

AVEO PHARMACEUTICALS INC

Form S-1

November 10, 2010

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As filed with the Securities and Exchange Commission on November 10, 2010

Registration No. 333-

**UNITED STATES**  
**SECURITIES AND EXCHANGE COMMISSION**

Washington, D.C. 20549

**FORM S-1**  
**REGISTRATION STATEMENT**

*UNDER*

*THE SECURITIES ACT OF 1933*

**AVEO PHARMACEUTICALS, INC.**

(Exact name of registrant as specified in its charter)

**Delaware**  
(State or other jurisdiction of

**2834**  
(Primary Standard Industrial

**04-3581650**  
(I.R.S. Employer

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incorporation or organization)

Classification Code Number)

Identification Number)

75 Sidney Street

Cambridge, Massachusetts 02139

(617) 299-5000

(Address, including zip code, and telephone number, including area code, of registrant's principal executive offices)

Tuan Ha-Ngoc

Chief Executive Officer

AVEO Pharmaceuticals, Inc.

75 Sidney Street

Cambridge, Massachusetts 02139

(617) 299-5000

(Name, address, including zip code, and telephone number, including area code, of agent for service)

*Copies to:*

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Approximate date of commencement of proposed sale to the public: From time to time after the effective date of this Registration Statement.

If any of the securities being registered on this Form are to be offered on a delayed or continuous basis pursuant to Rule 415 under the Securities Act of 1933, as amended (the "Securities Act"), check the following box.

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If this Form is filed to register additional securities for an offering pursuant to Rule 462(b) under the Securities Act, check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering.    "

If this Form is a post-effective amendment filed pursuant to Rule 462(c) under the Securities Act, check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering.    "

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If this Form is a post-effective amendment filed pursuant to Rule 462(d) under the Securities Act, check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering. ..

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer, or a smaller reporting company. See definitions of large accelerated filer, accelerated filer and smaller reporting company in Rule 12b-2 of the Exchange Act. (Check one):

Large accelerated filer .. Accelerated filer ..  
 Non-accelerated filer x (Do not check if a smaller reporting company) Smaller reporting company ..

**CALCULATION OF REGISTRATION FEE**

| <b>Title of Each Class of Securities to be Registered</b> | <b>Amount to be Registered(1)</b> | <b>Proposed Maximum Aggregate Offering Price per Share(2)</b> | <b>Proposed Maximum Aggregate Offering Price(2)</b> | <b>Amount of Registration Fee</b> |
|---|-----------------------------------|---|---|-----------------------------------|
| Common Stock, \$0.001 par value per share                 | 4,500,000                         | \$15.84   | \$71,280,000  | \$5,083                           |

- (1) Represents shares offered by the selling stockholders. Includes (i) 4.5 million shares held by the selling stockholders and (ii) an indeterminable number of additional shares of common stock, pursuant to Rule 416 under the Securities Act of 1933, as amended, that may be issued to prevent dilution from stock splits, stock dividends or similar transactions that could affect the shares to be offered by selling stockholders.
- (2) Estimated solely for the purpose of calculating the registration fee pursuant to Rule 457(c) under the Securities Act of 1933, as amended. The price per share and aggregate offering price are based on the average of the high and low prices of the registrant's common stock on November 3, 2010, as quoted on the Nasdaq Global Market.

**THE REGISTRANT HEREBY AMENDS THIS REGISTRATION STATEMENT ON SUCH DATE OR DATES AS MAY BE NECESSARY TO DELAY ITS EFFECTIVE DATE UNTIL THE REGISTRANT SHALL FILE A FURTHER AMENDMENT WHICH SPECIFICALLY STATES THAT THIS REGISTRATION STATEMENT SHALL THEREAFTER BECOME EFFECTIVE IN ACCORDANCE WITH SECTION 8(A) OF THE SECURITIES ACT OF 1933 OR UNTIL THE REGISTRATION STATEMENT SHALL BECOME EFFECTIVE ON SUCH DATE AS THE SECURITIES AND EXCHANGE COMMISSION, ACTING PURSUANT TO SAID SECTION 8(A), MAY DETERMINE.**



