be marketed in the United States generally include:

- Completion of preclinical laboratory tests, animal studies and formulation studies in compliance with the FDA s Good Laboratory Practices, or GLP, regulations;
- Submission to the FDA of an IND to support human clinical testing;
- Approval by an IRB at each clinical site before each trial may be initiated;
- Performance of adequate and well-controlled clinical trials in accordance with GCP to establish the safety and efficacy of the investigational drug product for each targeted indication or the safety, purity and potency of the biological product for its intended indication;
- Submission of an NDA or BLA to the FDA;
- Satisfactory completion of an FDA Advisory Committee review, if applicable;
- Satisfactory completion of an FDA inspection of the manufacturing facilities at which the investigational drug or biological product is produced to assess compliance with current good manufacturing practices, or cGMP, and to assure that the facilities, methods and controls are adequate to preserve the product s identity, strength, quality and purity; and
- FDA review and approval of the NDA or BLA.

In most cases, the NDA or BLA must be accompanied by a substantial user fee; there may be some instances in which the user fee is waived.

The FDA will initially review the NDA or BLA for completeness before it accepts the NDA or BLA for filing. The FDA has 60 days from its receipt of an NDA to determine whether the application will be accepted for filing based on the agency s threshold determination that it is sufficiently complete to permit substantive review. After the NDA submission is accepted for filing, the FDA reviews the NDA to determine, among other things, whether the proposed product is safe and effective for its intended use, and whether the product is being manufactured in accordance with cGMP to assure and preserve the product s identity, strength, quality and purity. The FDA reviews a BLA to determine, among other things, whether the product is safe, pure and potent and the facility in which it is manufactured, processed, packaged or held meets standards designed to assure the product s continued safety, purity and potency. The FDA may refer applications for novel drug or biological products or drug or biological products which present difficult questions of safety or efficacy to an advisory committee, typically a panel that includes clinicians and other experts, for review, evaluation and a recommendation as to whether the application should be approved and under what conditions. The FDA is not bound by the recommendations of an advisory committee, but it considers such recommendations carefully

when making decisions.

Before approving an NDA or BLA, the FDA will inspect the facilities at which the product is manufactured. The FDA will not approve the product unless it determines that the manufacturing processes and facilities are in compliance with cGMP requirements and adequate to assure consistent production of the product within required

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specifications. Additionally, before approving an NDA or BLA, the FDA will typically inspect one or more clinical sites to assure compliance with GCP. If the FDA determines the application, manufacturing process or manufacturing facilities are not acceptable, it will outline the deficiencies in the submission and often will request additional testing or information. Notwithstanding the submission of any requested additional information, the FDA ultimately may decide that the application does not satisfy the regulatory criteria for approval.

The testing and approval process requires substantial time, effort and financial resources, and each may take several years to complete. Data obtained from clinical activities are not always conclusive and may be susceptible to varying interpretations, which could delay, limit or prevent regulatory approval. The FDA may not grant approval on a timely basis, or at all. We may encounter difficulties or unanticipated costs in our efforts to develop our product candidates and secure necessary governmental approvals, which could delay or preclude us from marketing our products. Even if the FDA approves a product, it may limit the approved indications for use or place other conditions on any approvals that could restrict the commercial application of the products such as a requirement that we implement special risk management measures through a Risk Evaluation and Mitigation Strategy. After approval, some types of changes to the approved product, such as adding new indications, manufacturing changes and additional labeling claims, are subject to further testing requirements and FDA review and approval.

Post-Approval Regulation

After regulatory approval of a drug or biological product is obtained, we are required to comply with a number of post-approval requirements. For example, as a condition of approval of an NDA or BLA, the FDA may require post-marketing testing, including phase 4 clinical trials, and surveillance to further assess and monitor the product s safety and effectiveness after commercialization. Regulatory approval of oncology products often requires that patients in clinical trials be followed for long periods to determine the overall survival benefit of the drug or biologic. In addition, as a holder of an approved NDA or BLA, we would be required to report, among other things, certain adverse reactions and production problems to the FDA, to provide updated safety and efficacy information, and to comply with requirements concerning advertising and promotional labeling for any of our products. Also, quality control and manufacturing procedures must continue to conform to cGMP after approval to assure and preserve the long term stability of the drug or biological product. The FDA periodically inspects manufacturing facilities to assess compliance with cGMP, which imposes extensive procedural, substantive and record keeping requirements. In addition, changes to the manufacturing process are strictly regulated, and, depending on the significance of the change, may require prior FDA approval before being implemented. FDA regulations also require investigation and correction of any deviations from cGMP and impose reporting and documentation requirements upon us and any third party manufacturers that we may decide to use. Accordingly, manufacturers must continue to expend time, money and effort in the area of production and quality control to maintain compliance with cGMP and other aspects of regulatory compliance.

We rely, and expect to continue to rely, on third parties for the production of clinical and commercial quantities of our product candidates. Future FDA and state inspections may identify compliance issues at our facilities or at the facilities of our contract manufacturers that may disrupt production or distribution, or require substantial resources to correct. In addition, discovery of previously unknown problems with a product or the failure to comply with applicable requirements may result in restrictions on a product, manufacturer or holder of an approved NDA or BLA, including withdrawal or recall of the product from the market or other voluntary, FDA-initiated or judicial action that could delay or prohibit further marketing. Newly discovered or developed safety or effectiveness data may require changes to a product s approved labeling, including the addition of new warnings and contraindications, and also may require the implementation of other risk management measures. Also, new government requirements, including those resulting from new legislation, may be established, or the FDA s policies may change, which could delay or prevent regulatory approval of our products under development.

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Europe / Rest of World Government Regulation

In addition to regulations in the United States, we will be subject to a variety of regulations in other jurisdictions governing, among other things, clinical trials and any commercial sales and distribution of our products.

Whether or not we obtain FDA approval for a product, we must obtain the requisite approvals from regulatory authorities in foreign countries prior to the commencement of clinical trials or marketing of the product in those countries. Certain countries outside of the United States have a similar process that requires the submission of a clinical trial application much like the IND prior to the commencement of human clinical trials. In Europe, for example, a clinical trial application, or CTA, must be submitted to each country s national health authority and an independent ethics committee, much like the FDA and IRB, respectively. Once the CTA is approved in accordance with a country s requirements, clinical trial development may proceed.

The requirements and process governing the conduct of clinical trials, product licensing, pricing and reimbursement vary from country to country. In all cases, the clinical trials are conducted in accordance with GCP and the applicable regulatory requirements and the ethical principles that have their origin in the Declaration of Helsinki.

To obtain regulatory approval of an investigational drug or biological product under European Union regulatory systems, we must submit a marketing authorization application. The application used to file the NDA or BLA in the United States is similar to that required in Europe, with the exception of, among other things, country-specific document requirements.

For other countries outside of the European Union, such as countries in Eastern Europe, Latin America or Asia, the requirements governing the conduct of clinical trials, product licensing, pricing and reimbursement vary from country to country. In all cases, again, the clinical trials are conducted in accordance with GCP and the applicable regulatory requirements and the ethical principles that have their origin in the Declaration of Helsinki.

If we fail to comply with applicable foreign regulatory requirements, we may be subject to, among other things, fines, suspension or withdrawal of regulatory approvals, product recalls, seizure of products, operating restrictions and criminal prosecution.

Compliance

During all phases of development (pre- and post-marketing), failure to comply with the applicable regulatory requirements may result in administrative or judicial sanctions. These sanctions could include the FDA s imposition of a clinical hold on trials, refusal to approve pending applications, withdrawal of an approval, warning letters, product recalls, product seizures, total or partial suspension of production or distribution, product detention or refusal to permit the import or export of products, injunctions, fines, civil penalties or criminal prosecution. Any agency or judicial enforcement action could have a material adverse effect on us.

Available Special Regulatory Procedures

Formal Meetings

We are encouraged to engage and seek guidance from health authorities relating to the development and review of investigational drugs and biologics, as well as marketing applications. In the United States, there are different types of official meetings that may occur between us and the FDA. Each meeting type is subject to different procedures. Conclusions and agreements from each of these meetings are captured in the official final meeting minutes issued by the FDA.

The EMEA also provides the opportunity for dialogue with us. This is usually done in the form of Scientific Advice, which is given by the Scientific Advice Working Party of the Committee for Medicinal Products for Human Use, or CHMP. A fee is incurred with each Scientific Advice meeting.

Advice from either the FDA or EMEA is typically provided based on questions concerning, for example, quality (chemistry, manufacturing and controls testing), nonclinical testing and clinical studies, and

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pharmacovigilance plans and risk-management programs. Advice is not legally binding with regard to any future marketing authorization application of the product concerned. To obtain binding commitments from health authorities in the United States and the European Union, Special Protocol Assessment or Protocol Assistance procedures are available. Where the FDA agrees to a Special Protocol Assessment, or SPA, the agreement may not be changed by either the sponsor or the FDA except if the sponsor and the FDA agree to a change, or a senior FDA official determines that a substantial scientific issue essential to determining the safety or effectiveness of the product was identified after the testing began. A SPA is not binding if new circumstances arise, and there is no guarantee that a study will ultimately be adequate to support an approval even if the study is subject to a SPA.

Orphan Drug Designation

The FDA may grant orphan drug designation to drugs and biological products intended to treat a rare disease or condition that affects fewer than 200,000 individuals in the United States, or if it affects more than 200,000 individuals in the United States and there is no reasonable expectation that the cost of developing and making the drug or biological product for this type of disease or condition will be recovered from sales in the United States. In the European Union, the EMEA s Committee for Orphan Medicinal Products, or COMP, grants orphan drug designation to promote the development of products that are intended for the diagnosis, prevention or treatment of a life-threatening or chronically debilitating conditions affecting not more than 5 in 10,000 persons in the European Union Community. Additionally, designation is granted for products intended for the diagnosis, prevention or treatment of a life-threatening, seriously debilitating or serious and chronic condition and when, without incentives, it is unlikely that sales of the drug in the European Union would be sufficient to justify the necessary investment in developing the drug or biological product.

In the United States, orphan drug designation entitles a party to financial incentives such as opportunities for grant funding towards clinical trial costs, tax advantages and user-fee waivers. In addition, if a product receives the first FDA approval for the indication for which it has orphan designation, the product is entitled to orphan drug exclusivity, which means the FDA may not approve any other application to market the same drug or biological product for the same indication for a period of 7 years, except in limited circumstances, such as a showing of clinical superiority over the product with orphan exclusivity.

In the European Union, orphan drug designation also entitles a party to financial incentives such as reduction of fees or fee waivers and 10 years of market exclusivity is granted following drug or biological product approval. This period may be reduced to 6 years if the orphan drug designation criteria are no longer met, including where it is shown that the product is sufficiently profitable not to justify maintenance of market exclusivity.

Orphan drug designation must be requested before submitting an application for marketing approval. Orphan drug designation does not convey any advantage in, or shorten the duration of, the regulatory review and approval process.

Pediatric Development

In the United States, Section 505A of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355a, Pediatric Studies of Drugs) provides for an additional 6 months of marketing exclusivity for a drug if reports are filed of investigations studying the use of the drug product in a pediatric population in response to a written request from the FDA. Separate from this potential exclusivity benefit, NDAs and BLAs must contain data (or a proposal for post-marketing activity) to assess the safety and effectiveness of an investigational drug or biological product for the claimed indications in all relevant pediatric populations in order to support dosing and administration for each pediatric subpopulation for which the drug is safe and effective. The FDA may, on its own initiative or at the request of the applicant, grant deferrals for submission of some or all pediatric data until after approval of the product for use in adults or full or partial waivers if certain criteria are met. Discussions about pediatric development plans can be discussed with the FDA at any time, but usually occur any time between the end-of-phase 2 meeting and submission of the NDA or BLA.

For the EMEA, a Pediatric Investigation Plan, and/or a request for waiver or deferral, is required for submission prior to submitting a marketing authorization application.

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Authorization Procedures in the European Union

Medicines can be authorized in the European Union by using either the centralized authorization procedure or national authorization procedures.

Centralized procedure. The EMEA implemented the centralized procedure for the approval of human medicines to facilitate marketing authorizations that are valid throughout the European Union. This procedure results in a single marketing authorization issued by the EMEA that is valid across the European Union, as well as Iceland, Liechtenstein and Norway. The centralized procedure is compulsory for human medicines that are: derived from biotechnology processes, such as genetic engineering, contain a new active substance indicated for the treatment of certain diseases, such as HIV/AIDS, cancer, diabetes, neurodegenerative disorders or autoimmune diseases and other immune dysfunctions, and officially designated orphan medicines.

For medicines that do not fall within these categories, an applicant has the option of submitting an application for a centralized marketing authorization to the EMEA, as long as the medicine concerned is a significant therapeutic, scientific or technical innovation, or if its authorization would be in the interest of public health.

National authorization procedures. There are also two other possible routes to authorize medicinal products in several countries, which are available for investigational drug products that fall outside the scope of the centralized procedure:

Decentralised procedure. Using the decentralised procedure, an applicant may apply for simultaneous authorization in more than one European Union country of medicinal products that have not yet been authorized in any European Union country and that do not fall within the mandatory scope of the centralised procedure.

Mutual recognition procedure. In the mutual recognition procedure, a medicine is first authorized in one European Union Member State, in accordance with the national procedures of that country. Following this, further marketing authorizations can be sought from other European Union countries in a procedure whereby the countries concerned agree to recognize the validity of the original, national marketing authorization.

Priority Review / Standard Review (United States) and Accelerated Review (European Union)

Based on results of the phase 3 clinical trial(s) submitted in an NDA or BLA, upon the request of an applicant a priority review designation may be granted to a product by the FDA, which sets the target date for FDA action on the application at 6 months. Priority review is given where preliminary estimates indicate that a product, if approved, has the potential to provide a safe and effective therapy where no satisfactory alternative therapy exists, or a significant improvement compared to marketed products is possible. If criteria are not met for priority review, the standard FDA review period is 10 months. Priority review designation does not change the scientific/medical standard for approval or the quality of evidence necessary to support approval.

Under the Centralized Procedure in the European Union, the maximum timeframe for the evaluation of a marketing authorization application is 210 days (excluding clock stops, when additional written or oral information is to be provided by the applicant in response to questions asked by the CHMP. Accelerated evaluation might be granted by the CHMP in exceptional cases, when a medicinal product is expected to be of a major public health interest, defined by three cumulative criteria: the seriousness of the disease (e.g. heavy disabling or life-threatening diseases) to be treated; the absence or insufficiency of an appropriate alternative therapeutic approach; and anticipation of high therapeutic benefit. In this circumstance, EMEA ensures that the opinion of the CHMP is given within 150 days.

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Pharmaceutical Coverage, Pricing and Reimbursement

Significant uncertainty exists as to the coverage and reimbursement status of any drug products for which we obtain regulatory approval. In the United States and markets in other countries, sales of any products for which we receive regulatory approval for commercial sale will depend in part on the availability of reimbursement from third party payors. Third party payors include government health administrative authorities, managed care providers, private health insurers and other organizations. The process for determining whether a payor will provide coverage for a drug product may be separate from the process for setting the price or reimbursement rate that the payor will pay for the drug product. Third party payors may limit coverage to specific drug products on an approved list, or formulary, which might not include all of the FDA-approved drugs for a particular indication. Third party payors are increasingly challenging the price and examining the medical necessity and cost-effectiveness of medical products and services, in addition to their safety and efficacy. We may need to conduct expensive pharmacoeconomic studies in order to demonstrate the medical necessity and cost-effectiveness of our products, in addition to the costs required to obtain FDA approvals. Our product candidates may not be considered medically necessary or cost-effective. A payor s decision to provide coverage for a drug product does not imply that an adequate reimbursement rate will be approved. Adequate third party reimbursement may not be available to enable us to maintain price levels sufficient to realize an appropriate return on our investment in product development.

In 2003, the United States government enacted legislation providing a partial prescription drug benefit for Medicare recipients, which became effective at the beginning of 2006. Government payment for some of the costs of prescription drugs may increase demand for any products for which we receive marketing approval. However, to obtain payments under this program, we would be required to sell products to Medicare recipients through prescription drug plans operating pursuant to this legislation. These plans will likely negotiate discounted prices for our products. Federal, state and local governments in the United States continue to consider legislation to limit the growth of healthcare costs, including the cost of prescription drugs. Future legislation could limit payments for pharmaceuticals such as the drug candidates that we are developing.

Different pricing and reimbursement schemes exist in other countries. In the European Community, governments influence the price of pharmaceutical products through their pricing and reimbursement rules and control of national health care systems that fund a large part of the cost of those products to consumers. Some jurisdictions operate positive and negative list systems under which products may only be marketed once a reimbursement price has been agreed. To obtain reimbursement or pricing approval, some of these countries may require the completion of clinical trials that compare the cost-effectiveness of a particular product candidate to currently available therapies. Other member states allow companies to fix their own prices for medicines, but monitor and control company profits. The downward pressure on health care costs in general, particularly prescription drugs, has become very intense. As a result, increasingly high barriers are being erected to the entry of new products. In addition, in some countries, cross-border imports from low-priced markets exert a commercial pressure on pricing within a country.

The marketability of any products for which we receive regulatory approval for commercial sale may suffer if the government and third party payors fail to provide adequate coverage and reimbursement. In addition, an increasing emphasis on managed care in the United States has increased and we expect will continue to increase the pressure on pharmaceutical pricing. Coverage policies and third party reimbursement rates may change at any time. Even if favorable coverage and reimbursement status is attained for one or more products for which we receive regulatory approval, less favorable coverage policies and reimbursement rates may be implemented in the future.

Other Healthcare Laws and Compliance Requirements

In the United States, our activities are potentially subject to regulation by various federal, state and local authorities in addition to the FDA, including the Centers for Medicare and Medicaid Services (formerly the Health Care Financing Administration), other divisions of the U.S. Department of Health and Human Services (e.g., the Office of Inspector General), the U.S. Department of Justice and individual U.S. Attorney offices within the Department of Justice, and state and local governments. For example, sales, marketing and scientific/

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educational grant programs must comply with the anti-fraud and abuse provisions of the Social Security Act, the False Claims Act, the privacy provisions of the Health Insurance Portability and Accountability Act, or HIPAA, and similar state laws, each as amended. Pricing and rebate programs must comply with the Medicaid rebate requirements of the Omnibus Budget Reconciliation Act of 1990 and the Veterans Health Care Act of 1992, each as amended. If products are made available to authorized users of the Federal Supply Schedule of the General Services Administration, additional laws and requirements apply. Under the Veterans Health Care Act, or VHCA, drug companies are required to offer certain drugs at a reduced price to a number of federal agencies including U.S. Department of Veterans Affairs and U.S. Department of Defense, the Public Health Service and certain private Public Health Service designated entities in order to participate in other federal funding programs including Medicare and Medicaid. Recent legislative changes purport to require that discounted prices be offered for certain U.S. Department of Defense purchases for its TRICARE program via a rebate system. Participation under the VHCA requires submission of pricing data and calculation of discounts and rebates pursuant to complex statutory formulas, as well as the entry into government procurement contracts governed by the Federal Acquisition Regulations.

In order to distribute products commercially, we must comply with state laws that require the registration of manufacturers and wholesale distributors of pharmaceutical products in a state, including, in certain states, manufacturers and distributors who ship products into the state even if such manufacturers or distributors have no place of business within the state. Some states also impose requirements on manufacturers and distributors to establish the pedigree of product in the chain of distribution, including some states that require manufacturers and others to adopt new technology capable of tracking and tracing product as it moves through the distribution chain. Several states have enacted legislation requiring pharmaceutical companies to establish marketing compliance programs, file periodic reports with the state, make periodic public disclosures on sales, marketing, pricing, clinical trials and other activities, and/or register their sales representatives, as well as to prohibit pharmacies and other healthcare entities from providing certain physician prescribing data to pharmaceutical companies for use in sales and marketing, and to prohibit certain other sales and marketing practices. All of our activities are potentially subject to federal and state consumer protection and unfair competition laws.

Employees

As of February 1, 2010, we had 133 full-time employees, including a total of 33 employees with M.D. or Ph.D. degrees. Of our workforce, 88 employees are engaged in research and development. None of our employees is represented by labor unions or covered by collective bargaining agreements. We consider our relationship with our employees to be good.

Facilities

We sublease our principal facilities, which consist of approximately 55,200 square feet of research and office space located at 75 Sidney Street, Cambridge, Massachusetts, which sublease expires in February 2014, and approximately 7,407 square feet of office space located at 64 Sidney Street, Cambridge, Massachusetts, which sublease expires in April 2012. We believe that our existing facilities are sufficient for our current needs for the foreseeable future.

Legal Proceedings

We are not currently a party to any material legal proceedings.

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MANAGEMENT

The following table sets forth the name, age and position of each of our executive officers and directors as of February 1, 2010.

Name	Age	Position
Executive Officers		
Tuan Ha-Ngoc	57	Chief Executive Officer, President and Director
David Johnston	54	Chief Financial Officer
Elan Ezickson	46	Chief Business Officer
William Slichenmyer, M.D., Sc.M.	52	Chief Medical Officer
Jeno Gyuris, Ph.D.	50	Senior Vice President, Head of Research
Directors		
Kenneth M. Bate[(1)(2)]	59	Director
Douglas G. Cole, M.D.[(1)]	49	Director
Ronald A. DePinho, M.D.	54	Director
Anthony B. Evnin, Ph.D.[(1)(3)]	68	Director (Chairman of the Board)
Nicholas G. Galakatos[(2)]	52	Director
Russell Hirsch, M.D., Ph.D.[(2)]	47	Director
Raju Kucherlapati, Ph.D.[(3)]	67	Director
Kenneth E. Weg	71	Director
Robert C. Young, M.D.[(3)]	69	Director

(1) Member of the Audit Committee.