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**The information in this prospectus is not complete and may be changed. The selling stockholders named in this prospectus may not sell these securities until the registration statement filed with the Securities and Exchange Commission is effective. This prospectus is not an offer to sell these securities and the selling stockholders named in this prospectus are not soliciting offers to buy these securities in any jurisdiction where the offer or sale is not permitted.**

*PROSPECTUS (Subject to Completion)*

Issued November 10, 2010

**4,500,000 Shares**

**COMMON STOCK**

This prospectus relates to the resale of 4,500,000 shares of common stock previously issued by AVEO Pharmaceuticals, Inc. to certain accredited investors in connection with a private placement completed on November 3, 2010.

The selling stockholders identified in this prospectus, or their pledgees, donees, transferees or other successors-in-interest, may offer the shares from time to time through public or private transactions at prevailing market prices, at prices related to prevailing market prices or at privately negotiated prices. For additional information on the methods of sale that may be used by the selling stockholders, see the section entitled **Plan of Distribution** on page 38. For a list of the selling stockholders, see the section entitled **Selling Stockholders** on page 35.

We will not receive any of the proceeds from the sale of these shares by the selling stockholders.

We may amend or supplement this prospectus from time to time by filing amendments or supplements as required. You should read the entire prospectus and any amendments or supplements carefully before you make your investment decision.

Our common stock is traded on the NASDAQ Global Market under the symbol **AVEO**. On November 9, 2010, the closing sale price of our common stock on the NASDAQ Global Market was \$16.45 per share. You are urged to obtain current market quotations for the common stock.

*Investing in our common stock involves risks. See **Risk Factors** beginning on page 7.*

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 date of this prospectus is \_\_\_\_\_, 2010.

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**You should rely only on the information contained in this prospectus and in any amendments or supplements we may make to this prospectus. 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. If it is against the law in any jurisdiction to make an offer to sell these shares, or to solicit an offer from someone to buy these shares, then this prospectus does not apply to any person in that jurisdiction, and no offer or solicitation is made by this prospectus to any such person. 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.**

**As used herein, the term prospectus shall mean and include any amendments or supplements we may make to this prospectus from time to time except where the context provides otherwise.**



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**Table of Contents****PROSPECTUS SUMMARY**

*This summary highlights information contained elsewhere in this prospectus. This summary does not contain all of the information you should consider before investing in our common stock. You should read this entire prospectus carefully, especially the Risk Factors section beginning on page 7 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 phase 2 clinical 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 August 2010, we completed enrollment of our 517-patient phase 3 clinical trial of tivozanib in patients with advanced RCC, which we refer to as the TIVO-1 study. 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.

In addition to the TIVO-1 study, 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 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.

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 recently initiated a phase 2 clinical trial for non-small cell lung cancer. In 2007, we entered into an agreement with Merck & Co., Inc. (formerly Schering-Plough Corporation), or Merck, under which we granted Merck exclusive worldwide rights to co-develop and commercialize AV-299 and under which Merck funded all development and manufacturing expenses, subject to an agreed-upon budget. On September 28, 2010, we received notice from Merck of termination of the collaboration agreement effective as of December 27, 2010, at which point we will be responsible for funding all future development, manufacturing and commercialization costs for the AV-299 program.



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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 into 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.

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.

We have entered into an 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 have also entered into strategic partnerships with OSI Pharmaceuticals, Inc. (a wholly-owned subsidiary of Astellas US Holding Inc., a holding company owned by Astellas Pharma Inc.), or OSI and Merck where we have utilized, or granted rights to certain elements of, our Human Response Platform in the research and development of novel targets and 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 7. 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.



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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 September 30, 2010, we had an accumulated deficit of \$226.2 million. We anticipate that our operating losses will increase over the next several years.