(2) Member of the Compensation Committee.

(3) Member of the Nominating and Governance Committee.

Executive Officers

Tuan Ha-Ngoc has served as President and Chief Executive Officer of our company and as a member of our board of directors since June 2002. From 1999 to 2002, he was co-founder, President and Chief Executive Officer of deNovis, Inc., an enterprise-scale software development company for the automation of healthcare administrative functions. From 1998 to 1999, Mr. Ha-Ngoc was Corporate Vice President of Strategic Development for Wyeth, following Wyeth s acquisition of Genetics Institute, where Mr. Ha-Ngoc served as Executive Vice President with responsibility for corporate development, commercial operations and European and Japanese operations. Mr. Ha-Ngoc serves on the Board of Directors of Human Genome Sciences, Inc. as well as on the boards of a number of academic and nonprofit organizations, including the Harvard School of Dental Medicine, the Tufts School of Medicine, the MIT Koch Institute of Integrative Cancer Research, the Boston Philharmonic Orchestra, and the International Institute of Boston. He holds an M.B.A. from INSEAD and an M.A. in pharmacy from the University of Paris, France.

David Johnston has served as our Chief Financial Officer since October 2007. From 1998 to 2007, he served as Senior Vice President of Corporate Finance at Genzyme Corporation. Mr. Johnston sits on the Board of Directors of Tissue Banks International. Mr. Johnston holds a B.S. from Washington and Lee University and an M.B.A. from the University of Michigan.

Elan Ezickson has served as our Chief Business Officer since April 2003. From 1994 to 2003, he worked at Biogen in roles that included President of Biogen Canada, Program Executive and Associate General Counsel. Mr. Ezickson sits on the Board of Directors of the Greater Boston Food Bank. Mr. Ezickson holds a B.A in Political Science from Yale University and a J.D. from the Columbia University School of Law.

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William Slichenmyer, M.D., Sc.M. has served as our Chief Medical Officer since September 2009. Prior to joining our company, Dr. Slichenmyer served as Chief Medical Officer at Merrimack Pharmaceuticals from 2007 to September 2009. From 2000 to 2007 Dr. Slichenmyer worked at Pfizer Inc. in roles that included Global Head of Oncology Clinical Development as well as positions in medical affairs and regulatory affairs. Dr. Slichenmyer holds a B.A. and M.D. from Case Western Reserve University and an M.A. in clinical investigation from Johns Hopkins Oncology Center.

Jeno Gyuris, Ph.D. was named Senior Vice President, Head of Research in January 2010, and oversees all our research activities. Dr. Gyuris joined our company in 2002 and served as our Vice President, Molecular Technologies until January 2007 and as our Senior Vice President, Drug Discovery from January 2007 to January 2010. From 1993 to 2002, Dr. Gyuris worked at GPC Biotech AG, formerly Mitotix Inc., where he held positions of increasing responsibility, most recently Vice President of Molecular Technologies. Dr. Gyuris has received several research fellowships in Europe and the United States, and is the author of numerous patents and publications. Dr. Gyuris received his Ph.D. from University of Szeged, Szeged, Hungary.

Non-Employee Directors

Kenneth M. Bate has served as a director since December 2007. He is currently the President and Chief Executive Officer of Archemix Corp., a position he has held since April 2009. From 2006 to 2008 he served as President and Chief Executive Officer of NitroMed, Inc. From January 2005 to March 2006, he was employed at JSB Partners, a firm which Mr. Bate co-founded that provides banking and advisory services to biopharmaceutical companies. From 2002 to January 2005, Mr. Bate served as Head of Commercial Operations and Chief Financial Officer at Millennium Pharmaceuticals, Inc. Mr. Bate currently serves on the boards of Cubist Pharmaceuticals, Inc. and Archemix Corp. He holds a B.A. in Chemistry from Williams College and an M.B.A from The Wharton School of the University of Pennsylvania.

Douglas G. Cole, M.D. has served as a director since February 2006. Dr. Cole has been a general partner of Flagship Ventures, where he focuses on life science investments, since 2004. He currently serves on the Boards of Directors of several private companies, including Ensemble Discovery Corporation, Tetraphase Pharmaceuticals, Inc., Concert Pharmaceuticals, Inc., Quanterix Corporation, Agios Pharmaceuticals, Inc., Selecta Biosciences, Inc., and Avedro, Inc. Dr. Cole holds a B.A. magna cum laude in English from Dartmouth College and an M.D. from the University of Pennsylvania School of Medicine.

Ronald A. DePinho, M.D. is one of our co-founders and has served as a director since October 2001. Dr. DePinho has served as Professor of Medicine and Genetics at the Harvard Medical School since 1998. He is founder and director of the Belfer Institute for Applied Cancer Science and has been a member of the Departments of Medical Oncology, Medicine and Genetics at the Dana Farber Cancer Institute and Harvard Medical School since 1998. Dr. DePinho is a leading cancer researcher, recipient of numerous awards, and currently serves on a number of advisory boards for the public and private sectors. He is a member of the Institute of Medicine of the National Academies. He holds a B.S. in Biology from Fordham University and an M.D. with distinction in Microbiology and Immunology from the Albert Einstein College of Medicine.

Anthony B. Evnin, Ph.D. has served as a director since March 2002 and is Chairman of our Board. He has been a Partner at Venrock, where he focuses largely on life sciences investments and, in particular, biotechnology investments, since 1975. Dr. Evnin currently serves on the boards of Icagen, Inc., Infinity Pharmaceuticals, Inc., Pharmos Corporation and several private companies, including Acceleron Pharma Inc., Boston-Power, Inc. and Metabolex, Inc. His previous experience was as a manager of business development at Story Chemical Corporation and a research scientist at Union Carbide Corporation. Dr. Evnin is a Trustee of Rockefeller University and the Memorial Sloan-Kettering Cancer Center. Dr. Evnin holds a Ph.D. in Chemistry from the Massachusetts Institute of Technology and an A.B. from Princeton University.

Nicholas G. Galakatos, Ph.D. has served as a director since March 2002. He is a co-founder and Managing Director of Clarus Ventures, a global venture capital firm focused in the life sciences, since Clarus inception in 2005. He is also a General Partner of the MPM BioVentures II and MPM BioVentures III funds since 2000.

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From 1997 to 2000 Dr. Galakatos served as Vice President, New Business at Millennium Pharmaceuticals, Inc. He was a founder of TransForm Pharmaceuticals and Millennium Predictive Medicine and currently is the Lead Director at Affymax, Inc. He serves on the boards of a number of private companies, including Aerovance Inc., Link Medicine Corporation, Nanostring Technologies, Inc., Portola Pharmaceuticals, Inc. and Taligen Therapeutics, Inc. He holds a B.A in chemistry from Reed College and a Ph.D. in organic chemistry from the Massachusetts Institute of Technology.

Russell Hirsch, M.D., Ph.D. has served as a director since March 2002. He has been a Managing Director of Prospect Venture Partners since February 2001 and co-founded Prospect Venture Partners II, L.P., Prospect Venture Partners III, L.P. and Prospect Venture Partners IV, L.P. as dedicated life science funds. Dr. Hirsch serves on the board of Hansen Medical, Inc., as well as a number of private companies. Dr. Hirsch holds an M.D. and Ph.D. in Biochemistry from the University of California, San Francisco and a B.A. in Chemistry from the University of Chicago.

Raju Kucherlapati, Ph.D. has served as a director since October 2001. He has been a professor of Medicine at Harvard Medical School since 2001 and served as Scientific Director of the Harvard Medical School-Partners HealthCare Center for Genetics and Genomics from 2001 to 2008. Dr. Kucherlapati was a founder of Cell Genesys, Inc., Abgenix, Inc. and Millennium Pharmaceuticals, Inc. and currently serves on the board of Enlight Biosciences LLC. Dr. Kucherlapati holds a B.S. in Biology from P.R. College, Kakinada, India, a M.S. in Biology from Andhra University, Waltair, India and a Ph.D. from the University of Illinois at Urbana.

Kenneth E. Weg is one of our co-founders and has served as a director since January 2002. He has over 33 years of experience in the pharmaceutical industry with Bristol-Myers Squibb Company and Merck & Co., Inc. From 1993 to 1998 he was president, Worldwide Medicines Group of Bristol-Myers Squibb Company, responsible for all ethical pharmaceuticals and over-the-counter medicines on a global basis. Mr. Weg also served as Vice-Chairman of the Board. He retired from Bristol-Myers Squibb Company in February 2001. Mr. Weg also served as non-Executive Chairman of Millennium Pharmaceuticals, Inc. until that company was acquired by Takeda, Inc. in 2007. He is also a founder of Metamark Genetics, Inc, a molecular diagnostics company focused on oncology. Currently, Mr. Weg serves on the board at Fox Chase Cancer Center. He holds a B.A. in English Literature from Dartmouth College and an M.B.A. from Columbia University.

Robert C. Young, M.D. has served as a director since July 2009. Dr. Young is president of RCY Medicine, a consulting service focused on cancer center productivity, health care quality and health policy which he founded in July 2009. From 2007 to 2009 he served as chancellor of Fox Chase Cancer Center in Philadelphia and as president and chief executive officer from 1989 to 2007. Dr. Young is a past-president of the American Society of Clinical Oncology, the American Cancer Society and the International Gynecologic Cancer Society and past Chairman of the Board of Scientific Advisors of the National Cancer Institute. Dr. Young serves on the board of West Pharmaceutical Services, Inc. and Human Genome Sciences, Inc. He holds a B.Sc. in zoology from Ohio State University and an M.D. from Cornell University Medical College and is Board certified in Internal Medicine, Hematology and Medical Oncology.

Scientific Advisors

We have established a scientific advisory board comprised of leading experts in their fields. Our scientific advisors participate in advisory board meetings, as well as provide ad hoc individual consulting services to management. We regularly seek advice and input from these experienced scientific leaders on matters related to our research and development programs. The members of our scientific advisory board consist of experts across a range of key disciplines relevant to our programs and science. We intend to continue to leverage the broad expertise of our advisors by seeking their counsel on important topics relating to our drug discovery and development programs.

With the exception of Dr. Robinson, who is a full-time employee of our company, we pay our advisors a fee for their attendance at scientific advisory board meetings, reimburse them for their expenses, and have granted them options to purchase common stock under our 2002 Stock Incentive Plan. Members of our scientific advisory board also generally enter into consulting agreements with us covering, among other things, their respective financial arrangements and confidentiality, non-disclosure and proprietary rights matters.

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All of the scientific advisors are employed by or have consulting arrangements with other entities and devote only a small portion of their time to us, except for Dr. Robinson, who is a full-time employee of our company. Our current advisors are:

Name	Professional Affiliation
Ronald A. DePinho, M.D.	Co-chair of our Scientific Advisory Board. For a description of Dr. DePinho s professional affiliations, please see Non-Employee Directors
Murray O. Robinson, Ph.D.	Co-chair of our Scientific Advisory Board and Senior Vice President, Translational Medicine, of our company. He joined our company in 2003 after 12 years at Amgen, Inc., where he started and managed Amgen s internal cancer research program
Steven C. Clark, Ph.D.	Chief Scientific Officer of our company from July 2002 to 2007 with 28 years of drug discovery experience, including seven years as Vice President of Research at Genetics Institute and five years as Vice President of Discovery Research at Wyeth
Lewis Cantley, Ph.D.	Professor of System Biology, Chief, Division of Signal Transduction, Department of Medicine, Beth Israel Deaconess Medical Center
Lynda Chin, M.D.	Co-founder of our company and a Professor of Dermatology at the Harvard Medical School, Dana-Farber Cancer Institute and an associate member of the Broad Institute of MIT and Harvard
Douglas Hanahan, Ph.D.	Currently holds joint appointments in Lausanne, Switzerland and San Francisco, California. He is an American Cancer Society Research Professor in the Department of Biochemistry & Biophysics, and a member of the Comprehensive Cancer Center and the Diabetes Center at the University of California San Francisco. In addition, he is the Director of the Swiss Institute for Experimental Cancer Research and a Professor of Molecular Oncology at the Swiss Federal Institute of Technology Lausanne
H. Robert Horvitz, Ph.D.	Received the Nobel Prize in Physiology for Medicine in 2002. He is the David H. Koch Professor of Biology at the Massachusetts Institute of Technology; an Investigator of the Howard Hughes Medical Institute; Neurobiologist (Neurology) at the Massachusetts General Hospital; and a Member of the MIT McGovern Institute for Brain Research and the MIT Koch Institute for Integrative Cancer Research

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Name	Professional Affiliation
Tyler Jacks, Ph.D.	Director of the Koch Institute for Integrative Cancer Research at the Massachusetts Institute of Technology. He is also a Professor of Biology at MIT and an Investigator of the Howard Hughes Medical Institute
Raju Kucherlapati, Ph.D.	For a description of Dr. Kucherlapati s professional affiliations, please see Non-Employee Directors
David M. Livingston, M.D.	Deputy Director of the Dana-Farber/Harvard Cancer Center; Chief of the Charles A. Dana Division of Human Cancer Genetics, and the Emil Frei Professor of Genetics and Medicine at Harvard Medical School
Charles L. Sawyers, M.D.	An Investigator of the Howard Hughes Medical Institute and the inaugural Director of the HOPP at Memorial Sloan Kettering Cancer Center, where he is building a program of lab-based translational researchers across various clinical disciplines and institutional infrastructure to enhance the application of global genomics tools to clinical trials

Board Composition and Election of Directors

Our board of directors is currently comprised of 10 members, although we are authorized under our certificate of incorporation and bylaws to elect up to 11 members. The members of our board of directors were elected in compliance with the provisions of the voting agreement between us, our major stockholders and the founders of our company. The voting agreement will terminate upon the closing of this offering and we will have no further contractual obligations regarding the election of our directors. Our directors hold office until their successors have been elected and qualified or until their earlier death, resignation or removal. There are no family relationships among any of our directors or executive officers.

Board Committees and Independence

Rule 5605 of the NASDAQ Marketplace Rules requires a majority of a listed company s board of directors to be comprised of independent directors within one year of listing. In addition, NASDAQ Marketplace Rules require that, subject to specified exceptions, each member of a listed company s audit, compensation and nominating and governance committees be independent and that audit committee members also satisfy independence criteria set forth in Rule 10A-3 under the Securities Exchange Act of 1934, as amended. Under Rule 5605(a)(2), a director will only qualify as an independent director if, in the opinion of our board of directors, that person does not have a relationship that would interfere with the exercise of independent judgment in carrying out the responsibilities of a director. In order to be considered independent for purposes of Rule 10A-3, a member of an audit committee of a listed company may not, other than in his or her capacity as a member of the audit committee, the board of directors, or any other board committee: (1) accept, directly or indirectly, any consulting, advisory, or other compensatory fee from the listed company or any of its subsidiaries; or (2) be an affiliated person of the listed company or any of its subsidiaries.

In November 2009, our board of directors undertook a review of the composition of our board of directors and its committees and the independence of each director. Based upon information requested from and provided by each director concerning his background, employment and affiliations, including family relationships, our board of directors has determined that none of Kenneth Bate, Douglas Cole, Anthony Evnin, Nicholas Galakatos,

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Russell Hirsch, Raju Kurcherlapati, and Robert Young, representing seven of our ten directors, has a relationship that would interfere with the exercise of independent judgment in carrying out the responsibilities of a director and that each of these directors is independent as that term is defined under Rule 5605(a)(2) of the NASDAQ Marketplace Rules. Our board of directors also determined that Kenneth Bate, Douglas Cole, and Anthony Evnin, who comprise our audit committee, Nicholas Galakatos, Kenneth Bate and Russell Hirsch, who comprise our compensation committee, and Anthony Evnin, Robert Young and Raju Kucherlapati, who comprise our nominating and governance committee, satisfy the independence standards for such committees established by the Securities and Exchange Commission and the NASDAQ Marketplace Rules, as applicable. In making such determination, the board of directors considered the relationships that each such non-employee director has with our company and all other facts and circumstances the board of directors deemed relevant in determining independence, including the beneficial ownership of our capital stock by each non-employee director. Currently, our board of directors has determined that all current members satisfy the independence requirements for service on the audit committee.

Board Committees

Our board of directors has established an audit committee, a compensation committee and a nominating and governance committee. The composition of each committee will be effective upon the closing of this offering. Each committee will operate under a charter approved by our board. Following this offering, copies of each committee s charter will be posted on the Corporate Governance section of our website, www.aveopharma.com.

Audit Committee

The members of our audit committee are Kenneth Bate, Douglas Cole and Anthony Evnin. Kenneth Bate chairs the audit committee. Our board of directors has determined that Kenneth Bate is an audit committee financial expert as defined in applicable SEC rules. Upon the closing of this offering, our audit committee s responsibilities will include:

- appointing, approving the compensation of, and assessing the independence of our registered public accounting firm;
- overseeing the work of our registered public accounting firm, including through the receipt and consideration of reports from such firm;
- reviewing and discussing with management and the registered public accounting firm our annual and quarterly financial statements and related disclosures;
- monitoring our internal control over financial reporting, disclosure controls and procedures and code of business conduct and ethics;
- overseeing our internal audit function;
- discussing our risk management policies;
- establishing policies regarding hiring employees from the registered public accounting firm and procedures for the receipt and retention of accounting related complaints and concerns;
- meeting independently with our internal auditing staff, registered public accounting firm and management;

reviewing and approving or ratifying any related person transactions; and

preparing the audit committee report required by SEC rules.

All audit and non-audit services, other than de minimus non-audit services, to be provided to us by our independent registered public accounting firm must be approved in advance by our audit committee.

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Compensation Committee

The members of our compensation committee are Nicholas Galakatos, Kenneth Bate and Russell Hirsch. Nicholas Galakatos chairs the compensation committee. Upon the closing of this offering, our compensation committee s responsibilities will include:

- annually reviewing and approving corporate goals and objectives relevant to Chief Executive Officer compensation;
- determining our Chief Executive Officer s compensation;
- reviewing and approving, or making recommendations to our board with respect to, the compensation of our other executive officers;
- overseeing an evaluation of our senior executives;
- overseeing and administering our cash and equity incentive plans;
- reviewing and making recommendations to our board with respect to director compensation;
- reviewing and discussing annually with management our Compensation Discussion and Analysis disclosure required by SEC rules; and
- preparing the annual compensation committee report required by SEC rules.

Nominating and Governance Committee

The members of our nominating and governance committee are Anthony Evnin, Robert Young and Raju Kucherlapati. Anthony Evnin chairs the nominating and governance committee. Upon the closing of this offering, our nominating and governance committee s responsibilities will include:

- identifying individuals qualified to become members of our board;
- recommending to our board the persons to be nominated for election as directors and to each of our board s committees;
- reviewing and making recommendations to our board with respect to management succession planning;
- developing and recommending to our board corporate governance principles; and
- overseeing an annual evaluation of our board.

Compensation Committee Interlocks and Insider Participation

During 2009, the members of our compensation committee were Nicholas Galakatos, Russell Hirsch and Kenneth Bate. No member of our compensation committee is or has been a current or former officer or employee of our company. None of our executive officers served as a director or a member of a compensation committee (or other committee serving an equivalent function) of any other entity that had one or more executive officers serving as a director or member of our compensation committee during the fiscal year ended December 31, 2009. For a description of transactions between us and members of the compensation committee and entities affiliated with such members, please see Certain Relationships and Related Person Transactions.

Code of Business Conduct and Ethics

We have adopted a written code of business conduct and ethics that applies to our directors, officers and employees, including our principal executive officer, principal financial officer, principal accounting officer or controller, or persons performing similar functions. Following this offering, a current copy of the code will be posted on the Corporate Governance section of our website, www.aveopharma.com.

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EXECUTIVE AND DIRECTOR COMPENSATION

Compensation Discussion and Analysis

Overview

This section discusses the principles underlying our policies and decisions with respect to the compensation of our executive officers who are named in the Summary Compensation Table for the Years Ended December 31, 2008 and 2009, or our named executive officers, and the most important factors relevant to an analysis of these policies and decisions.

Our named executive officers are:

- Tuan Ha-Ngoc, President and Chief Executive Officer;
- David Johnston, Chief Financial Officer;
- Elan Ezickson, Chief Business Officer;
- Jeno Gyuris, Senior Vice President, Head of Research; and
- William Slichenmyer, Chief Medical Officer.

Our compensation committee is responsible for establishing and administering our policies governing the compensation for our named executive officers, including salaries, cash incentives and equity incentive compensation. Our compensation committee consists of three members of our board of directors, all of whom have extensive experience in our industry. Our compensation committee is composed entirely of non-employee independent directors. Our compensation committee also considers the recommendations of our Chief Executive Officer when determining the appropriate mix of compensation for each of our executive officers, including our named executive officers. However, our Chief Executive Officer does not provide input on his own compensation.

We believe that the compensation of our named executive officers should focus executive behavior on the achievement of near-term corporate goals as well as long-term business objectives and strategies. We place significant emphasis on pay-for-performance compensation programs, which reward our executives when we achieve certain financial and business goals and create stockholder value. We use a combination of base salary, annual cash incentive compensation programs, a long-term equity incentive compensation program and a broad based benefits program to create a competitive compensation package for our executive management team. Because we believe that the performance of every employee is important to our success, we are mindful of the effect our executive compensation and incentive program has on all of our employees.

Objectives of our Executive Compensation Program

Our compensation committee has designed our overall executive compensation program to achieve the following objectives:

- attract and retain talented and experienced executives;
- motivate and reward executives whose knowledge, skills and performance are critical to our success;

provide a competitive compensation package that aligns the interests of our named executive officers and stockholders by including a significant variable component which is weighted heavily toward performance-based rewards;

ensure fairness among the executive management team by recognizing the contributions each executive makes to our success; and

foster a shared commitment among executives by aligning their individual goals with our corporate goals and the creation of shareholder value.

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Basis for Historical and Future Compensation Policies and Decisions

We use a mix of short-term compensation, consisting of base salaries and cash incentive bonuses, and long-term compensation, consisting of equity incentive compensation, to provide a total compensation structure that is designed to achieve our objectives.

In arriving at the amount and types of initial compensation for each of our named executive officers, we consider the following factors:

- the individual s particular background and circumstances, including prior relevant work experience and compensation paid prior to joining us;
- the individual s role with us and the compensation paid to similar persons in the companies represented in the compensation data that we review (as further discussed below);
- the demand for people with the individual s specific expertise and experience at the time of hire;
- performance goals and other expectations for the individual s position;
- comparison to other executives within our company having similar levels of expertise and experience;
- recommendations from our compensation consultant; and
- uniqueness of industry skills.

We annually re-assess the compensation of our named executive officers and determine whether any adjustments should be made. In determining whether to adjust the compensation of any of our named executive officers, we generally take into account the following factors:

- our understanding of compensation generally paid by similarly situated companies to their executives with similar roles and responsibilities;
- formal market data regarding base salary, cash incentives and equity compensation from a leading life science compensation survey of national biopharmaceutical and biotechnology companies;
- the roles and responsibilities of our executives, including any increases or decreases in responsibilities; and
- the contributions and performance of each named executive officer.

In 2007, our compensation committee retained an independent compensation consultant, Nancy Arnosti, to assist the compensation committee in developing our overall executive and director compensation program for our 2007 fiscal year and thereafter. Our compensation committee also considers publicly available compensation data and subscription compensation survey data for national and regional companies in the biotechnology industry to help guide its executive compensation decisions at the time of hiring and for subsequent adjustments in compensation.

Our compensation committee has particularly relied on data from the annual life science compensation survey of Radford Biotechnology Surveys. Specifically, our compensation committee analyzed the base salary, performance bonus and equity components of compensation from the Radford pre-IPO report for companies with over $80.0 million of investment and the Radford Global Life Sciences survey for small US-based companies with 50-149 employees as well as medium-sized US-based companies with employee populations ranging from 150-500 employees. Historically, this market data included survey results from a broad group of biopharmaceutical and biotechnology companies and our compensation committee deemed the survey to be adequate for our purposes because it indicated the ranges of compensation paid by the companies with which we competed for executive talent. However, due to the varied types and stages of companies included in this survey, the compensation data ranges were wide.

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In October 2009, the compensation committee retained Ms. Arnosti to review all compensation and employment arrangements for our executive officers, including base salary, performance bonus, equity ownership, change in control and severance arrangements. In addition, a peer group of publicly traded companies in the life science industry at a stage of development, market capitalization and size comparable to ours was developed to guide future compensation decisions. This peer group consists of companies the compensation committee believes are generally comparable to our company and against which the compensation committee believes we compete for executive talent. The companies included in this peer group are: Affymax, Inc., Alnylam Pharmaceuticals, Inc., Ariad Pharmaceuticals, Inc., AVI Biopharma, Inc., BioCryst Pharmaceuticals, Inc., Cell Therapeutics, Inc., Cypress Bioscience, Inc., Cytokinetics, Inc., Depomed, Inc., Durect Corporation, Dyax Corp., Endo Pharmaceuticals, Halozyme Therapeutics, Inc., Immunogen, Inc., Immunomedics, Inc., Infinity Pharmaceuticals, Inc., Inspire Pharmaceuticals, Inc., Intermune, Inc., Jazz Pharmaceuticals, Inc., Lexicon Pharmaceuticals, Inc., Ligand Pharmaceuticals Incorporated, Micromet, Inc., Momenta Pharmaceuticals, Inc., OraSure Technologies, Inc., Osiris Therapeutics Inc., Sequenom, Inc., Spectrum Pharmaceuticals, Inc., Supergen, Inc., Targacept, Inc., Vical Inc., Xenoport, Inc. and Xoma Ltd.

The CEO s Role in the Compensation Process

The compensation committee uses, in addition to its own judgment and experience, and the resources and tools described above, the recommendations of our Chief Executive Officer to determine the appropriate mix of compensation for each of our other executive officers. Our Chief Executive Officer does not participate in the determination of his own compensation.

Executive Compensation Components

Our executive compensation program is primarily comprised of:

- base salary;
- annual incentive cash compensation; and
- equity compensation.

Our compensation committee has not adopted a formal policy for allocating between long-term and short-term compensation, between cash and non-cash compensation or among the different forms of non-cash compensation. Instead, the compensation committee, after reviewing information provided by our compensation consultant and other relevant data, determines subjectively what it believes to be the appropriate level and mix of the various compensation components.

We generally strive to provide our named executive officers with a balance of short-term and long-term incentives to encourage consistently strong performance. We have historically relied upon base salary and equity compensation as the primary mechanism to attract members of our leadership team. While we believe that the annual incentive cash component of our compensation package encourages our executives to focus on our near-term performance, generally performance over a one-year period, we rely upon equity-based awards to encourage our executives to focus on our performance over several years. In addition, we provide our executives with benefits that are generally available to our salaried employees, including medical, dental, group life and accidental death, dismemberment and long and short term disability insurance, and matching contributions in our 401(k) plan.

Base Salary. Base salary is used to recognize the experience, skills, knowledge and responsibilities required of all our employees, including our named executive officers. Generally, we believe that executive base salaries should be targeted near the median of the range of salaries for executives in similar positions at comparable companies. When establishing base salaries for 2009 and 2010, our board of directors, upon the recommendation of our compensation committee, considered the overall economic environment, the degree to which the company achieved its business goals and objectives, and each individual s performance. In addition, with respect to our named executive officers, other than Mr. Ha-Ngoc, our compensation committee considered the recommendations of Mr. Ha-Ngoc in determining appropriate base salary levels.

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In January 2009, upon the recommendation of the compensation committee, our board of directors decided to increase the base salary of each of our named executive officers for 2009 by approximately 2% over their respective 2008 base salaries and to increase their base salaries a further 1% upon achievement of a strategic partnership. This incremental 1% increase became effective upon the achievement of our strategic partnership with Biogen Idec in March 2009. Our compensation committee made its recommendation after it decided that the increase in base salaries for these executives in 2009 was necessary in order to appropriately retain and motivate our leadership team in a highly competitive environment. In making its decision, our compensation committee based its analysis on what similar companies in our industry pay their executive officers and its review of the Radford pre-IPO report for companies with over $80.0 million of investment and the Radford Global Life Sciences survey for small US-based companies with 50-149 employees.

In February 2010, upon the recommendation of the compensation committee, our board of directors decided to increase the base salary of each of our named executive officers for 2010 by approximately 2.5% over their respective 2009 base salaries. Dr. Gyuris also received an additional increase in connection with his promotion to Senior Vice President, Head of Research. Our compensation committee made its recommendation based on its analysis, with input from our consultant, Ms. Arnosti, of executive officer pay for the peer group companies described above and its review of the Radford Global Life Sciences survey for small US-based companies with 50-149 employees and the Radford Global Life Sciences survey for medium-sized US-based companies with 150-500 employees.

For 2009 and 2010, our board of directors, upon the recommendation of our compensation committee, established annual base salaries for our named executive officers as follows:

Name	2009 Annual Base Salary	2010 Annual Base Salary
Tuan Ha-Ngoc	$ 412,000	$ 422,300
David Johnston	$ 289,823	$ 297,070
Elan Ezickson	$ 305,138	$ 312,766
Jeno Gyuris	$ 256,174	$ 285,634
William Slichenmyer	$ 340,000[1]	$ 342,833

(1) Our board of directors established an annual base salary for Dr. Slichenmyer of $340,000 in connection with his hiring as chief medical officer in September 2009. When determining Dr. Slichenmyer s salary, our board of directors considered Dr. Slichenmyer s salary with his previous employer, the internal equity among his peers at the company and his responsibilities at the company.

We believe that the base salaries established for our named executive officers for 2010 are aligned with our executive compensation objectives stated above and are competitive with those of similarly-situated companies.

Annual Cash Incentive Program. We have designed our annual cash incentive program to reward our named executive officers upon the achievement of specified annual corporate and individual goals which are approved in advance by our compensation committee and board of directors. Our cash incentive program emphasizes pay-for-performance and is intended to closely align executive compensation with achievement of specified operating results as the cash incentive amount is calculated on the basis of percentage of corporate goals achieved. The compensation committee communicates the bonus criteria to the named executive officers at the beginning of each fiscal year. The performance goals established by the compensation committee are based on the business strategy of the company and the objective of building shareholder value. There are three steps to determine if and the extent to which an annual cash incentive award is payable to a named executive officer. First, at the beginning of the fiscal year, the compensation committee determines the target annual cash incentive award for the named executive officer based on a percentage of the officer s annual base salary for that year. Second, at the beginning of the fiscal year, the compensation committee establishes the specific performance goals that must be met in order for the officer to receive the award. Third, shortly after the end of the fiscal year, the compensation committee determines the extent to which these performance goals are met and the amount of the award. The board of directors considers, and if it deems appropriate approves, the recommendation of the compensation committee at each of these steps.

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Fiscal Year 2009. For our fiscal year ended December 31, 2009, our compensation committee, with board approval, set corporate and individual goals for our named executive officers.

For 2009, the corporate goals, which accounted for 70% of the cash incentive for each of our named executive officers (other than our Chief Executive Officer), the weighting of each goal, and the compensation committee s quantitative assessment of the degree to which each goal was actually achieved, were as follows:

Corporate Goal	Target Score	Actual Score
Initiate tivozanib phase 3 clinical trial and demonstrate safety in phase 1 combination study	35%	30%(1)
Complete first-in-human AV-299 study and initiate one phase 1b/2a clinical trial	10	10(2)
Advance antibody pipeline and other research goals	20	20(3)
Secure additional funding through partnerships	30	25(4)
Achieve year-end cash target of at least $50 million	5	5(5)
Totals	100%	90%

(1) We initiated patient screening for our phase 3 clinical trial of tivozanib in December 2009 and we received safety data in October 2009 in connection with the phase 1 clinical trial of tivozanib in combination with Torisel, which showed that tivozanib can be safely administered at full doses with Torisel.
(2) We completed the phase 1 clinical trial of AV-299 in patients in September 2009 and we initiated the phase 1b portion of a clinical trial to test the combination of AV-299 with another targeted agent in December 2009.
(3) We achieved proof-of-concept in several of our antibody programs and achieved other specific translational research goals related to our pre-clinical and clinical development programs.
(4) We entered into an exclusive option and license agreement with Biogen Idec in March 2009 and we entered into an expanded collaboration and license agreement with OSI Pharmaceuticals in July 2009.
(5) Our cash balance as of December 31, 2009 was $51.3 million.

For 2009, the individual goals for each of our named executive officers (other than our Chief Executive Officer) accounted for 30% of their performance incentive. The individual goals for those named executive officers are primarily related to the corporate goals for which they are most responsible and, to a lesser extent, individual development goals or department specific goals, subject to discretionary adjustments that our compensation committee deems appropriate. Our Chief Executive Officer makes recommendations to the compensation committee as to the degree to which those named executive officers have satisfied their individual goals.

Mr. Johnston s individual goals related to monitoring the financial and cash management of our company, maintaining relationships with the financial community and supporting the equity financings related to our partnering efforts. The compensation committee deemed Mr. Johnston s individual goals to be achieved in full based on our 2009 year-end cash balance, the engagement of the underwriters for our initial public offering and the completion of private financings in conjunction with the Biogen Idec and OSI Pharmaceuticals strategic partnerships consummated in March 2009 and July 2009, respectively.

Mr. Ezickson s individual goals related to securing two partnership transactions and overseeing intellectual property and legal activities as well as program management and market development initiatives. The compensation committee deemed Mr. Ezickson s individual goals to be exceeded, as described below, based on our successful completion of the Biogen Idec and OSI Pharmaceuticals strategic partnerships, the issuance of four patents and his leadership in conjunction with our public offering process, specifically as it related to responsibilities outside of his normal duties.

Dr. Gyuris s individual goals related to leading our drug discovery efforts to advance the AV-203, RON, Notch and other ongoing antibody programs. The compensation committee deemed Dr. Gyuris s individual goals to be achieved in full based on substantial preclinical progress made in the AV-203, RON and Notch programs.

Dr. Slichenmyer s individual goals related to leading the clinical and regulatory efforts to advance the development of tivozanib and AV-299. The compensation committee deemed Dr. Slichenmyer s individual goals to be achieved in full based on the initiation of patient screening for our phase 3 clinical trial of tivozanib in December 2009 and the initiation of the phase 1b portion of a clinical trial to test the combination of AV-299 with another targeted agent in December 2009.

With input from our Chief Executive Officer, our compensation committee determined that each of these named executive officers achieved 100% of their individual goals other than Mr. Ezickson for whom the

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compensation committee determined, in its discretion, performed at a level of 105% of his individual goal target in view of his leadership in conjunction with our public offering process, specifically as it related to responsibilities outside of his normal duties.

The cash incentive payment for our Chief Executive Officer is based solely on the achievement of our overall corporate goals described above. As indicated above, the compensation committee determined that the corporate goals were achieved at the 90% level and, as such, Mr. Ha-Ngoc received a cash incentive payment equal to 90% of his target amount.

Our compensation committee has the authority to make discretionary adjustments to our annual cash incentive program, including the ability to modify the corporate and individual performance targets and the level of awards that our named executive officers receive in conjunction with their performance against the targets. In reaching its determinations as to the payouts for 2009 cash incentive compensation the compensation committee used its discretion to deem our filing of a registration statement for our initial public offering as a factor relevant to the achievement of our corporate partnership goal because the public offering undertaking was a suitable alternative to corporate partnerships for advancing our liquidity and growth goals.

For the fiscal year ended December 31, 2009, the compensation committee established a target incentive payment for each of our named executive officers based on a percentage of their 2009 annual base salary. The following table sets forth each named executive officer s target incentive payment (both as a percentage of his annual base salary and in actual dollars), the total cash incentive award paid, and the total award paid as a percentage of the target award.

Name	2009 Annual Base Salary	Target Percentage of 2009 Annual Base Salary (%)	Target 2009 Annual Cash Incentive Award ($)	Total Cash Incentive Award Paid for 2009	Total Cash Incentive Award as a Percentage of Target Cash Incentive Award
Tuan Ha-Ngoc	$ 412,000	50%	$ 206,000	$ 185,400	90.0%
David Johnston	$ 289,823	30%	$ 86,947	$ 80,861	93.0%
Elan Ezickson	$ 305,138	30%	$ 91,541	$ 86,507	94.5%
Jeno Gyuris	$ 256,174	30%	$ 76,852	$ 71,473	93.0%
William Slichenmyer	$ 340,000	40%	$ 45,333[1]	$ 42,160	93.0%

(1) The target 2009 annual cash incentive award for Dr. Slichenmyer has been pro rated to reflect the date of commencement of his employment, which was September 14, 2009.

Fiscal Year 2010. For our fiscal year ended December 31, 2010, our compensation committee, with board approval, set corporate and individual goals for our named executive officers.

For 2010, the corporate goals, which will account for 80% of the cash incentive for each of our named executive officers (other than our Chief Executive Officer), consist of the following:

Corporate Goal	Target Score (%)
Advance development of tivozanib by enrolling targeted number of patients in phase 3 clinical trial, by initiating clinical trial to expand into indication beyond RCC monotherapy and by initiating other supportive clinical trials	40
Secure funding adequate to end 2010 fiscal year with a cash balance of at least $50 million	40
Advance development of AV-299 by enrolling first patient in a phase 2 clinical trial	10
Advance the antibody pipeline	10
Total	100

The cash incentive payment for our Chief Executive Officer is based solely on the achievement of our overall corporate goals described above, subject to discretionary adjustments that our compensation committee deems appropriate.

For 2010, the individual goals for each of our named executive officers (other than our Chief Executive Officer) account for 20% of their performance incentive. The individual goals for those named executive officers

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are primarily related to the corporate goals for which they are most responsible and, to a lesser extent, individual development goals or department specific goals, subject to discretionary adjustments that our compensation committee deems appropriate. Following the completion of the 2010 fiscal year, our Chief Executive Officer will make recommendations to the compensation committee as to the degree to which those named executive officers have satisfied their individual goals. Mr. Johnston s individual goals relate to leading the public offering process, monitoring the financial and cash management of our company, maintaining relationships with the financial community and putting in place necessary compliance processes. Mr. Ezickson s individual goals relate to securing partnership transactions and overseeing intellectual property and legal activities as well as program management and market development initiatives. Dr. Gyuris s individual goals relate to leading our drug discovery efforts to advance the AV-203, RON, Notch and other ongoing antibody programs. Dr. Slichenmyer s individual goals relate to leading the clinical and regulatory efforts to advance the development of tivozanib and AV-299.

The compensation committee believes the 2010 goals described above for each of the named executive officers can be achieved only with significant effort and operational success on the part of such executives and the company.

For the fiscal year ended December 31, 2010, the compensation committee established a target incentive payment for each of our named executive officers based on a percentage of their 2010 annual base salary as set forth below:

Name	2010 Annual Base Salary	Target Percentage of 2010 Annual Base Salary (%)	Target 2010 Annual Cash Incentive Award ($)
Tuan Ha-Ngoc	$ 422,300	50%	$ 211,150
David Johnston	$ 297,070	30%	$ 89,121
Elan Ezickson	$ 312,766	30%	$ 93,830
Jeno Gyuris	$ 285,634	30%	$ 85,690
William Slichenmyer	$ 342,833	40%	$ 137,133

Equity Compensation. We use stock options to attract, retain, motivate and reward our named executive officers. Through our equity-based grants, we seek to align the interests of our named executive officers with our stockholders, reward and motivate both near-term and long-term executive performance and provide an incentive for retention. Our decisions regarding the amount and type of equity incentive compensation, the allocation of equity and relative weighting of these awards within total executive compensation have been based on market practices of similarly-situated companies and our negotiations with our executives in connection with their initial employment. While annual incentive cash compensation is designed to encourage shorter-term performance, generally performance over a one-year period, equity-based awards are designed to encourage our named executives performance over several years.

We grant stock option awards to our employees, including our named executive officers, upon the commencement of their employment and, generally, on an annual basis, as part of our overall compensation program. Historically, all grants of stock options to our named executive officers have been made by our board of directors at regularly scheduled meetings during the year upon the recommendation of our compensation committee. The exercise price of each award is equal to the fair market value of the award on the date of grant, which is the date of the board meeting approving such grant. The following factors are considered in determining the amount of equity incentive awards, if any, to grant to our named executive officers:

- the number of shares subject to, and exercise prices of, outstanding options, both vested and unvested, held by our executives;
- the vesting schedule of the unvested stock options held by our executives; and
- the amount and percentage of total equity on a diluted basis held by our executives.

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All historical stock option grants have been made at exercise prices that our board of directors determined to equal the fair market value of our shares of common stock on the respective grant dates.

Fiscal Year 2009. In April 2009, as part of the annual performance evaluations of our named executive officers, our board of directors granted to our named executive officers the following stock options to purchase shares of our common stock, each at an exercise price of $8.48 per share, which was determined to equal the fair market value of our common stock on the date of grant:

Name	Number of Shares of Common Stock Underlying Option
Tuan Ha-Ngoc	57,499
David Johnston	12,499
Elan Ezickson	14,999
Jeno Gyuris	12,499

On October 8, 2009, our board of directors granted Dr. Slichenmyer stock options to purchase an aggregate of 187,500 shares of our common stock in connection with his hiring. The options have an exercise price of $9.64 per share, which was determined to equal the fair market value of our common stock on the date of grant. Our board made this stock option grant to Dr. Slichenmyer as part of Dr. Slichenmyer s initial compensation package in order to provide him with an equity award that is comparable to what he could receive from companies with which we compete for talent and in consideration of the internal equity with the other named executive officers.

The stock options we granted to our named executive officers in 2009 provide them with the right to purchase shares of our common stock at a fixed exercise price for a period of up to 10 years, subject to continued employment with our company. These stock options are earned on the basis of continued service to us and vest and become exercisable over a period of four years in equal monthly installments. Options granted upon hiring, including the foregoing option granted to Dr. Slichenmyer, vest and become exercisable over four years, with 25% of the shares underlying the grant vesting on the first anniversary of the grant date and the remaining shares vesting on a pro-rata basis monthly thereafter.

Fiscal Year 2010. In February 2010, as part of the annual individual performance evaluations of our named executive officers, our board of directors upon the recommendation of our compensation committee granted to our named executive officers the options set forth in the table below to purchase shares of our common stock. The board also granted our named executive officers an additional award of milestone-based options to purchase shares of common stock, as set forth below, to further incentivize shareholder value creation in 2010. Both stock option awards to our named executive officers were granted with a term of 10 years (subject to continued employment with our company) and an exercise price of $12.24 per share, which was determined to equal the fair market value of our common stock on the date of grant. Our compensation committee made its recommendation based on its analysis, with input from our consultant, Ms. Arnosti, of executive officer equity for the peer group companies described above and its review of the Radford Global Life Sciences survey for small US-based companies with 50-149 employees and the Radford Global Life Sciences survey for medium-sized US-based companies with 150-500 employees.

Name	Number of Shares of Common Stock Underlying Annual Performance Option(1)	Number of Shares of Common Stock Underlying Milestone-Based Option(2)	Total Number of Shares of Common Stock Underlying Option
Tuan Ha-Ngoc	39,999	61,250	101,249
David Johnston	14,999	12,500	27,499
Elan Ezickson	18,749	16,250	34,999
Jeno Gyuris	14,999	10,000	24,999
William Slichenmyer		12,500	12,500

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(1) These options vest and become exercisable over a period of four years in equal monthly installments.
(2) 50% of the shares underlying these options vest and become exercisable if we end the 2010 fiscal year with a cash balance at least 40% over the 2010 budget while accomplishing our research and development goals and the remainder of the shares underlying these options vest on the first anniversary of achieving such cash balance goal.

Vesting of options granted to any employee, including our named executive officers, fully accelerate if such employee is terminated without cause within one year following a change in control of the company. Vesting and exercise rights cease shortly after termination of employment except in the case of death or disability. Prior to the exercise of an option, the holder has no rights as a stockholder with respect to the shares subject to such option, including voting rights and the right to receive dividends or dividend equivalents.

We do not have any equity ownership guidelines for our executives.

Other Benefits. We believe that establishing competitive benefit packages for our employees is an important factor in attracting and retaining highly qualified personnel. Named executive officers are eligible to participate in all of our employee benefit plans, such as medical, dental, group life and accidental death and dismemberment insurance and our 401(k) plan, in each case on the same basis as other employees. Under our 401(k) plan, we match 50% on every dollar contributed by an employee up to a maximum of 5% of the employee s salary. The match vests at 25% per year over four years. Consistent with our compensation philosophy, we intend to continue to maintain our current benefits for our named executive officers. The compensation committee in its discretion may revise, amend or add to the officer s executive benefits and perquisites if it deems it advisable.

In certain circumstances, we sometimes award cash signing bonuses when executives first join us. Whether a signing bonus is paid and the amount of the bonus is determined on a case-by-case basis under the specific hiring circumstances. For example, we will consider paying signing bonuses to compensate for amounts forfeited by an executive upon terminating prior employment, to assist with relocation expenses or to create additional incentive for an executive to join our company in a position where there is high market demand. Dr. Slichenmyer, who was hired as our chief medical officer in September 2009, received a signing bonus payment as follows: $20,000 upon commencing employment; $60,000 upon the first anniversary of his employment; and $50,000 upon our initiation of a phase 2 clinical trial of AV-299.

Severance and Change in Control Benefits

Our named executive officers are entitled to receive severance benefits in connection with a termination of their employment not in connection with a change in control. Please refer to Employment Agreements and Severance Arrangements for a more detailed discussion of these benefits. Additionally, pursuant to our Key Employee Change in Control Severance Benefit Plan, certain of our key employees, including our named executive officers, are entitled to severance payments if we terminate their employment without cause or if they leave their employment with us for good reason within 18 months of a change in control of our company. We have provided more detailed information about these benefits, along with estimates of their value under various circumstances, under Potential Payments and Benefits Upon Termination and a Change in Control below.

We believe providing these benefits helps us compete for executive talent. After reviewing the practices of comparable companies, we believe that our severance and change in control benefits are generally in line with severance packages offered to executives by such companies.

Our practice in the case of change in control benefits has been to structure these as double trigger benefits. This means that the change in control does not itself trigger benefits; rather, benefits are paid only if the employment of the executive is terminated during a specified period after the change in control. We believe a

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double trigger benefit maximizes shareholder value because it prevents an unintended windfall to executives in the event of a friendly change in control, while still providing them appropriate incentives to cooperate in negotiating any change in control in which they believe they may lose their jobs.

Tax and Accounting Considerations

Because we currently have a history of operating losses and we have net operating loss carryforwards that would have the effect of offsetting any future taxable gains, we generally do not consider the tax implications of our executive compensation programs to be meaningful to our operating or financial results. Section 162(m) of the Internal Revenue Code of 1986, as amended, or the Code, generally disallows a tax deduction for compensation in excess of $1.0 million paid to our chief executive officer and our three other officers (other than our chief financial officer) whose compensation is required to be reported to our stockholders pursuant to the Exchange Act by reason of being among the three other most highly paid executive officers. Qualifying performance-based compensation is not subject to the deduction limitation if specified requirements are met. The compensation committee may, in its judgment, authorize compensation payments that do not comply with the exemptions in Section 162(m) when it believes that such payments are appropriate to attract and retain executive talent.

We account for equity compensation paid to our employees in accordance with ASC 718, which requires us to measure and recognize compensation expense in our financial statements for all share-based payments based upon an estimate of their fair value over the service period of the award. We record cash compensation as an expense at the time the obligation is accrued.

Summary Compensation Table for the Years Ended December 31, 2008 and 2009

The following table sets forth information for the years ended December 31, 2008 and 2009 regarding compensation awarded to, earned by or paid to our Chief Executive Officer, our Chief Financial Officer, and our three other most highly compensated executive officers during fiscal years 2008 and 2009.

Name and Principal Position	Year	Salary ($)	Bonus ($)	Option Awards ($)[2]	Non-Equity Incentive Plan Compensation ($)[3]	All Other Compensation ($)[4]	Total ($)
Tuan Ha-Ngoc,	2009	$ 411,572		$ 378,780	$ 185,400	$ 9,737	$ 985,489
Chief Executive Officer	2008	$ 400,000		$ 286,983	$ 180,000	$ 9,362	$ 876,345
David Johnston,	2009	$ 289,509		$ 171,290	$ 80,861	$ 7,580	$ 549,240
Chief Financial Officer	2008	$ 280,000	$ 100,000[1]	$ 151,619	$ 75,600	$ 7,157	$ 614,376
Elan Ezickson,	2009	$ 304,907		$ 109,951	$ 86,507	$ 7,130	$ 508,495
Chief Business Officer	2008	$ 296,250		$ 86,245	$ 79,988	$ 6,726	$ 469,209
Jeno Gyuris,	2009	$ 255,981		$ 102,663	$ 71,473	$ 6,954	$ 437,071
Senior Vice President, Head of Research	2008	$ 248,713		$ 82,913	$ 55,960	$ 6,555	$ 394,141
William Slichenmyer,	2009	$ 102,137	$ 20,000[5]	$ 96,584	$ 42,160	$ 2,213	$ 263,094
Chief Medical Officer							

(1) Bonus amount for Mr. Johnston of $100,000 represents the payment of a signing bonus in connection with Mr. Johnston s employment, which became due on January 31, 2008, 90 days following his start of employment.

(2) The assumptions we used in valuing options are described under the caption Stock-Based Compensation in Note 14 to our financial statements included in this prospectus. This column reflects compensation expense that would be recorded under ASC 718 as stock-based compensation in our financial statements for the indicated year in connection with options we granted in the indicated year and in prior years, adjusted to disregard the effects of any estimate of forfeitures related to service-based vesting.

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(3) Our compensation committee determined to pay Tuan Ha-Ngoc, David Johnston, Elan Ezickson, Jeno Gyuris and William Slichenmyer annual cash incentive plan awards equal to 90%, 93.0%, 94.5%, 93.0%, and 93.0% of such executive officer s target award, respectively, for performance in fiscal 2009. See Grants of Plan-Based Awards for the Year Ended December 31, 2009 below for additional information related to these awards. Our compensation committee determined to pay our executive officers 90% of their target awards under our annual cash incentive program for performance in fiscal 2008. The bonus earned on the basis of actual performance relative to target bonus metrics has been reported in this column as non-equity incentive plan compensation.

(4) Amounts represent the value of perquisites and other personal benefits, which are further detailed below.

Name	Year	Matched 401(k) Contribution ($)	Group Life Insurance ($)	Total ($)
Tuan Ha-Ngoc,	2009	$ 6,125	$ 3,612	$ 9,737
Chief Executive Officer	2008	$ 5,750	$ 3,612	$ 9,362
David Johnston,	2009	$ 6,125	$ 1,455	$ 7,580
Chief Financial Officer	2008	$ 5,750	$ 1,407	$ 7,157
Elan Ezickson,	2009	$ 6,125	$ 1,005	$ 7,130
Chief Business Officer	2008	$ 5,750	$ 976	$ 6,726
Jeno Gyuris,	2009	$ 6,125	$ 829	$ 6,954
Senior Vice President, Head of Research	2008	$ 5,750	$ 805	$ 6,555
William Slichenmyer, Chief Medical Officer	2009	$ 1,706	$ 507	$ 2,213

(5) Bonus amount for Dr. Slichenmyer represents the payment of a signing bonus in connection with Dr. Slichenmyer s employment.

Grants of Plan-Based Awards for the Year Ended December 31, 2009

The following table sets forth information for the year ended December 31, 2009 regarding grants of plan-based awards made during fiscal 2009 to our named executive officers.

Name	Grant Date	Estimated Future Payouts Under Non-Equity Incentive Plan Awards[1] Target ($)	All Other Option Awards: Number of Securities Underlying Options (#)[2]	Exercise or Base Price of Option Awards ($/sh)[3]	Grant Date Fair Value of Stock and Option Awards ($)[4]
Tuan Ha-Ngoc	4/1/2009	$ 206,000	57,499	$ 8.48	$ 362,940
David Johnston	4/1/2009	$ 86,947	12,499	$ 8.48	$ 78,900
Elan Ezickson	4/1/2009	$ 91,541	14,999	$ 8.48	$ 94,680
Jeno Gyuris	4/1/2009	$ 76,852	12,499	$ 8.48	$ 78,900
William Slichenmyer	10/8/2009	$ 45,333	187,500	$ 9.64	$ 1,305,675

(1)

Represents the target payout levels under the annual cash incentive program. Target payouts for Tuan Ha-Ngoc, David Johnston, Elan Ezickson, Jeno Gyuris and William Slichenmyer represented 50%, 30%, 30%, 30% and 40% of base salary, respectively. The actual payout with respect to each named executive officer is shown above in the Summary Compensation Table for the Years Ended December 31, 2008 and 2009 in the column titled Non-Equity Incentive Plan Compensation. The board retains broad discretion to increase or decrease awards based on achievement of our corporate goals and individual performance.

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Additional information regarding the design of the annual cash incentive program, including a description of the corporate goals and individual performance applicable to 2009 awards, is described above in Executive Compensation Components.

(2) For the vesting schedules of these awards, please see footnotes 2 and 3 of the Outstanding Equity Awards at December 31, 2009 table below. These awards are subject to acceleration upon termination of employment as further described in the Severance and Change in Control Benefits section above and the Employment Agreements and Severance Arrangements and Potential Payments and Benefits Upon Termination and a Change in Control sections below.

(3) For a discussion of our methodology for determining the fair value of our common stock, see the Management s Discussion and Analysis of Financial Condition and Results of Operations Critical Accounting Policies and Significant Judgments and Estimates section of this prospectus.

(4) Valuation of these options is based on the aggregate dollar amount of share-based compensation recognized for financial statement reporting purposes computed in accordance with ASC 718 over the term of these options, excluding the impact of estimated forfeitures related to service-based vesting conditions. The assumptions used by us with respect to the valuation of stock and option awards are set forth in Note 14 to our financial statements included elsewhere in this prospectus.

Outstanding Equity Awards at December 31, 2009

The following table sets forth information regarding outstanding equity awards held as of December 31, 2009 by our named executive officers.

	Option awards[1]			
Name	Number of Securities Underlying Unexercised Options Exercisable (#)	Number of Securities Underlying Unexercised Options Unexercisable (#)	Option Exercise Price ($)	Option Expiration Date
Tuan Ha-Ngoc	13,177	44,322	$ 8.48[2]	4/1/2019
	29,947	32,552	$ 6.44[4]	1/31/2018
	174,088	64,661	$ 5.20[5]	5/9/2017
	85,677	1,823	$ 2.00[6]	2/9/2016
	250,000		$ 1.32[7]	2/1/2015
	50,000		$ 0.48[8]	5/22/2012
David Johnston	2,864	9,635	$ 8.48[2]	4/1/2019
	94,791	80,209	$ 5.60[9]	10/31/2017
Elan Ezickson	3,437	11,562	$ 8.48[2]	4/1/2019
	17,968	19,531	$ 6.44[4]	1/31/2018
	36,458	13,542	$ 5.20[5]	5/9/2017
	24,479	521	$ 2.00[6]	2/9/2016
	50,000		$ 1.32[7]	2/1/2015
	37,500		$ 0.48[10]	5/2/2013
Jeno Gyuris	2,864	9,635	$ 8.48[2]	4/1/2019
	14,375	15,625	$ 6.44[4]	1/31/2018
	36,458	13,542	$ 5.20[5]	5/9/2017
	36,718	782	$ 2.00[6]	2/9/2016
	30,000		$ 1.32[7]	2/1/2015
	45,000		$ 0.48[11]	2/28/2013
William Slichenmyer	0	187,500	$ 9.64[3]	10/8/2019

(1) All option awards held by our named executive officers are subject to vesting acceleration upon termination of employment, as further described in the Severance and Change in Control Benefits section above

and the Employment Agreements and Severance Arrangements and Potential Payments and Benefits Upon Termination and a Change in Control sections below.

(2) These options vest in equal monthly installments through January 1, 2013.

(3) These options will vest as to 25% of the shares on September 14, 2010 and in equal monthly installments as to the remaining shares through September 14, 2013.

(4) These options vest in equal monthly installments through January 1, 2012.

(5) These options vest in equal monthly installments through January 1, 2011.

(6) These options vest in equal monthly installments through January 1, 2010.

(7) These options are fully vested as of January 1, 2009.

(8) These options are fully vested as of December 31, 2005.

(9) These options vested as to 25% of the shares on October 31, 2008, and as to an additional 1/48 of the shares per month thereafter. Pursuant to the terms of the option agreements, these options will vest as to an additional aggregate 37,500 shares upon successful completion of a qualifying public offering (as such term is defined in our certificate of incorporation) or a change in control, as defined by Mr. Johnston s option agreements.

(10) These options are fully vested as of April 28, 2007.

(11) These options are fully vested as of January 13, 2007.

Employment Agreements and Severance Arrangements

Tuan Ha-Ngoc Employment Agreement. We entered into an employment agreement with Tuan Ha-Ngoc, our President and Chief Executive Officer, in December 2008. Mr. Ha-Ngoc s annual base salary is currently $422,300. Mr. Ha-Ngoc s base salary is reviewed annually by our board of directors. Pursuant to the agreement, Mr. Ha-Ngoc had the opportunity to earn an annual performance bonus for each calendar year he is employed by us of up to 35% (which may be increased from time to time at the discretion of our board of directors) of his base salary based on the achievement of criteria agreed to by Mr. Ha-Ngoc and the board of directors, each year. The board of directors has currently set Mr. Ha-Ngoc s annual performance bonus potential at 50% of his base salary. If all of the criteria for the award of any annual bonus are exceeded in any calendar year, the board, in its sole discretion, may award an amount that exceeds the 50% target. The amount and components of any bonus award are determined in the sole discretion of the board, or its designee, and are based solely on company-wide performance. Mr. Ha-Ngoc also received a sign-on bonus of $120,000 in connection with the commencement of his employment with us.

Upon appointment as our President and Chief Executive Officer, and as provided in the employment agreement, Mr. Ha-Ngoc was granted 200,000 shares of restricted stock at a purchase price of $0.48 per share, which have vested in full. Upon appointment, Mr. Ha-Ngoc was also granted a stock option to purchase 50,000 shares of our common stock at an exercise price of $0.48 per share, which options are fully vested. Mr. Ha-Ngoc is also eligible to receive on an annual basis, and has received, additional grants of stock options, as determined in the sole discretion of the board of directors or our compensation committee, as the case may be. To date, Mr. Ha-Ngoc has received options to purchase an aggregate of 847,496 shares of common stock.

Severance and Change in Control Agreements with Named Executive Officers. We have entered into individual severance and change in control agreements with each of our named executive officers. All benefits payable pursuant to a severance and change in control agreement are contingent upon the executive officer executing a release of claims in our favor in a form satisfactory to us. In addition, each of our key executive officers is subject to non-competition and non-solicitation covenants as part of their individual agreements, subject to certain exceptions.

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Pursuant to the terms of our severance and change in control agreement with Mr. Ha-Ngoc, he is entitled, in the event that his employment is terminated without cause, due to a disability or for good reason to the following:

- to continue to receive compensation after termination of his employment with us at a rate equal to his then-current base salary for the lesser of 18 months or the time at which he finds comparable employment;
- to receive a lump sum payment of his annual bonus target pro-rated through the date of his termination; and
- to continue his health insurance for the lesser of 18 months or the time at which he receives such benefits from a new employer.

Pursuant to the terms of our severance and change in control agreement with each of David Johnston, Elan Ezickson, Jeno Gyuris and William Slichenmyer, each such executive officer is entitled, in the event that his employment is terminated without cause, due to a disability or for good reason to the following:

- to continue to receive compensation after termination of his respective employment with us at a rate equal to his then-current base salary for the lesser of 12 months or the time at which he finds comparable employment;
- to receive a lump sum payment of his annual bonus target pro-rated through the date of his termination; and
- to continue his health insurance for the lesser of 12 months or the time at which he receives such benefits from a new employer.

As defined in each named executive officer s severance and change in control agreement, cause means any of the following, as determined by our board of directors:

- the conviction of or plea of not guilty or nolo contedere to a felony or a crime involving dishonesty or any felony;
- willful misconduct resulting in material harm to our company;
- commission of an act of fraud, embezzlement, theft or dishonesty against the company resulting in material harm to our company;
- repeated and continuing failure to follow the proper and lawful directions of our chief executive officer (other than with respect to Mr. Ha-Ngoc) or our board of directors after a written demand is delivered that specifically identifies the manner in which the chief executive officer or our board of directors believes that he has failed to follow such instructions;
- current alcohol or prescription drug abuse affecting work performance, or current illegal use of drugs regardless of the effect on work performance;
- material violation of our code of conduct that causes harm to our company; or

material breach of any term of his severance and change in control agreement, or any other applicable confidentiality and/or non-competition agreements with us.

However, in the case of Tuan Ha-Ngoc, a termination for cause can only be made (i) upon the determination of at least 67% of the non-interested members of our board of directors and (ii) Mr. Ha-Ngoc is given at least 30 days to cure any violation.

As defined in each named executive officer s severance and change in control agreement, termination for good reason means the executive officer s voluntary termination of employment due to any of following occurring without his written consent:

the requirement that such employee perform his duties outside a radius of 50 miles from our corporate headquarters in Cambridge, MA;

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any material diminution in such employee s duties, responsibilities or authority;

a reduction in his base salary (unless such reduction is effected in connection with a general and proportionate reduction of compensation all employees of his pay level); or

the material breach by us of any term or condition of his severance and change in control agreement or another applicable employment agreement.

The right to terminate employment for good reason requires that an executive give us written notice of termination and an opportunity to cure the condition giving rise to good reason within 30 days of receiving such notice. The delivery of the notice and the date of termination must occur within 90 and 180 days, respectively, of the condition giving rise to good reason.

If an executive s employment is terminated within 18 months following a change in control of our company, the individual severance and change in control agreements provide that all severance payments be made pursuant to our key employee change in control severance benefits plan.

Key Employee Change in Control Severance Benefits Plan. In addition to individual severance and change in control agreements, our named executives officers and other key employees participate in our Key Employee Change in Control Severance Benefits Plan. No payments are made pursuant to individual severance and change in control agreements if payments are made under this plan. All benefits payable under the plan are contingent upon the participant executing a release of claims in our favor in a form satisfactory to us. Pursuant to the terms of the plan, if we terminate a named executive officer s employment without cause or if they leave their employment with us for good reason within 18 months following a change in control of our company, such named executive officer is entitled to the following benefits:

continued receipt of compensation after termination at a rate equal to such executive s then-current base salary for 12 months (18 months in the case of Mr. Ha-Ngoc);

payment of a sum equal to (i) such individual s pro rata target bonus plus (ii) an amount equal to one times his target bonus (1.5 times his target bonus, in the case of Mr. Ha-Ngoc); and

continued health insurance for 12 months (18 months in the case of Mr. Ha-Ngoc).

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Potential Payments and Benefits Upon Termination and a Change in Control

Our named executive officers are entitled to certain benefits in the event their employment is terminated without cause, due to a disability or for good reason, as described above. The following table describes the potential payments and benefits to each of our named executive officers following a termination of employment without cause, due to a disability or for good reason on December 31, 2009. Actual amounts payable to each executive listed below upon termination can only be determined definitively at the time of each executive s actual departure. In addition to the amounts shown in the table below, each executive would receive payments for amounts of base salary and vacation time accrued through the date of termination and payment for any reimbursable business expenses incurred. For information relating to compensation earned by each of our named executive officers, see our Summary Compensation Table For the Years Ended December 31, 2008 and 2009 above.

Name	Benefits ($)	Termination Without Cause, Due To a Disability or For Good Reason	Termination Without Cause or For Good Reason Within 18 Months of a Change in Control
Tuan Ha-Ngoc, Chief Executive Officer	Base Salary	$ 618,000[1]	$ 618,000[5]
	Bonus	$ 206,000[2]	$ 515,000[6]
	Healthcare Benefits	$ 23,667[3]	$ 23,667[7]
	Market Value of Awards Vesting on Termination[4]	$	$ 697,444
	Total	$ 847,667	$ 1,854,111
David Johnston, Chief Financial Officer	Base Salary	$ 289,823[1]	$ 289,823[5]
	Bonus	$ 86,947[2]	$ 173,894[6]
	Healthcare Benefits	$ 15,778[3]	$ 15,778[7]
	Market Value of Awards Vesting on Termination[4]	$	$ 486,159[8]
	Total	$ 392,548	$ 965,654
Elan Ezickson, Chief Business Officer	Base Salary	$ 305,138[1]	$ 305,138[5]
	Bonus	$ 91,541[2]	$ 183,082[6]
	Healthcare Benefits	$ 15,778[3]	$ 15,778[7]
	Market Value of Awards Vesting on Termination[4]	$	$ 215,880
	Total	$ 412,457	$ 719,878
Jeno Gyuris, Senior Vice President, Head of Research	Base Salary	$ 256,174[1]	$ 256,174[5]
	Bonus	$ 76,852[2]	$ 153,704[6]
	Healthcare Benefits	$ 15,778[3]	$ 15,778[7]
	Market Value of Awards Vesting on Termination[4]	$	$ 193,779
	Total	$ 348,804	$ 619,435
William Slichenmyer Chief Medical Officer	Base Salary	$ 340,000[1]	$ 340,000[5]
	Bonus	$ 45,333[2]	$ 181,333[6]
	Healthcare Benefits	$ 15,778[3]	$ 15,778[7]
	Market Value of Awards Vesting on Termination[4]	$	$ 315,000

Total	$ 401,111	$ 852,111

(1) Represents the executive officer s base salary payable over 12 months, or in the case of Mr. Ha-Ngoc, 18 months. Severance is equal to payment of the executive s base salary until the earlier of (i) 12 months (in the case of Mr. Ha-Ngoc, 18 months) following the date of termination and (ii) the date on which the executive commences full-time employment or a full-time consulting relationship with substantially equivalent compensation.

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(2) Represents the executive s severance bonus payable within 30 days of the date of termination. Severance bonus is equal to payment of the executive s target annual incentive plan bonus pro-rated through the date of termination.

(3) Represents the cost of continued COBRA benefits for the executive and any qualified beneficiary. COBRA benefits are payable until the earlier of (i) 12 months (in the case of Mr. Ha-Ngoc, 18 months) (or as long as such eligibility for the executive and each qualified beneficiary continues) from the date such benefits would otherwise end under the applicable plan terms and (ii) the date the Employee becomes eligible for group health coverage through another employer. This value is based upon the type of insurance coverage we carried for each executive officer as of December 31, 2009 and is valued at the premiums in effect on December 31, 2009.

(4) This amount is equal to (a) the number of options that would vest as a direct result of the employment termination subsequent to a change in control multiplied by (b) the excess of $11.32, which represents the fair market value of our common stock as of December 31, 2009, over the exercise price of the options.

(5) Represents the executive s base salary payable over 12 months (in the case of Mr. Ha-Ngoc, 18 months) following the date of termination.

(6) Represents the executive s severance bonus payable over 12 months (in the case of Mr. Ha-Ngoc, 18 months) following the date of termination. Severance bonus is in addition to the executive s target annual incentive plan bonus pro-rated through the date of termination.

(7) Represents the cost of continued COBRA benefits for the executive and any qualified beneficiary for 12 months (in the case of Mr. Ha-Ngoc, 18 months) following the date of termination.

(8) Pursuant to the terms of his option agreements, Mr. Johnston s options will vest as to an additional aggregate 37,500 shares upon successful completion of a qualifying public offering (as such term is defined in our certificate of incorporation) or a change in control, as defined by Mr. Johnston s option agreements.

Stock Option and Other Compensation Plans

2002 Stock Incentive Plan

Our stock incentive plan, which we refer to as the 2002 stock plan, was originally adopted by our board of directors on February 2, 2002 and approved by our stockholders on February 12, 2002. On February 2, 2010 and February 11, 2010, respectively, our board of directors and stockholders approved an amendment to our 2002 stock plan to increase the number of shares of common stock authorized for issuance from 4,269,062 shares to 6,144,062 shares.

The 2002 stock plan provides for the grant of incentive stock options, nonstatutory stock options, restricted stock and other stock-based awards. Our employees, officers, directors, consultants and advisors are eligible to receive awards under the 2002 stock plan; however, incentive stock options may only be granted to our employees. In accordance with the terms of the 2002 stock plan, our board of directors, or a committee or subcommittee appointed by our board of directors, administers the 2002 stock plan and, subject to any limitations in the 2002 stock plan, selects the recipients of awards and determines:

the number of shares of our common stock covered by options and the dates upon which the options become exercisable;

the exercise price of options;

the duration of the options;

the methods of payment of the exercise price; and

the number of shares of our common stock subject to any restricted stock or other stock-based awards and the terms and conditions of such awards, including conditions for repurchase, issue price and repurchase price.

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The 2002 stock plan also permits our board of directors to delegate authority to an executive officer to grant awards to all of our employees, except executive officers, provided that our board of directors will fix the terms of the awards to be granted by such executive officer, including the exercise price of such awards and the maximum number of shares subject to awards that such executive officer may make.

Pursuant to the terms of the 2002 stock plan, in the event of a proposed liquidation or dissolution of our company, our board of directors will provide that all unexercised options will become exercisable in full at least 10 business days prior to the effective date of the liquidation or dissolution and will terminate upon the liquidation or dissolution, except to the extent exercised before such date. Our board of directors may specify the effect of a liquidation or dissolution on any restricted stock award or other award granted under the 2002 stock plan at the time of the grant of the award.

Upon the occurrence of a Reorganization Event (as defined in the 2002 stock plan), or the signing of an agreement with respect to a Reorganization Event, all outstanding options will be assumed or equivalent options substituted by the successor corporation. Notwithstanding the foregoing, if the acquiring or succeeding corporation in a Reorganization Event does not agree to assume or substitute for outstanding options, or in the event of our liquidation or dissolution, our board of directors will provide that all unexercised options will become exercisable in full prior to the Reorganization Event and the options, if unexercised, will terminate on the date the Reorganization Event takes place. If under the terms of the Reorganization Event holders of our common stock receive cash for their shares, our board may instead provide for a cash-out of the value of any outstanding options less the applicable exercise price and any applicable tax withholdings.

If on or prior to the first anniversary of a Change In Control Event (as defined in the 2002 stock plan), regardless of whether such event also constitutes a Reorganization Event, an option holder s employment with us or our succeeding corporation is terminated by us or the succeeding corporation without Cause (as defined in the 2002 stock plan), all options held by such employee will become immediately exercisable in full.

Upon the occurrence of a Reorganization Event, or the signing of an agreement with respect to a Reorganization Event, our repurchase and other rights with respect to shares of common stock subject to outstanding restricted stock awards will inure to the benefit of our successor and will apply to the cash, securities or other property into which our common stock is then converted in the same manner and to the same extent as they applied to our common stock subject to such restricted stock awards.

If on or prior to the first anniversary of a Change In Control Event, regardless of whether such event also constitutes a Reorganization Event, a restricted stock holder s employment with us or our succeeding corporation is terminated by us or the succeeding corporation without Cause, all shares of restricted stock outstanding under any award held by such employee will become immediately free of all restrictions and conditions.

As of February 1, 2010, there were options to purchase 3,248,207 shares of common stock outstanding under the 2002 stock plan at a weighted average exercise price of $4.56 per share, 277,216 shares of common stock had been issued pursuant to the exercise of options granted under the 2002 stock plan and 344,999 shares of common stock (net of forfeitures) had been issued pursuant to restricted stock awards granted under the plan. As of February 1, 2010, there were 398,611 shares of common stock reserved but not granted under the 2002 stock plan.

After the effective date of the 2010 Stock Incentive Plan described below, we will grant no further stock options or other awards under the 2002 stock plan; however, any shares of common stock reserved for issuance under the 2002 stock plan that remain available for issuance and any shares of common stock subject to awards under the 2002 stock plan that expire, terminate, or are otherwise surrendered, canceled, forfeited or repurchased without having been fully exercised or resulting in any common stock being issued shall be rolled into the 2010 Stock Incentive Plan up to a specified number of shares.

2010 Stock Incentive Plan

Our 2010 Stock Incentive Plan, which we refer to as the 2010 stock plan, will become effective upon the closing of this offering, and was adopted by our board of directors on February 2, 2010 and approved by our

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stockholders on February 11, 2010. The 2010 stock plan provides for the grant of incentive stock options, nonstatutory stock options, restricted stock awards, restricted stock unit awards, stock appreciation rights and other stock-based and cash-based awards. Upon effectiveness of the 2010 stock plan, the number of shares of our common stock that will be reserved for issuance under the 2010 stock plan will be the number of shares of our common stock reserved for issuance under the 2002 stock plan that remain available for grant under the 2002 stock plan immediately prior to the closing of this offering plus the number of shares of our common stock subject to awards granted under the 2002 stock plan which expire, terminate or are otherwise surrendered, cancelled, forfeited or repurchased by us at their original issuance price pursuant to a contractual repurchase right, up to a maximum of 2,500,000 shares.

Our employees, officers, directors, consultants and advisors are eligible to receive awards under our 2010 stock plan; however, incentive stock options may only be granted to our employees. The maximum number of shares of our common stock with respect to which awards may be granted to any participant under the plan is 250,000 per fiscal year.

In accordance with the terms of the 2010 stock plan, our board of directors has authorized our compensation committee to administer the 2010 stock plan. Pursuant to the terms of the 2010 stock plan, our compensation committee will select the recipients of awards and determine:

- the number of shares of our common stock covered by options and the dates upon which the options become exercisable;
- the exercise price of options;
- the duration of the options;
- the methods of payment of the exercise price; and
- the number of shares of our common stock subject to any restricted stock or other stock-based awards and the terms and conditions of such awards, including conditions for repurchase, issue price and repurchase price.

The 2010 stock plan provides our non-employee directors with an automatic grant of options to purchase 18,750 shares of common stock upon commencement of service on our board of directors and an automatic grant of options to purchase an additional 12,500 shares of common stock on the date of each annual meeting, provided that in the case of the options granted on the date of our annual meeting, such director must (i) be serving as a director immediately prior to and after our annual meeting and (ii) have served on our board of directors for at least six months. Unless otherwise determined by our board, both initial and annual option grants will vest in twelve equal monthly installments beginning on the date of grant. Our board of directors has the authority to provide for different vesting provisions and conditions than those set forth in the 2010 stock plan, to increase or decrease the number of shares subject to such options and to substitute stock appreciation rights, restricted stock awards or other stock-based awards in lieu of some or all of such options.

We will be required to make equitable adjustments in connection with the 2010 stock plan and any outstanding awards to reflect stock splits, stock dividends, recapitalizations, spin-offs and other similar changes in capitalization.

Upon the occurrence of a Reorganization Event (as defined in the 2010 stock plan), or the signing of an agreement with respect to a Reorganization Event, all outstanding options will be assumed or equivalent options substituted by the successor corporation. Notwithstanding the foregoing, if the acquiring or succeeding corporation in a Reorganization Event does not agree to assume or substitute for outstanding options, or in the event of our liquidation or dissolution, our board of directors will provide that all unexercised options will become exercisable in full prior to the Reorganization Event and the options, if unexercised, will terminate on the date the Reorganization Event takes place. If under the terms of the Reorganization Event holders of our common stock receive cash for their shares, our board may instead provide for a cash-out of the value of any outstanding options less the applicable exercise price and any applicable tax withholdings.

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If on or prior to the first anniversary of a Change In Control Event (as defined in the 2010 stock plan), regardless of whether such event also constitutes a Reorganization Event, an option holder s employment with us or our succeeding corporation is terminated by us or the succeeding corporation without Cause (as defined in the 2010 stock plan), all options held by such employee will become immediately exercisable in full.

Upon the occurrence of a Reorganization Event, or the signing of an agreement with respect to a Reorganization Event, our repurchase and other rights with respect to shares of common stock subject to outstanding restricted stock awards will inure to the benefit of our successor and will apply to the cash, securities or other property into which our common stock is then converted in the same manner and to the same extent as they applied to our common stock subject to such restricted stock awards.

If on or prior to the first anniversary of a Change In Control Event, regardless of whether such event also constitutes a Reorganization Event, a restricted stock holder s employment with us or our succeeding corporation is terminated by us or the succeeding corporation without Cause, all shares of restricted stock outstanding under any award held by such employee will become immediately free of all restrictions and conditions.

No award may be granted under the 2010 stock plan more than 10 years from the date the 2010 stock plan was approved by our stockholders. Our board of directors may amend, suspend or terminate the 2010 stock plan at any time, except that stockholder approval will be required to comply with applicable law or stock market requirements.

2010 Employee Stock Purchase Plan

Our 2010 Employee Stock Purchase Plan, which we refer to as the 2010 ESPP, was adopted, subject to the closing of this offering, by our board of directors on February 2, 2010 and approved by our stockholders on February 11, 2010. The 2010 ESPP provides eligible employees with the opportunity to purchase up to an aggregate of 250,000 shares of our common stock.

All of our employees, including directors who are employees, are eligible to participate in the 2010 ESPP provided that:

such person is customarily employed by us for more than 20 hours per week and for more than five months in a calendar year;

such person has been employed by us for at least six months prior to enrolling in the 2010 ESPP; and

such person was our employee on the first day of the applicable offering period under the 2010 ESPP.

No employee is eligible to receive an option to purchase shares of our common stock that would result in the employee owning 5% or more of the total combined voting power or value of our stock immediately after the grant of such option.

We will make one or more offerings to our employees to purchase stock under the 2010 ESPP. Unless otherwise determined by our board of directors, the commencement date of our first purchase plan period will be July 1, 2010 and subsequent offering periods will begin each January 1 and July 1 (or the first business day thereafter) and continue for six months. Payroll deductions made during each purchase plan period will be held for the purchase of our common stock at the end of each purchase plan period.

On the offering commencement date of each purchase plan period, we will grant to each eligible employee who is then a participant in the 2010 ESPP an option to purchase shares of our common stock. The employee may authorize up to a maximum of 15% of his or her base pay to be deducted by us during the purchase plan period. Each employee who continues to be a participant in the 2010 ESPP on the last business day of the purchase plan period is deemed to have exercised the option, to the extent of accumulated payroll deductions within the 2010 ESPP ownership limits. Under the terms of the 2010 ESPP, the option exercise price shall be determined by our board of directors for each purchase plan period and the option exercise price will be at least 85% of the applicable closing price. If our board of directors does not make a determination of the option exercise price, the option exercise price will be 85% of the lesser of the closing price of our common stock on either (a) the first business day of the purchase plan period or (b) the last business day of the purchase plan

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period. In no event may an employee purchase in any one purchase plan period a number of shares that exceeds the number of shares determined by dividing (a) the product of $2,083 and the number of full months in the purchase plan period by (b) the closing price of a share of our common stock on the commencement date of the purchase plan period. Our board of directors may, in its discretion, change the date on which purchase plan periods may commence and may choose a different purchase plan period of 24 months or less for each offering.

An employee who is not a participant on the last day of the offering period is not entitled to exercise any option, and the employee s accumulated payroll deductions will be refunded. An employee s rights under the purchase plan terminate upon voluntary withdrawal from the purchase plan at any time, or when the employee ceases employment for any reason.

We will be required to make equitable adjustments in connection with the 2010 ESPP and any outstanding awards to reflect stock splits, reverse stock splits, stock dividends, recapitalizations, combination of shares, reclassification of shares, spin-offs and other similar changes in capitalization.

Upon the occurrence of a Reorganization Event (as defined in the 2010 ESPP), our board is authorized to take any one or more of the following actions as to outstanding options under the 2010 ESPP:

- provide that options will be assumed, or substantially equivalent options will be substituted, by the acquiring or succeeding corporation (or an affiliate thereof);
- upon written notice to employees, provide that all outstanding options will be terminated as of the effective date of the Reorganization Event and that all such outstanding options will become exercisable to the extent of accumulated payroll deductions as of a date specified by the Board;
- upon written notice to employees, provide that all outstanding options will be cancelled as of a date prior to the effective date of the Reorganization Event and that all accumulated payroll deductions will be returned to participating employees on such date;
- upon the occurrence of a Reorganization Event in which holders of our common stock will receive a cash payment for each share surrendered in the Reorganization Event, provide that participants will receive a cash payment equal to the acquisition price times the number of shares of common stock subject to the participant s option minus the aggregate option price of such option, in exchange for termination of such option; and
- provide that, in connection with a liquidation or dissolution of our company, options will convert into the right to receive liquidation proceeds (net of the option price).

Our board of directors may at any time, and from time to time, amend the 2010 ESPP. We will obtain stockholder approval for any amendment if such approval is required by Section 423 of the Code. Further, our board may not make any amendment that would cause the 2010 ESPP to fail to comply with Section 423 of the Code. Our board of directors may terminate the 2010 ESPP at any time. Upon termination, we will refund all amounts in the accounts of participating employees.

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Director Compensation

Mr. Ha-Ngoc, our President and Chief Executive Officer, has not received any compensation in connection with his service as a director. The compensation that we pay to our President and Chief Executive Officer is discussed under Compensation Discussion and Analysis above.

The following table sets forth information for the year ended December 31, 2009 regarding the compensation awarded to, earned by or paid to our non-employee directors.

Name	Fees Earned or Paid In Cash[1]	Option Awards[2]	All Other Compensation[3]	Total
Kenneth Bate[4][5]	$ 21,500	$ 24,466		$ 45,966
Douglas Cole[4][5]		$ 32,940		$ 32,940
Ronald DePinho[4][5]	$ 9,500	$ 32,940	$ 100,000	$ 142,440
Anthony Evnin[4][5]		$ 32,940		$ 32,940
Nicholas Galakatos[4][5]		$ 32,940		$ 32,940
Robert Higgins[4][5]		$ 32,940		$ 32,940
Russell Hirsch[4][5]		$ 32,940		$ 32,940
Raju Kucherlapati[4][5]	$ 9,500	$ 32,940	$ 23,000	$ 65,440
Kenneth Weg[4][5]		$ 32,940		$ 32,940
Robert Young[4][5]	$ 9,500	$ 32,804		$ 42,304

(1) Fees earned or paid in cash consist of: (A) for Mr. Bate, prior to the adoption of our director compensation policy in June 2009, $7,500 in retainer fees and $2,000 in the aggregate for attending board meetings during the first half of fiscal year 2009; and $7,500 in retainer fees ($3,750 per quarter), $2,500 for his service as our audit committee chairman and $2,000 in the aggregate for attending board meetings during the second half of fiscal year 2009; (B) for Dr. DePinho, $7,500 in retainer fees ($3,750 per quarter) and $2,000 in the aggregate for attending board meetings; (C) for Dr. Kucherlapati, $7,500 in retainer fees ($3,750 per quarter) and $2,000 in the aggregate for attending board meetings; and (D) for Dr. Young, $7,500 in retainer fees ($3,750 per quarter) and $2,000 in the aggregate for attending board meetings.

(2) The assumptions we used in valuing options are described under the caption Stock-Based Compensation in Note 14 to our financial statements included in this prospectus. This column reflects compensation expense that would be recorded under ASC 718 as stock-based compensation in our financial statements for the indicated year in connection with options we granted in the indicated year and in prior years, adjusted to disregard the effects of any estimate of forfeitures related to service-based vesting.

(3) Pursuant to their consulting agreements, which are described in further detail below, for the fiscal year ended December 31, 2009, Dr. DePinho received $100,000 and Dr. Kucherlapati received $23,000 as compensation for providing scientific and business advice to us and for attending meetings of our scientific advisory board.

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(4) The grant date fair value for options awarded to our directors during the fiscal year ended December 31, 2009 calculated in accordance with ASC 718 is as follows:

Name	Option Awards	Grant Date Fair Value [1]
Kenneth Bate	10,000	$ 39,200[2]
Douglas Cole	10,000	$ 65,880
Ronald DePinho	10,000	$ 65,880
Anthony Evnin	10,000	$ 65,880
Nicholas Galakatos	10,000	$ 65,880
Robert Higgins	10,000	$ 65,880
Russell Hirsch	10,000	$ 65,880
Raju Kucherlapati	10,000	$ 65,880
Kenneth Weg	10,000	$ 65,880
Robert Young	10,000	$ 65,608

(1) Options were granted at fair value on June 16, 2009 (with the exception of Mr. Young, whose options were granted on July 17, 2009) at $8.72 per share. The options were later determined to have a fair value of $10.04 per share, pursuant to our retrospective valuation. Options vest over one year in twelve equal monthly installments.

(2) Mr. Bate was granted an option to purchase 20,000 shares of our common stock on December 11, 2007 in connection with his service on our board of directors. Of the 20,000 shares granted, 10,000 shares were vested and the remaining 10,000 unvested shares were cancelled during 2009. The board then granted Mr. Bate an option to purchase 10,000 shares of our common stock under our director compensation policy adopted in June 2009 referred to below. Under ASC 718, this cancellation and regrant was considered a modification resulting in expense of $24,466 being recorded during 2009.

(5) The following table reflects the aggregate number of stock awards and the aggregate number of option awards outstanding for our directors as of December 31, 2009:

Name	Option Awards
Kenneth Bate[1]	20,000
Douglas Cole[2]	10,000
Ronald DePinho[3]	20,000
Anthony Evnin[2]	10,000
Nicholas Galakatos[2]	10,000
Robert Higgins[4]	4,166
Russell Hirsch[2]	10,000
Raju Kucherlapati[5]	7,709
Kenneth Weg[2]	10,000
Robert Young[6]	6,750

(1) Consists of (A) an option to purchase 10,000 shares of our common stock at an exercise price of $6.36 per share and (B) an option to purchase 10,000 shares of our common stock at an exercise price of $8.72 per share.

(2) Option to purchase 10,000 shares of our common stock at an exercise price of $8.72 per share.

(3) Consists of (A) an option to purchase 10,000 shares of our common stock at an exercise price of $6.68 per share and (B) an option to purchase 10,000 shares of our common stock at an exercise price of $8.72 per share.

(4) Option to purchase 4,166 shares of our common stock at an exercise price of $8.72 per share.

(5) Consists of (A) an option to purchase 1,875 shares of our common stock at an exercise price of $6.88 per share and (B) an option to purchase 5,834 shares of our common stock at an exercise price of $8.72 per share.

(6) Option to purchase 6,750 shares of our common stock at an exercise price of $8.72 per share.

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In June 2009, the board of directors adopted our director compensation policy, pursuant to which directors are compensated for their services on our board as follows:

Upon the initial election to our board of directors and the date upon which such director is re-elected at our annual shareholders meeting, each non-employee director receives an option to purchase 10,000 shares of common stock exercisable at the then fair market value of our common stock. These options expire ten years from the date of grant, subject to the director s continued service on our board, and are fully exercisable on the first anniversary of the vesting commencement date. Pursuant to the terms of the option agreements governing the grants to our directors, in the event a director resigns from the board, the vesting of any options granted for service on the board ceases as of such date, and such director has a period of up to three months from the date of resignation to exercise any option granted as compensation for service on the board of directors to the extent vested on the date of resignation.

Our non-employee directors who (i) are not affiliated with a venture capital firm holding our preferred stock and (ii) do not themselves hold shares of our preferred stock are paid for their service on our board of directors as follows:

- annual retainer fee of $15,000;
- in-person attendance fee of $1,000 per meeting;
- audit committee chairperson annual fee of $5,000; and
- compensation committee chairperson annual fee of $5,000.

Each member of our board is also entitled to be reimbursed for reasonable travel and other expenses incurred in connection with attending meetings of the board of directors and any committee on which he or she serves.

In November 2009, we approved a new director compensation policy, which we amended in February 2010, which will become effective upon the consummation of our public offering and will supercede the policy approved in June 2009. Under this new policy, our non-employee directors will be compensated as follows:

Upon the initial election to our board of directors, each non-employee director will receive an option to purchase 18,750 shares of common stock exercisable at the then fair market value of our common stock. Upon the date each director is re-elected at our annual shareholders meeting, such director will receive an option to purchase 12,500 shares of our common stock exercisable at the then fair market value of our common stock. Director options will be granted pursuant to our 2010 Stock Incentive Plan, as described in further detail above under Stock Option and Other Compensation Plans.

Our non-employee directors will be paid for their service on our board as follows:

- annual retainer fee for chairman of the board of $40,000;
- annual retainer fee of $20,000 (other than chairman);

in-person attendance fee for board meetings of $1,000 per meeting;

annual retainer fee for members of audit committee (other than chairperson of audit committee) of $6,000;

audit committee chairperson annual retainer fee of $12,500;

annual retainer fee for members of compensation committee (other than chairperson of compensation committee) of $4,000;

compensation committee chairperson annual retainer fee of $7,500;

annual retainer fee for members of nominating and governance committee (other than chairperson) of $3,000; and

nominating and governance committee chairperson annual retainer fee of $5,000.

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Each annual fee is payable in arrears in four equal quarterly installments on the last day of each quarter, provided that the amount of such payment will be prorated for any portion of the quarter that the director was not serving on our board. Each non-employee director will also be reimbursed for reasonable travel and other expenses incurred in connection with attending meetings of the board of directors and any committee on which he or she serves.

Consulting Agreement with Dr. Ronald DePinho. We entered into a consulting arrangement with Dr. DePinho dated as of January 1, 2008, pursuant to which he provides scientific and business advice as well as attends meetings of our scientific advisory board. The consulting agreement may be terminated by either party upon 30 days written notice. Pursuant to his consulting agreement, Dr. DePinho receives an annual retainer of $100,000 payable in equal quarterly installments for his services. In 2009, Dr. DePinho received $100,000 for consulting services provided under this agreement.

Consulting Agreement with Dr. Raju Kucherlapati. We entered into a consulting agreement with Dr. Kucherlapati dated as of January 1, 2008, pursuant to which Dr. Kucherlapati provides scientific and business advice as well as attends meetings of our scientific advisory board. The consulting agreement may be terminated by either party upon 30 days written notice. Pursuant to his consulting agreement, Dr. Kucherlapati receives $10,000 for each full-day meeting of the scientific advisory board he attends, $3,000 for each half-day meeting he attends and $10,000 for each meeting during which he chairs a topic for discussion. In 2009, Dr. Kucherlapati received $23,000 for consulting services provided under this agreement.

Limitation of Liability and Indemnification

Our certificate of incorporation that will be in effect upon the closing of this offering limits the personal liability of directors for breach of fiduciary duty to the maximum extent permitted by the Delaware General Corporation Law. Our certificate of incorporation provides that no director will have personal liability to us or to our stockholders for monetary damages for breach of fiduciary duty or other duty as a director. However, these provisions do not eliminate or limit the liability of any of our directors:

for any breach of their duty of loyalty to us or our stockholders;

for acts or omissions not in good faith or which involve intentional misconduct or a knowing violation of law;

for voting or assenting to unlawful payments of dividends or other distributions; or

for any transaction from which the director derived an improper personal benefit.

Any amendment to or repeal of these provisions will not eliminate or reduce the effect of these provisions in respect of any act or failure to act, or any cause of action, suit or claim that would accrue or arise prior to any amendment or repeal or adoption of an inconsistent provision. If the Delaware General Corporation Law is amended to provide for further limitations on the personal liability of directors of corporations, then the personal liability of our directors will be further limited to the greatest extent permitted by the Delaware General Corporation Law.

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

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CERTAIN RELATIONSHIPS AND RELATED PERSON TRANSACTIONS

Since January 1, 2007, we have engaged in the following transactions with our directors, executive officers and stockholders that beneficially own more than 5% of our voting securities, and affiliates or immediate family members of our directors, executive officers and stockholders that beneficially own more than 5% of our voting securities.

On April 13, 2005 and August 31, 2005, we sold an aggregate of 2,333,334 shares of our series C convertible preferred stock at a price per share of $3.00 to Merck for an aggregate purchase price of $7,000,002. As described below, Schering Corporation purchased 4,000,000 shares of our series D convertible preferred stock at a price per share of $2.50 for an aggregate purchase price of $10,000,000. Subsequent to Merck s merger with Schering-Plough, the parent entity of Schering Corporation, as of November 3, 2009, Merck may be deemed to beneficially hold more than 5% of our voting securities. Upon the closing of this offering, these shares will convert into shares of our common stock.

On March 26, 2007, April 10, 2007 and April 27, 2007, we sold an aggregate of 21,165,510 shares of our series D convertible preferred stock at a price per share of $2.50 to accredited investors, for an aggregate purchase price of $52,913,775. Upon the closing of this offering, these shares will convert into shares of common stock. The table below sets forth the number of shares of our series D convertible preferred stock sold to our directors and stockholders that beneficially own more than 5% of our voting securities and their affiliates and immediate family members in connection with our series D convertible preferred stock financing:

Name	Shares of Series D Convertible Preferred Stock	Aggregate Purchase Price
Affiliates of MPM BioVentures[1]	776,307	$ 1,940,767.50
Affiliates of Highland Capital Partners[2]	2,005,155	$ 5,012,887.50
Affiliates of Venrock[3]	802,062	$ 2,005,155.00
Affiliates of Prospect Venture Partners II, LP[4]	661,781	$ 1,654,452.50
Affiliates of Flagship Ventures[5]	400,981	$ 1,002,452.50
Kenneth E. Weg[6]	165,969	$ 414,922.50
Heidrich Community Property Trust UDT 8/84[7]	100,306	$ 250,765.00
Biogen Idec Inc.	4,010,803	$ 10,027,007.50
Schering Corporation	4,000,000	$ 10,000,000.00
Total	12,923,364	$ 32,308,410.00

(1) Consists of 524,785 shares purchased by MPM BioVentures II-QP, L.P., 184,761 shares purchased by MPM BioVentures GmbH & Co. Parallel-Beteiligungs KG, 57,834 shares purchased by MPM BioVentures II, L.P. and 8,927 shares purchased by MPM Asset Management Investors 2002 BV2 LLC. Nicholas Galakatos, a member of our board of directors, is a General Partner of the MPM BioVentures II and BioVentures III funds.

(2) Consists of 1,254,977 shares purchased by Highland Capital Partners VI Limited Partnership, 688,019 shares purchased by Highland Capital Partners VI-B Limited Partnership and 62,159 shares purchased by Highland Entrepreneurs Fund VI Limited Partnership. Robert Higgins, a former member of our board of directors who resigned from our board on December 15, 2009, is a co-founder of Highland Capital Partners.

(3) Consists of 641,650 shares purchased by Venrock Associates III, L.P., 144,371 shares purchased by Venrock Associates and 16,041 shares purchased by Venrock Entrepreneurs Fund III, L.P. Anthony Evnin, a member of our board of directors, is a Partner at Venrock.

(4) Consists of 651,855 shares purchased by Prospect Venture Partners II, L.P., or PVP II, and 9,926 shares purchased by Prospect Associates II, L.P., or PA II. Russell Hirsch, a member of our board of directors, is Managing Director of Prospect Management Company II, LLC, the respective General Partner of PVP II and PA II.

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(5) Consists of 378,126 shares purchased by Applied Genomic Technology Capital Fund, L.P. and 22,855 shares purchased by AGTC Advisors Fund, L.P. Douglas Cole, a member of our board of directors, is a general partner of Flagship Ventures.

(6) These shares were originally purchased by The Weg Family Limited Partnership and were subsequently transferred to Kenneth E. Weg. Kenneth E. Weg is a member of our board of directors.

(7) A. Grant Heidrich was a member of our board of directors from January 2002 to April 2007. A. Grant Heidrich is trustee of the Heidrich Community Property Trust UDT 8/84.

In November 2003, we entered into a license and collaboration agreement with Merck to discover and validate oncology targets. In August 2005, we entered into our second collaboration with Merck, a license and research collaboration agreement relating to the use of our Human Response Platform. Please see Management s Discussion and Analysis of Financial Condition and Results of Operations Strategic Partnerships Merck, Business Strategic Partnerships and Business Strategic Partnerships Merck for information on these agreements with Merck.

On March 23, 2007, we entered into a research, development and license agreement with Schering-Plough (through its subsidiary Schering Corporation). Please see Business Strategic Partnerships and Business Strategic Partnerships Schering-Plough (now Merck) for information on our agreement with Schering-Plough.

On October 25, 2007, we sold an aggregate of 1,833,334 shares of our series C convertible preferred stock at a price per share of $3.00 to OSI Pharmaceuticals, Inc., or OSI, a holder of more than 5% of our voting securities upon the closing of such sale, for an aggregate purchase price $5,500,002. Upon the closing of this offering, these shares will convert into shares of common stock. This sale and purchase was made in connection with the effectiveness of our collaboration and license agreement with OSI on October 25, 2007, which has subsequently been amended and restated. Please see Business Strategic Partnerships and Business Strategic Partnerships OSI Pharmaceuticals for information on our amended and restated collaboration and license agreement with OSI.

Until December 2007, we employed Steven Clark as our Chief Scientific Officer. For the fiscal year ended December 31, 2007, we paid him a base salary of $307,060 and an annual bonus of $76,765, pursuant to the terms of his employment agreement. Dr. Clark s annual bonus was based on the achievement of performance-based milestones approved by our board of directors. On January 1, 2008, Dr. Clark executed a letter agreement in connection with his appointment as Chairman of our Scientific Advisory Board, for which he was paid a base salary of $184,236 during the year ended December 31, 2008. In addition, Dr. Clark was eligible to participate in our standard benefits program. This letter agreement terminated all obligations under his previous employment agreement with us. For the fiscal year 2009, Dr. Clark received $163,036 in connection with his service as an advisor to our company and his service on our Scientific Advisory Board. Since January 1, 2007, Dr. Clark has been granted options to purchase an aggregate of 19,249 shares of our common stock at an exercise price of $5.20 per share, which was the fair market value of our common stock on the date of grant. As of the date hereof, Dr. Clark holds options to purchase 111,228 shares of our common stock. As of January 1, 2010, we entered into a consulting agreement with Dr. Clark under which he provides strategic consulting services to us for up to three days per month as well as services as a member of our Scientific Advisory Board.

On March 18, 2008, we sold an aggregate of 125,000 shares of our common stock to The Weg Family Limited Partnership at a price per share of $0.004, for an aggregate purchase price of $500. The price per share represented the exercise price of a warrant to purchase 125,000 shares of our common stock that had been held by The Weg Family Limited Partnership, but had expired unexercised in March 2007. Kenneth E. Weg, a member of our board of directors, is a member of the Weg Family LLC, which is the General Partner of the Weg Family Limited Partnership.

On July 1, 2008, we entered into a consultation and scientific advisory board agreement with Lynda Chin, an immediate family member of Ronald DePinho. Pursuant to the agreement, Dr. Chin provides scientific and business advice, as well as attends meetings of our scientific advisory board. The consultation and scientific advisory board agreement may be terminated by either party upon 30 days written notice. This agreement replaced a previous consulting agreement we had in place with Dr. Chin. From January 1, 2007 to February 1, 2010, Dr. Chin received $274,000 pursuant to her consulting arrangements with us.

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On March 18, 2009, we sold an aggregate of 7,500,000 shares of our series E convertible preferred stock at a price per share of $4.00 to Biogen Idec Inc., a holder of more than 5% of our voting securities upon the closing of such sale, for an aggregate purchase price of $30,000,000. Upon the closing of this offering, these shares will convert into shares of common stock. This sale and purchase was made in connection with the execution of our option and license agreement with Biogen Idec International GmbH, a subsidiary of Biogen Idec Inc., on March 18, 2009. Please see Business Strategic Partnerships and Business Strategic Partnerships Biogen Idec for information on our option and license agreement with Biogen Idec International GmbH.

On July 16, 2009, we sold an aggregate of 3,750,000 shares of our series E convertible preferred stock at a price per share of $4.00 to OSI, a holder of more than 5% of our voting securities upon the closing of such sale, for an aggregate purchase price of $15,000,000. Upon the closing of this offering, these shares will convert into shares of common stock. This sale and purchase was made in connection with the execution of our amended and restated collaboration and license agreement with OSI on July 16, 2009. Please see Business Strategic Partnerships and Business Strategic Partnerships OSI Pharmaceuticals for information on our amended and restated collaboration and license agreement with OSI.

Agreements With Our Stockholders

We have entered into an investor rights agreement with holders of our convertible preferred stock and warrants to purchase shares of our convertible preferred stock. The investor rights agreement contains a right of first refusal provision that provides that we shall not make certain issuances of our securities unless we first offer such securities to certain holders of preferred stock in accordance with the terms of the investor rights agreement. The right of first refusal provision of the investor rights agreement does not apply to and will terminate upon the closing of this offering. The investor rights agreement also provides that holders of preferred stock and warrants to purchase shares of our preferred stock have the right to (a) demand that we file a registration statement, subject to certain limitations, and (b) request that their shares be covered by a registration statement that we are otherwise filing. See Description of Capital Stock Registration Rights for a further discussion of these registration rights.

We have also entered into a right of first refusal and co-sale agreement with holders of convertible preferred stock and certain other stockholders. This agreement provides the holders of preferred stock a right of purchase and of co-sale in respect of sales of securities by certain holders of common stock. These rights of purchase and co-sale will terminate upon the closing of this offering.

We have also entered into a voting agreement with our equity holders that contains agreements with respect to the election of our board of directors and its composition. The voting agreement will terminate upon the closing of this offering.

Each of the transactions noted above were entered into prior to our adoption of a written related party transaction policy, which is described below.

Executive Compensation and Employment Arrangements

Please see Executive and Director Compensation for information on compensation arrangements with our executive officers, including option grants and agreements with executive officers.

Director Compensation

Please see Executive and Director Compensation for information on compensation arrangements for our directors generally and for information on consulting arrangements we have with Dr. DePinho and Dr. Kucherlapati. From January 1, 2007 to February 1, 2010, Dr. DePinho and Dr. Kucherlapati have received $300,000 and $77,000, respectively, under these consulting arrangements.

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Policies and Procedures for Related Person Transactions

Our board of directors has adopted written policies and procedures for the review of any transaction, arrangement or relationship in which we are a participant, the amount involved exceeds $120,000 and one of our executive officers, directors, director nominees or 5% stockholders (or their immediate family members), each of whom we refer to as a related person, has a direct or indirect material interest.

If a related person proposes to enter into such a transaction, arrangement or relationship, which we refer to as a related person transaction, the related person must report the proposed related person transaction to our Corporate Counsel. The policy calls for the proposed related person transaction to be reviewed and, if deemed appropriate, approved by the audit committee of our board of directors. Whenever practicable, the reporting, review and approval will occur prior to entry into the transaction. If advance review and approval is not practicable, the committee will review, and, in its discretion, may ratify the related person transaction. The policy also permits the chairman of the committee to review and, if deemed appropriate, approve proposed related person transactions that arise between committee meetings, subject to ratification by the committee at its next meeting. Any related person transactions that are ongoing in nature will be reviewed annually.

A related person transaction reviewed under the policy will be considered approved or ratified if it is authorized by the committee after full disclosure of the related person s interest in the transaction. As appropriate for the circumstances, the committee will review and consider:

- the related person s interest in the related person transaction;
- the approximate dollar value of the amount involved in the related person transaction;
- the approximate dollar value of the amount of the related person s interest in the transaction without regard to the amount of any profit or loss;
- whether the transaction was undertaken in the ordinary course of our business;
- whether the terms of the transaction are no less favorable to us than terms that could have been reached with an unaffiliated third party;
- the purpose of, and the potential benefits to us of, the transaction; and
- any other information regarding the related person transaction or the related person in the context of the proposed transaction that would be material to investors in light of the circumstances of the particular transaction.

The committee may approve or ratify the transaction only if the committee determines that, under all of the circumstances, the transaction is in or is not inconsistent with our best interests. The committee may impose any conditions on the related person transaction that it deems appropriate.

In addition to the transactions that are excluded by the instructions to the SEC s related person transaction disclosure rule, our board of directors has determined that the following transactions do not create a material direct or indirect interest on behalf of related persons and, therefore, are not related person transactions for purposes of this policy:

- interests arising solely from the related person s position as an executive officer of another entity (whether or not the person is also a director of such entity), that is a participant in the transaction, where (a) the related person and all other related persons own in the aggregate less than a 10% equity interest in such entity, (b) the related person and his or her immediate family members are not

involved in the negotiation of the terms of the transaction and do not receive any special benefits as a result of the transaction, (c) the amount involved in the transaction equals less than the greater of $200,000 or 5% of the annual consolidated gross revenues of the company receiving payment under the transaction; and

a transaction that is specifically contemplated by provisions of our charter or by-laws.

The policy provides that transactions involving compensation of executive officers shall be reviewed and approved by the compensation committee in the manner specified in its charter.

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PRINCIPAL STOCKHOLDERS

The following table sets forth information with respect to the beneficial ownership of our common stock as of February 1, 2010 by:

- each person, or group of affiliated persons, who is known by us to beneficially own more than 5% of our voting securities;
- each of our directors and named executive officers; and
- all of our directors and executive officers as a group.

The number of shares beneficially owned by each stockholder is determined under rules issued by the SEC. Under these rules, beneficial ownership includes any shares as to which the individual or entity has sole or shared voting power or investment power. In addition, these rules provide that shares of common stock subject to options or warrants that are currently exercisable or exercisable within 60 days of February 1, 2010 are considered outstanding and beneficially owned by the person holding the options or warrants for the purpose of calculating the percentage ownership of that person but not for the purpose of calculating the percentage ownership of any other person. Except as otherwise noted below, each of the stockholders listed has sole voting and investment power with respect to the shares beneficially owned by the stockholder, subject to community property laws where applicable.

The column entitled Percentage of Shares Beneficially Owned Before the Offering is based on a total of 20,644,831 shares of our common stock outstanding as of February 1, 2010, assuming conversion of all outstanding shares of our preferred stock into common stock upon the closing of this offering. The column entitled Percentage of Shares Beneficially Owned After the Offering is based on 29,644,831 shares of common stock to be outstanding after this offering, including the 9,000,000 shares that we are selling in this offering, but assumes no exercise of the underwriters over-allotment option. The percentage of common stock owned by each of the stockholders after this offering does not include any common stock that these stockholders may purchase in this offering.

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Except as otherwise set forth below, the address of the beneficial owner is c/o AVEO Pharmaceuticals, Inc., 75 Sidney Street, 4th Floor, Cambridge, Massachusetts 02139.

Name and Address of Beneficial Owner	Shares Beneficially Owned Prior to the Offering: Number of Shares Owned	+	Common Stock Underlying Options Exercisable Within 60 Days	=	Total Securities Beneficially Owned	Percentage of Shares Beneficially Owned: Before the Offering	After the Offering
Holders of more than 5% of our voting securities							
Biogen Idec Inc.[1]	2,877,700		0		2,877,700	13.9%	9.7%
Entities affiliated with MPM Capital[2]	2,208,961		7,500		2,216,461	10.7%	7.5%
Entities affiliated with Highland Capital Partners[3]	2,039,748		0		2,039,748	9.9%	6.9%
Entities affiliated with Venrock[4]	1,646,959		7,500		1,654,459	8.0%	5.6%
Entities affiliated with Prospect Venture Partners II, L.P.[5]	1,611,891		0		1,611,891	7.8%	5.4%
Merck & Co., Inc.[6]	1,583,333		0		1,583,333	7.7%	5.3%
OSI Pharmaceuticals, Inc.[7]	1,395,833		0		1,395,833	6.8%	4.7%
Directors and Named Executive Officers							
Kenneth M. Bate[8]	3,750		17,500		21,250	*	*
Douglas C. Cole[9]	869,474		7,500		876,974	4.2%	3.0%
Ronald A. DePinho[10]	592,524		20,208		612,732	3.0%	2.1%
Anthony B. Evnin[11]	1,646,959		7,500		1,654,459	8.0%	5.6%
Nicholas G. Galakatos[12]	2,208,961		7,500		2,216,461	10.7%	7.5%
Tuan Ha-Ngoc[13]	199,999		634,607		834,606	3.9%	2.8%
Russell Hirsch[14]	1,611,891		7,500		1,619,391	7.8%	5.5%
Raju Kucherlapati[15]	159,374		2,082		161,456	*	*
Kenneth E. Weg[16]	607,261		7,500		614,761	3.0%	2.1%
Robert C. Young[17]	2,250		4,250		6,500	*	*
Elan Ezickson[18]	12,500		178,905		191,405	*	*
Jeno Gyuris[19]	0		173,905		173,905	*	*
David Johnston[20]	0		109,634		109,634	*	*
William Slichenmyer	0		0		0	*	*
All current executive officers and directors as a group (14 persons)[21]	7,914,943		1,178,591		9,093,534	41.7%	29.5%

* Represents beneficial ownership of less than one percent of our outstanding common stock.

(1) Consists of 2,877,700 shares of common stock held by Biogen Idec Inc. issuable upon conversion of preferred stock. Biogen Idec Inc. is a publicly-traded corporation. Its address is 14 Cambridge Center, Cambridge, Massachusetts 02142.

(2) Consists of (a) 25,402 shares of common stock held by MPM Asset Management Investors 2002 BV2 LLC, or INV02, issuable upon conversion of preferred stock, (b) 525,732 shares of common stock held by MPM BioVentures GmbH & Co. Parallel-Beteiligungs KG, or BV2KG, issuable upon conversion of preferred stock, (c) 164,567 shares of common stock held by MPM BioVentures II, L.P., or BV2LP, issuable upon conversion of preferred stock, (d) 1,493,260 shares of common stock held by MPM BioVentures II-QP, L.P., or BV2QP, issuable upon conversion of preferred stock and (e) 7,500 shares of common stock issuable upon exercise of stock options held by Nicholas Galakatos. Dr. Galakatos, a member of our board of directors, is an investment manager of INV02 and may be deemed to have voting and investment power

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over shares held of record by INV02. MPM Asset Management II LLC is the sole general partner of MPM Asset Management II, L.P., which is the special limited partner of BV2KG and the sole general partner of BV2LP and BV2QP. Dr. Galakatos is an investment manager of MPM Asset Management II LLC, which has ultimate voting and investment power over shares held of record by BV2KG, BV2LP and BV2QP, and he may be deemed to have voting and investment power over shares held of record by BV2KG, BV2LP and BV2QP. Under the terms of the relevant operative agreements with MPM Capital, shares issuable upon exercise of the stock option held by Dr. Galakatos are held for the benefit of MPM Capital and may only be exercised at the direction of MPM Capital. Dr. Galakatos disclaims beneficial ownership over all such shares except to the extent of his pecuniary interest therein. The address of MPM Capital is 200 Clarendon Street, Boston, Massachusetts 02116.

(3) Consists of (a) 1,276,821 shares of common stock held by Highland Capital Partners VI Limited Partnership, or Highland Capital VI, issuable upon conversion of preferred stock, (b) 699,696 shares of common stock held by Highland Capital Partners VI-B Limited Partnership, or Highland Capital VI-B, issuable upon conversion of preferred stock and (c) 63,231 shares of common stock held by Highland Entrepreneurs Fund VI Limited Partnership, or Highland Entrepreneurs Fund, issuable upon conversion of preferred stock. Highland Management Partner VI Limited Partnership, or HMP, is the general partner of Highland Capital VI and Highland Capital VI-B. HEF VI Limited Partnership, or HEF, is the general partner of Highland Entrepreneurs Fund. Highland Management Partners VI, Inc., or Highland Management, is the general partner of both HMP and HEF. Voting and investment power over all shares held by record by Highland Capital VI, Highland Capital VI-B and Highland Entrepreneurs Fund is shared by Robert F. Higgins, Paul A. Maeder, Daniel J. Nove, Robert J. Davis, Sean M. Dalton, Corey M. Mulloy and Fergal J. Mullen, the managing directors of Highland Management. The address of Highland Capital Partners is 92 Hayden Avenue, Lexington, Massachusetts 02421.

(4) Consists of (a) 296,452 shares of common stock held by Venrock Associates issuable upon conversion of preferred stock, (b) 1,317,569 shares of common stock held by Venrock Associates III, L.P., or VA III, issuable upon conversion of preferred stock, (c) 32,938 shares of common stock held by Venrock Entrepreneurs Fund III, L.P., or VEF III, issuable upon conversion of preferred stock and (d) 7,500 shares of common stock issuable upon exercise of a stock option held by Anthony B. Evnin. Dr. Evnin is a General Partner of Venrock Associates, a New York limited partnership. Venrock Management III, LLC, or VM III, a Delaware limited liability company, is the sole General Partner of VA III. VEF Management III, LLC, or VEFM III, a Delaware limited liability company, is the sole General Partner of VEF III. Dr. Evnin is a Member of VM III and VEFM III. Dr. Evnin expressly disclaims beneficial ownership over all shares held by Venrock Associates, VA III, VEF III, VM III and VEFM III, except to the extent of his indirect pecuniary interest therein. VM III and VEFM III expressly disclaim beneficial ownership over all shares held by Venrock Associates, VA III and VEF III, except to the extent of their indirect pecuniary interest therein. The stock option held by Dr. Evnin, and shares of common stock issuable upon exercise of such stock option, are held for the sole and exclusive benefit of VR Management, LLC, a Delaware limited liability company and an affiliate of Venrock Associates, VA III, VEF III, VM III and VEFM III. Dr. Evnin expressly disclaims beneficial ownership over such stock option and all shares of common stock issuable thereunder. The address of Venrock is 530 Fifth Avenue, 22nd Floor, New York, New York 10036.

(5) Consists of (a) 1,587,714 shares of common stock held by Prospect Ventures Partners II, L.P., or PVP II, issuable upon conversion of preferred stock and (b) 24,177 shares of common stock held by Prospect Associates II, L.P., or PA II, issuable upon conversion of preferred stock. James B. Tananbaum, M.D., Alexander E. Barkas, Ph.D., David Schnell, M.D. and Russell C. Hirsch, M.D., Ph.D., the managing members of Prospect Management Company II, LLC, the respective General Partner of PVP II and PA II, share voting and investment power over the shares held by PVP II and PA II, but disclaim beneficial ownership, except to the extent of their pecuniary interest therein. The address of Prospect Venture Partners is 435 Tasso Street, Suite 200, Palo Alto, California 94301.

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(6) Consists of (a) 583,333 shares of common stock held by Merck Sharpe & Dohme Corp., a subsidiary of Merck & Co., Inc., issuable upon conversion of preferred stock and (b) 1,000,000 shares of common stock held by Schering Corporation, a subsidiary of Merck & Co., Inc., issuable upon conversion of preferred stock. Merck & Co., Inc. is a publicly-traded corporation. Its address is One Merck Drive, Whitehouse Station, NJ 08889.

(7) Consists of 1,395,833 shares of common stock held by OSI Pharmaceuticals, Inc. issuable upon conversion of preferred stock. OSI Pharmaceuticals, Inc. is a publicly-traded corporation. Its address is 14 Pinelawn Road, Melville, New York 11747.

(8) Consists of (a) 3,750 shares of common stock and (b) 17,500 shares of common stock issuable upon exercise of stock options.

(9) Consists of (a) 49,559 shares of common stock held by AGTC Advisors Fund, L.P., or AGTC, issuable upon conversion of preferred stock, (b) 819,915 shares of common stock held by Applied Genomic Technology Capital Fund, L.P., or AGTC Fund, issuable upon conversion of preferred stock and (c) 7,500 shares of common stock issuable upon exercise of stock options. NewcoGen Group, Inc., or NewcoGen Inc., is the general partner of AGTC Partners, L.P., which is the general partner of each of AGTC and AGTC Fund. NewcoGen Inc. is a wholly-owned subsidiary of Flagship Ventures Management, Inc. Flagship Ventures General Partner LLC is the general partner of Flagship Ventures Management, Inc. Noubar B. Afeyan Ph.D. and Edwin M. Kania, Jr. are the directors of Flagship Ventures Management, Inc. and the managers of Flagship Ventures General Partners LLC and may be deemed to have beneficial ownership with respect to all shares held by AGTC and AGTC Fund. Dr. Cole, a member of our board of directors, disclaims beneficial ownership over shares held by AGTC and AGTC Fund.

(10) Consists of (a) 250,012 shares of common stock, (b) 75,000 shares of common stock held by George D. Yancopoulos and his successors, as Trustee of The Ronald A. DePinho and Lynda Chin Family Trust, (c) 25,000 shares of common stock held by George Yancopoulos and his successors, as Trustee of The Ronald DePinho and Lynda Chin Family Trust, (d) 242,512 shares of common stock held by Dr. Chin, Dr. DePinho s wife, (e) 16,250 shares of common stock issuable upon exercise of stock options and (f) 3,958 shares of common stock issuable upon exercise of stock options held by Dr. Chin, Dr. DePinho s wife. George Yancopoulos is the trustee of the trusts described above and he exercises sole voting and investment power over the shares held of record by such trusts.

(11) Consists of (a) 1,646,959 shares of common stock held by entities affiliated with Venrock issuable upon conversion of preferred stock and (b) 7,500 shares of common stock issuable upon exercise of a stock option. Dr. Evnin, a member of our board of directors, is a General Partner of Venrock Associates, a New York limited partnership, and a Member of VM III and VEFM III. Dr. Evnin expressly disclaims beneficial ownership over all shares held by Venrock Associates, VA III, VEF III, VM III and VEFM III, except to the extent of his indirect pecuniary interest therein. The stock option held by Dr. Evnin, and shares of common stock issuable upon exercise of such stock option, are held for the sole and exclusive benefit of VR Management, LLC, a Delaware limited liability company and an affiliate of Venrock Associates, VA III, VEF III, VM III and VEFM III. Dr. Evnin expressly disclaims beneficial ownership over such stock option and all shares of common stock issuable thereunder.

(12) Consists of (a) 2,208,961 shares of common stock issuable upon conversion of preferred stock held by entities affiliated with MPM Capital and (b) 7,500 shares of common stock issuable upon exercise of stock options. Dr. Galakatos, a member of our board of directors, is an investment manager of INV02 and may be deemed to have voting and investment power over shares held of record by INV02. Dr. Galakatos is an investment manager of MPM Asset Management II LLC, which has ultimate voting and investment power over shares held of record by BV2KG, BV2LP and BV2QP, and he may be deemed to have voting and investment power over shares held of record by BV2KG, BV2LP and BV2QP. Under the terms of the relevant operative agreements with MPM Capital, shares issuable upon exercise of the stock option held by Dr. Galakatos are held for the benefit of MPM Capital and may only be exercised at the direction of MPM Capital. Dr. Galakatos disclaims beneficial ownership over all such shares except to the extent of his pecuniary interest therein.

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(13) Consists of (a) 199,999 shares of common stock held by Gabriel Schmergel, Trustee, or his successors in trust, of the Tuan Ha-Ngoc 2009 GRAT and (b) 634,607 shares of common stock issuable upon exercise of stock options. Gabriel Schmergel is the trustee of the trust described above and he exercises sole voting and investment over the shares held of record by such trust.

(14) Consists of (a) 1,587,714 and 24,177 shares of common stock held by PVP II and PA II, respectively, issuable upon conversion of preferred stock and (b) 7,500 shares of common stock issuable upon exercise of stock options. Dr. Hirsch is a Managing Director of Prospect Management Company II, LLC, the respective General Partner of PVP II and PA II. James B. Tananbaum, M.D., Alexander E. Barkas, Ph.D., David Schnell, M.D. and Dr. Hirsch, the managing members of Prospect Management Company II, LLC, the respective General Partner of PVP II and PA II, share voting and investment power over the shares held by PVP II and PA II, but disclaim beneficial ownership, except to the extent of their pecuniary interest therein.

(15) Consists of (a) 44,470 shares of common stock, (b) 19,053 shares of common stock held by Raju Kucherlapati as custodian for David Kucherlapati under the Massachusetts Uniform Transfers to Minors Act, (c) 42,078 shares of common stock held by Raju Kucherlapati c/f David Kucherlapati, (d) 3,773 shares of common stock held by Raju Kucherlapati Custodian FBO David Kucherlapati UTMA MA until age 21, (e) 50,000 shares of common stock held by Raju Kucherlapati Grantor Retained Annuity Trust No. 1 and (f) 2,082 shares of common stock issuable upon exercise of stock options. Dr. Kucherlapati, a member of our board of directors, is the trustee of the trusts described in this footnote and he exercises sole voting and investment power over the shares held of record by such trusts.

(16) Consists of (a) 41,492 shares of common stock issuable upon conversion of preferred stock, (b) 125,000 shares of common stock held by The Weg Family Limited Partnership, (c) 430,769 shares of common stock held by The Weg Family Limited Partnership issuable upon conversion of preferred stock, (d) 10,000 shares of common stock held by Clearview Venture Partners, LLC and (e) 7,500 shares of common stock issuable upon exercise of stock options. Mr. Weg, a member of our board of directors, is a member of The Weg Family Limited Partnership and may be deemed to have voting and investment power over shares held of record by it. Mr. Weg is also a founder and a member of the board of directors of Clearview Venture Partners, LLC and may be deemed to have voting and investment power over shares held of record by it. Mr. Weg disclaims beneficial ownership over shares held of record by The Weg Family Limited Partnership and Clearview Venture Partners, LLC except to the extent of his pecuniary interest therein.

(17) Consists of (a) 1,250 shares of common stock, (b) 4,250 shares of common stock issuable upon exercise of stock options and (c) 1,000 shares of common stock held by Ms. Young, Dr. Young s wife.

(18) Consists of (a) 12,500 shares of common stock and (b) 178,905 shares of common stock issuable upon exercise of stock options.

(19) Consists of 173,905 shares of common stock issuable upon exercise of stock options.

(20) Consists of 109,634 shares of common stock issuable upon exercise of stock options.

(21) Consists of and aggregate of (a) 7,914,943 shares of common stock and (b) 1,178,591 shares of common stock issuable upon exercise of stock options.

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DESCRIPTION OF CAPITAL STOCK

The following description of our capital stock and provisions of our certificate of incorporation and by-laws are summaries and are qualified by reference to the certificate of incorporation and the by-laws that will be in effect upon the closing of this offering. We have filed copies of these documents with the SEC as exhibits to our registration statement of which this prospectus forms a part. The description of the capital stock reflects changes to our capital structure that will occur upon the closing of this offering.

Upon the closing of this offering, our authorized capital stock will consist of 100,000,000 shares of common stock, par value $0.001 per share, and 5,000,000 shares of preferred stock, par value $0.001 per share, all of which preferred stock will be undesignated.

Upon the closing of this offering, all of the outstanding shares of our convertible preferred stock will convert into a total of 18,979,155 shares of our common stock. In addition, upon the closing of this offering and after giving effect to the conversion of our convertible preferred stock into common stock, warrants to purchase an aggregate of 182,200 shares of common stock will remain outstanding.

Common Stock

As of February 1, 2010, there were 20,644,831 shares of our common stock outstanding and held of record by 154 stockholders, assuming the conversion of all outstanding shares of our convertible preferred stock into shares of our common stock.

Holders of our common stock are entitled to one vote for each share held on all matters submitted to a vote of stockholders and do not have cumulative voting rights. An election of directors by our stockholders shall be determined by a plurality of the votes cast by the stockholders entitled to vote on the election. Holders of common stock are entitled to receive proportionately any dividends as may be declared by our board of directors, subject to any preferential dividend rights of any series of preferred stock that we may designate and issue in the future.

In the event of our liquidation or dissolution, the holders of common stock are entitled to receive proportionately our net assets available for distribution to stockholders after the payment of all debts and other liabilities and subject to the prior rights of any outstanding preferred stock. Holders of common stock have no preemptive, subscription, redemption or conversion rights. Our outstanding shares of common stock are, and the shares offered by us in this offering will be, when issued and paid for, validly issued, fully paid and nonassessable. The rights, preferences and privileges of holders of common stock are subject to and may be adversely affected by the rights of the holders of shares of any series of preferred stock that we may designate and issue in the future.

Preferred Stock

Under the terms of our certificate of incorporation that will become effective upon the closing of this offering, our board of directors is authorized to direct us to issue shares of preferred stock in one or more series without stockholder approval. Our board of directors has the discretion to determine the rights, preferences, privileges and restrictions, including voting rights, dividend rights, conversion rights, redemption privileges and liquidation preferences, of each series of preferred stock.

The purpose of authorizing our board of directors to issue preferred stock and determine its rights and preferences is to eliminate delays associated with a stockholder vote on specific issuances. The issuance of preferred stock, while providing flexibility in connection with possible acquisitions, future financings and other corporate purposes, could have the effect of making it more difficult for a third party to acquire, or could discourage a third party from seeking to acquire, a majority of our outstanding voting stock. Upon the closing of this offering, there will be no shares of preferred stock outstanding, and we have no present plans to issue any shares of preferred stock.

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Options

As of February 1, 2010, options to purchase 3,248,207 shares of common stock at a weighted average exercise price of $4.56 per share were outstanding.

Delaware Anti-Takeover Law and Certain Charter and By-law Provisions

Delaware Law

We are subject to Section 203 of the Delaware General Corporation Law. Subject to certain exceptions, Section 203 prevents a publicly held Delaware corporation from engaging in a business combination with any interested stockholder for three years following the date that the person became an interested stockholder, unless either the interested stockholder attained such status with the approval of our board of directors, the business combination is approved by our board of directors and stockholders in a prescribed manner or the interested stockholder acquired at least 85% of our outstanding voting stock in the transaction in which it became an interested stockholder. A business combination includes, among other things, a merger or consolidation involving us and the interested stockholder and the sale of more than 10% of our assets. In general, an interested stockholder is any entity or person beneficially owning 15% or more of our outstanding voting stock and any entity or person affiliated with or controlling or controlled by such entity or person. The restrictions contained in Section 203 are not applicable to any of our existing stockholders that will own 15% or more of our outstanding voting stock upon the closing of this offering.

Stockholder Action; Special Meeting of Stockholders; Advance Notice Requirements for Stockholder Proposals and Director Nominations

Our certificate of incorporation and our by-laws provide that any action required or permitted to be taken by our stockholders at an annual meeting or special meeting of stockholders may only be taken if it is properly brought before such meeting and may not be taken by written action in lieu of a meeting. Our certificate of incorporation and our by-laws also provide that, except as otherwise required by law, special meetings of the stockholders can only be called by the chairman of our board, our chief executive officer or our board of directors. In addition, our by-laws establish an advance notice procedure for stockholder proposals to be brought before an annual meeting of stockholders, including proposed nominations of candidates for election to the board of directors. Stockholders at an annual meeting may only consider proposals or nominations specified in the notice of meeting or brought before the meeting by or at the direction of the board of directors, or by a stockholder of record on the record date for the meeting, who is entitled to vote at the meeting and who has delivered timely written notice in proper form to our secretary of the stockholder s intention to bring such business before the meeting. These provisions could have the effect of delaying until the next stockholder meeting stockholder actions that are favored by the holders of a majority of our outstanding voting stock. These provisions also could discourage a third party from making a tender offer for our common stock, because even if it acquired a majority of our outstanding voting stock, it would be able to take action as a stockholder, such as electing new directors or approving a merger, only at a duly called stockholders meeting and not by written consent.

Super-Majority Voting

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

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Authorized But Unissued Shares

Authorized but unissued shares of common stock and preferred stock are available for future issuance without stockholder approval, subject to any limitations imposed by the listing standards of the NASDAQ Global Market. These additional shares may be used for a variety of corporate finance transactions, acquisitions and employee benefit plans. The existence of authorized but unissued and unreserved common stock and preferred stock could make more difficult or discourage an attempt to obtain control of us by means of a proxy contest, tender offer, merger or otherwise.

Registration Rights

Upon the closing of this offering, holders of an aggregate of 18,937,663 shares of our common stock and holders of warrants to purchase 25,000 shares of our common stock will have the right to require us to register these shares under the Securities Act under specified circumstances.

Demand and Form S-3 Registration Rights

Beginning twelve months after the closing of this offering, subject to specified limitations, these stockholders may require that we register all or part of these securities for sale under the Securities Act on two occasions. In addition, these stockholders may from time to time make demand for registrations on Form S-3, a short form registration statement, when we are eligible to use this form.

Incidental Registration Rights

If we register any of our common stock, either for our own account or for the account of other security holders, these stockholders are entitled to notice of the registration and to include their shares of common stock in the registration.

Limitations and Expenses

Other than in a demand registration, with specified exceptions, a holder s right to include shares in a registration is subject to the right of the underwriters to limit the number of shares included in the offering. All fees, costs and expenses of any demand registrations and any registrations on Form S-3 will be paid by us, and all selling expenses, including underwriting discounts and commissions, will be paid by the holders of the securities being registered.

Transfer Agent and Registrar

The transfer agent and registrar for our common stock is Computershare Trust Company, N.A.

NASDAQ Global Market

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

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SHARES ELIGIBLE FOR FUTURE SALE

Sales of substantial amounts of our common stock in the public market, or the perception that such sales may occur, could adversely affect the market price of our common stock. Although our common stock has been approved for listing on the NASDAQ Global Market, we cannot assure you that there will be an active public market for our common stock.

Prior to this offering, there was no public market for our common stock. Upon the closing of this offering, we will have outstanding an aggregate of 29,644,831 shares of our common stock, after giving effect to the issuance of 9,000,000 shares of common stock offered by us in this offering and assuming no exercise of options or warrants after February 1, 2010. Of these shares, all shares sold in this offering will be freely tradable without restriction or further registration under the Securities Act, except for any shares purchased by our affiliates, as that term is defined in Rule 144 under the Securities Act, whose sales would be subject to the Rule 144 resale restrictions described below, other than the holding period requirement.

The remaining 20,644,831 shares of our common stock held by existing investors will be restricted securities, as that term is defined in Rule 144 under the Securities Act. These restricted securities are eligible for public sale only if they are registered under the Securities Act or if they qualify for an exemption from registration under Rules 144 or 701 under the Securities Act, which are summarized below.

Subject to the lock-up agreements with the underwriters described below and the provisions of Rules 144 and 701 under the Securities Act, these restricted securities will be available for sale in the public market as follows:

Date	Number of Shares
On the date of this prospectus	16,250
90 days after the date of this prospectus	88,934
At various times beginning 180 days after the date of this prospectus	20,539,647

In addition, of the 3,248,207 shares of our common stock that were subject to stock options outstanding as of February 1, 2010, options to purchase 2,289,198 shares of common stock were vested as of February 1, 2010. Upon the closing of this offering, we will have outstanding warrants to purchase an aggregate of 182,200 shares of our common stock at a weighted average exercise price of $9.52 per share. Shares received upon exercise of these options or warrants will be eligible for sale subject to the lock up agreements described below and Rules 144 and 701 under the Securities Act. In addition, an aggregate of 2,125,000 additional shares of common stock will be available under our 2010 stock incentive plan and 2010 employee stock purchase plan upon the closing of this offering. We plan to register these shares on Form S-8, as described in more detail below under Equity Plans.

Lock-Up Agreements

We and each of our directors and executive officers and holders of substantially all of our outstanding capital stock, who collectively own 20,539,647 shares of our common stock based on shares outstanding as of February 1, 2010, have agreed, subject to certain exceptions, not to directly or indirectly sell or dispose of any shares of our common stock or any securities convertible into or exchangeable or exercisable for shares of our common stock for a period of 180 days after the date of this prospectus, and in specific circumstances, up to an additional 34 days, without the prior written consent of J.P. Morgan Securities Inc. and Morgan Stanley & Co. Incorporated. For additional information, see the section of this prospectus entitled Underwriting. Upon the expiration of the applicable lock-up periods, substantially all of the shares subject to such lock-up restrictions will become eligible for sale, subject to the limitations discussed above.

In addition, certain of our stockholders are subject to restrictions in their respective option agreements and restricted stock agreements whereby they have agreed not to sell, make short sale of, loan, grant any options for the purpose of, or otherwise dispose of any shares of our common stock without our prior written consent or that of the underwriters managing the offering for a period of 180 days from the effective date of the registration statement, and to execute any agreement reflecting these provisions as may be requested by us or the managing underwriters at the time of the offering. Certain of our stockholders are also subject to restrictions in an investor rights agreement whereby they have agreed not to sell or otherwise transfer or dispose of any of our securities for a period of 180 days following the offering.

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Rule 144

In general, under Rule 144, beginning 90 days after the date of this prospectus, a person who is not our affiliate and has not been our affiliate at any time during the preceding three months will be entitled to sell any shares of our common stock that such person has beneficially owned for at least six months, including the holding period of any prior owner other than one of our affiliates, without regard to volume limitations. Sales of our common stock by any such person would be subject to the availability of current public information about us if the shares to be sold were beneficially owned by such person for less than a year. But sales of our common stock by any such person would not be subject to the manner of sale, volume limitation or notice filing provisions of Rule 144 at any time.

Beginning 90 days after the date of this prospectus, a person who is an affiliate of ours, or who was an affiliate at any time during the preceding three months, and who has beneficially owned shares of our common stock for at least six months, including the holding period of any prior owner other than one of our affiliates, would be entitled to sell within any three-month period a number of shares that does not exceed the greater of:

- 1% of the number of shares of our common stock then outstanding, which will equal approximately shares immediately after this offering; or
- the average weekly trading volume in our common stock on the NASDAQ Global Market during the four calendar weeks preceding the filing of a Notice of Proposed Sale of Securities Pursuant to Rule 144 with respect to such sale.

Sales under Rule 144 by our affiliates are also subject to manner of sale provisions and notice requirements and to the availability of current public information about us.

Rule 701

In general, subject to the lock-up agreements summarized above, under Rule 701 of the Securities Act, any of our employees, directors, officers, consultants or advisors who purchased shares from us in connection with a qualified compensatory stock plan or other written agreement is entitled to sell such shares 90 days after the date of this prospectus in compliance with the manner of sale provisions in Rule 144, but without compliance with the other restrictions, including the availability of public information about us, holding period and volume limitations, contained in Rule 144.

The SEC has indicated that Rule 701 will apply to typical stock options granted by us before the date of this prospectus, along with the shares acquired upon exercise of such options, including exercises after the date of this prospectus.

Equity Plans

We intend to file one or more registration statements on Form S-8 under the Securities Act to register all shares of common stock subject to outstanding stock options and common stock issuable under our 2002 stock plan, 2010 stock plan and 2010 ESPP. We expect to file the registration statement covering shares offered pursuant to our stock plans shortly after the date of this prospectus, permitting the resale of such shares by nonaffiliates in the public market without restriction under the Securities Act and the sale by affiliates in the public market, subject to compliance with the resale provisions of Rule 144.

Registration Rights

Upon the closing of this offering, the holders of 18,937,663 shares of our common stock and holders of warrants to purchase 25,000 shares of our common stock will be entitled to various rights with respect to the registration of these shares under the Securities Act. Registration of these shares under the Securities Act would result in these shares becoming fully tradable without restrictions under the Securities Act immediately upon the effectiveness of registration, except for shares purchased by affiliates. For a detailed description of these registration rights, see Description of Capital Stock Registration Rights .

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

The following is a general discussion of material U.S. federal income and estate tax considerations relating to ownership and disposition of our common stock by a non-U.S. holder. For purposes of this discussion, the term non-U.S. holder means a beneficial owner of our common stock that is not, for U.S. federal income tax purposes:

- an individual who is a citizen or resident of the United States;
- a corporation, or other entity treated as a corporation for U.S. federal income tax purposes, created or organized in or under the laws of the United States or of any political subdivision of the United States;
- an estate the income of which is subject to U.S. federal income taxation regardless of its source; or
- a trust, if a U.S. court is able to exercise primary supervision over the administration of the trust and one or more U.S. persons have authority to control all substantial decisions of the trust or if the trust has a valid election to be treated as a U.S. person under applicable U.S. Treasury regulations.

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

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

- insurance companies;
- tax-exempt organizations;
- financial institutions;
- brokers or dealers in securities;
- regulated investment companies;
- pension plans;

controlled foreign corporations;

passive foreign investment companies;

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

certain U.S. expatriates.

In addition, this discussion does not address the tax treatment of partnerships, other entities or arrangements treated as partnerships or other entities which are transparent for U.S. federal income tax purposes. Partnerships, other entities or arrangements treated as partnerships, or other transparent entities that will hold our common stock, and owners of interests in any such entities or arrangements, should consult their own tax advisors regarding the tax consequences of the ownership and disposition of our common stock through a partnership or other transparent entity, as applicable.

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

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Dividends

As discussed under the Dividend Policy section of this prospectus, we do not currently expect to pay dividends. In the event that we pay distributions on our common stock, those distributions generally will constitute dividends for U.S. federal income tax purposes to the extent paid from our current or accumulated earnings and profits, as determined under U.S. federal income tax principles. If a distribution exceeds our current and accumulated earnings and profits, the excess will be treated as a tax-free return of the non-U.S. holder s investment, up to such holder s tax basis in the common stock. Any remaining excess will be treated as capital gain, subject to the tax treatment described below under the heading Gain on Disposition of Common Stock.

Dividends paid to a non-U.S. holder generally will be subject to withholding of U.S. federal income tax at a 30% rate or such lower rate as may be specified by an applicable income tax treaty between the United States and such holder s country of residence. If we determine, at a time reasonably close to the date of payment of a distribution on our common stock, that the distribution will not constitute a dividend because we do not anticipate having current or accumulated earnings and profits, we intend not to withhold any U.S. federal income tax on the distribution as permitted by U.S. Treasury Regulations.

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

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

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

Gain on Disposition of Common Stock

A non-U.S. holder generally will not be subject to U.S. federal income tax on gain recognized on a disposition of our common stock unless:

- the gain is effectively connected with the non-U.S. holder s conduct of a trade or business in the United States, and, if an applicable income tax treaty so requires, the gain is attributable to a permanent establishment maintained by the non-U.S. holder in the United States; in these cases, the non-U.S. holder will be taxed on a net income basis at the regular graduated rates and in the manner applicable to U.S. persons, and, if the non-U.S. holder is a foreign corporation, an additional branch profits tax at a rate of 30%, or a lower rate as may be specified by an applicable income tax treaty, may apply;

- the non-U.S. holder is an individual present in the United States for 183 days or more in the taxable year of the disposition and certain other requirements are met, in which case the non-U.S. holder will be subject to a 30% tax, or such lower rate as may be specified by an applicable income tax treaty, on the net gain derived from the disposition; or

- we are or have been a U.S. real property holding corporation as defined in the Code during the shorter of the five-year period ending on the date of disposition or your holding period of our common stock, provided however that if, on the date of disposition, our common stock is regularly traded on an

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established securities market, within the meaning of Section 897(c)(3) of the Code, these rules will apply only if you actually or constructively hold more than five percent of such regularly traded common stock at any time during the applicable period that is specified in the Code. Generally, a corporation is a U.S. real property holding corporation if the fair market value of its U.S. real property interests equals or exceeds 50% of the sum of the fair market value of its worldwide real property interests plus its other assets used or held for use in a trade or business. We believe that we are not currently, and we do not anticipate becoming, a U.S. real property holding corporation for U.S. federal income tax purposes.

Information Reporting and Backup Withholding Tax

We must report annually to the IRS and to each non-U.S. holder the gross amount of the distributions on our common stock paid to such holder and the tax withheld, if any, with respect to such distributions. Non-U.S. holders may have to comply with specific certification procedures to establish that the holder is not a U.S. person (as defined in the Code) in order to avoid backup withholding at the applicable rate, currently 28%, with respect to dividends on our common stock. Generally, a holder will comply with such procedures if it provides a properly executed, applicable IRS Form W-8 or otherwise meets documentary evidence requirements for establishing that it is a non-U.S. holder, or otherwise establishes an exemption.

Information reporting and backup withholding generally will apply to the proceeds of a disposition of our common stock by a non-U.S. holder effected by or through the U.S. office of any broker, U.S. or foreign, unless the holder certifies its status as a non-U.S. holder and satisfies certain other requirements, or otherwise establishes an exemption. Generally, information reporting and backup withholding will not apply to a payment of disposition proceeds to a non-U.S. holder where the transaction is effected outside the United States through a non-U.S. office of a broker. However, for information reporting purposes, dispositions effected through a non-U.S. office of a broker with substantial U.S. ownership or operations generally will be treated in a manner similar to dispositions effected through a U.S. office of a broker. Non-U.S. holders should consult their own tax advisors regarding the application of the information reporting and backup withholding rules to them.

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

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

Federal Estate Tax

Common stock owned or treated as owned by an individual who is a non-U.S. holder (as specially defined for U.S. federal estate tax purposes) at the time of death will be included in the individual s gross estate for U.S. federal estate tax purposes and, therefore, may be subject to U.S. federal estate tax, unless an applicable estate tax or other treaty provides otherwise.

The preceding discussion of material U.S. federal tax considerations is for general information only. It is not tax advice. Prospective investors should consult their own tax advisors regarding the particular U.S. federal, state, local and non-U.S. tax consequences of purchasing, holding and disposing of our common stock, including the consequences of any proposed changes in applicable laws.

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UNDERWRITING

We are offering the shares of common stock described in this prospectus through a number of underwriters. J.P. Morgan Securities Inc. and Morgan Stanley & Co. Incorporated are acting as joint book-running managers of the offering and as representatives of the underwriters. We have entered into an underwriting agreement with the underwriters. Subject to the terms and conditions of the underwriting agreement, we have agreed to sell to the underwriters, and each underwriter has severally agreed to purchase, at the public offering price less the underwriting discounts and commissions set forth on the cover page of this prospectus, the number of shares of common stock listed next to its name in the following table:

Name	Number of Shares
J.P. Morgan Securities Inc.	3,825,000
Morgan Stanley & Co. Incorporated	3,375,000
Leerink Swann LLC	1,350,000
Canaccord Adams Inc.	450,000
Total	9,000,000

The underwriters are committed to purchase all the shares of common stock offered by us if they purchase any shares. The underwriting agreement also provides that if an underwriter defaults, the purchase commitments of non-defaulting underwriters may also be increased or the offering may be terminated.

The underwriters propose to offer the shares of common stock directly to the public at the public offering price set forth on the cover page of this prospectus and to certain dealers at that price less a concession not in excess of $0.378 per share. After the initial public offering of the shares, the offering price and other selling terms may be changed by the underwriters. Sales of shares made outside of the United States may be made by affiliates of the underwriters. The representatives have advised us that the underwriters do not intend to confirm discretionary sales in excess of 5% of the shares of common stock offered in this offering.

The underwriters have an option to purchase up to 1,350,000 additional shares of common stock from us to cover sales of shares by the underwriters which exceed the number of shares specified in the table above. The underwriters have 30 days from the date of this prospectus to exercise this over-allotment option. If any shares are purchased with this over-allotment option, the underwriters will purchase shares in approximately the same proportion as shown in the table above. If any additional shares of common stock are purchased, the underwriters will offer the additional shares on the same terms as those on which the shares are being offered.

The underwriting discounts and commissions are equal to the public offering price per share of common stock less the amount paid by the underwriters to us per share of common stock. The underwriting discounts and commissions are $0.63 per share. The following table shows the per share and total underwriting discounts and commissions payable by us to the underwriters assuming both no exercise and full exercise of the underwriters option to purchase additional shares.

	Without Over-Allotment Exercise	With Full Over-Allotment Exercise
Per Share	$ 0.63	$ 0.63
Total	$ 5,670,000	$ 6,520,500

We estimate that the total expenses of this offering, including registration, filing and listing fees, printing fees and legal and accounting expenses, but excluding the underwriting discounts and commissions, will be approximately $2.75 million, all of which is payable by us.

A prospectus in electronic format may be made available on the web sites maintained by one or more underwriters, or selling group members, if any, participating in the offering. The underwriters may agree to

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allocate a number of shares to underwriters and selling group members for sale to their online brokerage account holders. Internet distributions will be allocated by the representatives to underwriters and selling group members that may make Internet distributions on the same basis as other allocations.

We have agreed that we will not, subject to limited exceptions, (i) offer, pledge, sell, contract to sell, sell any option or contract to purchase, purchase any option or contract to sell, grant any option, right or warrant to purchase or otherwise transfer or dispose of, directly or indirectly, or file with the SEC a registration statement under the Securities Act relating to, any shares of our common stock or securities convertible into or exchangeable or exercisable for any shares of our common stock, or publicly disclose the intention to make any offer, sale, pledge, disposition or filing, or (ii) enter into any swap or other arrangement that transfers all or a portion of the economic consequences associated with the ownership of any shares of common stock or any such other securities (regardless of whether any of these transactions are to be settled by the delivery of shares of common stock or such other securities, in cash or otherwise), in each case without the prior written consent of J.P. Morgan Securities Inc. and Morgan Stanley & Co. Incorporated for a period of 180 days after the date of this prospectus. Notwithstanding the foregoing, if (1) during the last 17 days of the 180-day restricted period, we issue an earnings release or material news or a material event relating to our company occurs; or (2) prior to the expiration of the 180-day restricted period, we announce that we will release earnings results during the 16-day period beginning on the last day of the 180-day period, the restrictions described above shall continue to apply until the expiration of the 18-day period beginning on the issuance of the earnings release or the occurrence of the material news or material event.

Our directors and executive officers and substantially all of our equity holders have entered into lock-up agreements with the underwriters prior to the commencement of this offering pursuant to which each of these persons or entities, with limited exceptions, for a period commencing on the date of the lock-up agreement and ending 180 days after the date of this prospectus, may not, without the prior written consent of J.P. Morgan Securities Inc. and Morgan Stanley & Co. Incorporated, (1) offer, pledge, sell, contract to sell, sell any option or contract to purchase, purchase any option or contract to sell, grant any option, right or warrant to purchase, or otherwise transfer or dispose of, directly or indirectly, any shares of our common stock or any securities convertible into or exercisable or exchangeable for shares of our common stock (including, without limitation, common stock or such other securities which may be deemed to be beneficially owned by such directors, executive officers, managers and members in accordance with the rules and regulations of the SEC and securities which may be issued upon exercise of a stock option or warrant), or publicly disclose the intention to make any offer, sale, pledge, disposition or filing, or (2) enter into any swap or other agreement that transfers, in whole or in part, any of the economic consequences of ownership of the common stock or such other securities, whether any such transaction described in clause (1) or (2) above is to be settled by delivery of common stock or such other securities, in cash or otherwise, or (3) make any demand for or exercise any right with respect to the registration of any shares of our common stock or any security convertible into or exercisable or exchangeable for our common stock. Notwithstanding the foregoing, if (1) during the last 17 days of the 180-day restricted period, we issue an earnings release or material news or a material event relating to our company occurs; or (2) prior to the expiration of the 180-day restricted period, we announce that we will release earnings results during the 16-day period beginning on the last day of the 180-day period, the restrictions described above shall continue to apply until the expiration of the 18-day period beginning on the issuance of the earnings release or the occurrence of the material news or material event.

We have agreed to indemnify the underwriters against certain liabilities, including liabilities under the Securities Act.

In connection with this offering, the underwriters may engage in stabilizing transactions, which involves making bids for, or purchasing and selling shares of, common stock in the open market for the purpose of preventing or retarding a decline in the market price of the common stock while this offering is in progress. These stabilizing transactions may include making short sales of the common stock, which involves the sale by the underwriters of a greater number of shares of common stock than they are required to purchase in this offering, and purchasing shares of common stock on the open market to cover positions created by short sales. Short sales may be covered shorts, which are short positions in an amount not greater than the underwriters

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over-allotment option referred to above, or may be naked shorts, which are short positions in excess of that amount. The underwriters may close out any covered short position either by exercising their over-allotment option, in whole or in part, or by purchasing shares in the open market. In making this determination, the underwriters will consider, among other things, the price of shares available for purchase in the open market compared to the price at which the underwriters may purchase shares through the over-allotment option. A naked short position is more likely to be created if the underwriters are concerned that there may be downward pressure on the price of the common stock in the open market that could adversely affect investors who purchase in this offering. To the extent that the underwriters create a naked short position, they will purchase shares in the open market to cover the position.

The underwriters have advised us that, pursuant to Regulation M of the Securities Act, they may also engage in other activities that stabilize, maintain or otherwise affect the price of the common stock, including the imposition of penalty bids. This means that if the representatives of the underwriters purchase common stock in the open market in stabilizing transactions or to cover short sales, the representatives can require the underwriters that sold those shares as part of this offering to repay the underwriting discount received by them.

These activities may have the effect of raising or maintaining the market price of the common stock or preventing or retarding a decline in the market price of the common stock, and, as a result, the price of the common stock may be higher than the price that otherwise might exist in the open market. If the underwriters commence these activities, they may discontinue them at any time. The underwriters may carry out these transactions on the NASDAQ Global Market, in the over-the-counter market or otherwise.

Other than in the United States, no action has been taken by us or the underwriters that would permit a public offering of the shares of common stock offered by this prospectus in any jurisdiction where action for that purpose is required. The shares of common stock offered by this prospectus may not be offered or sold, directly or indirectly, nor may this prospectus or any other offering material or advertisements in connection with the offer and sale of any such shares of common stock be distributed or published in any jurisdiction, except under circumstances that will result in compliance with the applicable rules and regulations of that jurisdiction. Persons into whose possession this prospectus comes are advised to inform themselves about and to observe any restrictions relating to the offering and the distribution of this prospectus. This prospectus does not constitute an offer to sell or a solicitation of an offer to buy any shares of common stock offered by this prospectus in any jurisdiction in which such an offer or a solicitation is unlawful.

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