We will need to raise substantial additional funds as we seek 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 and Biogen Idec. 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 decline and the development and commercialization of our product candidates would be interrupted. In addition, if OSI 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](http://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 AVEO 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 by the selling stockholders | 4.5 million shares   |
| Use of proceeds                                  | We will not receive any proceeds from the sale of the shares in this offering. For more information, see <a href="#">Use of Proceeds</a> on page 34.   |
| Risk factors                                     | You should read the <a href="#">Risk Factors</a> section of this prospectus beginning on page 7 for a discussion of factors to consider carefully before deciding to invest in shares of our common stock. |
| NASDAQ Global Market symbol                      | AVEO   |

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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. We derived the summary statements of operations data for the nine months ended September 30, 2009 and 2010 and the balance sheet data as of September 30, 2010 from our unaudited 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.

|  | 2007                                  | Years Ended<br>December 31,<br>2008 | 2009        | Nine Months Ended<br>September 30,<br>2009 2010<br>(unaudited) |             |
|--|---------------------------------------|-------------------------------------|-------------|--|-------------|
|  | (in thousands, except per share data) |                                     |             |  |             |
| <b>Statement of operations data:</b>   |                                       |                                     |             |  |             |
| Revenue  | \$ 11,034                             | \$ 19,660                           | \$ 20,719   | \$ 14,683  | \$ 32,725   |
| <b>Operating expenses:</b>   |                                       |                                     |             |  |             |
| Research and development   | 29,248                                | 41,821                              | 51,792      | 38,326   | 68,867      |
| General and administrative   | 6,502                                 | 9,164                               | 10,120      | 7,504  | 10,199      |
| <b>Total operating expenses</b>  | 35,750                                | 50,985                              | 61,912      | 45,830   | 79,066      |
| <b>Loss from operations</b>  | (24,716)                              | (31,325)                            | (41,193)    | (31,147)   | (46,341)    |
| <b>Other income and expense:</b>   |                                       |                                     |             |  |             |
| Other income (expense), net  |                                       | 18                                  | (333)       | (273)  | 722         |
| Loss on loan extinguishment  |                                       | (248)                               |             |  | (582)       |
| Interest expense   | (2,437)                               | (2,086)                             | (2,811)     | (2,141)  | (2,361)     |
| Interest income  | 2,171                                 | 1,168                               | 144         | 121  | 87          |
| <b>Other income (expense), net</b>   | (266)                                 | (1,148)                             | (3,000)     | (2,293)  | (2,134)     |
| Net loss before taxes  | (24,982)                              | (32,473)                            | (44,193)    | (33,440)   | (48,475)    |
| <b>Tax benefit</b>   |                                       |                                     | 100         | 63   |             |
| <b>Net loss</b>  | \$ (24,982)                           | \$ (32,473)                         | \$ (44,093) | \$ (33,377)  | \$ (48,475) |
| <b>Net loss per share applicable to common stockholders-basic and diluted</b>                            | \$ (17.89)                            | \$ (21.08)                          | \$ (27.43)  | \$ (20.87)   | \$ (2.13)   |
| <b>Weighted average number of common shares used in net loss per share calculation-basic and diluted</b> | 1,396                                 | 1,541                               | 1,607       | 1,599  | 22,773      |

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|   | As of September 30,<br>2010<br>(unaudited, in thousands) |
|---|--|
| <b>Balance Sheet Data:</b>                                |  |
| Cash, cash equivalents, and marketable securities         | \$ 87,022  |
| Working capital   | 57,325   |
| Total assets  | 96,512   |
| Loans payable, including current portion, net of discount | 23,140   |
| Accumulated deficit                                       | (226,200)  |
| Total stockholders' equity                                | 23,411   |



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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 are currently conducting our phase 3 clinical trial for tivozanib as well as five phase 1 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, are in the preclinical research stage. The clinical and commercial success of tivozanib will depend on a number of factors, including the following:

completion of our phase 3 clinical trial and timely enrollment in, and completion of, our other on-going or planned clinical trials;

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 tivozanib;

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 tivozanib 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 price of our common stock 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 EMA, for the treatment of advanced RCC, as well as the treatment of hepatocellular carcinoma. Based on our discussions with the FDA and the EMA, we set the number of patients to be enrolled in the clinical trial at a number we expect will be 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 before we may successfully 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 EMA, 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 EMA 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 EMA 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 EMA 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.

***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.

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We have completed a phase 2 clinical trial of our lead product candidate, tivozanib, and are currently conducting 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, has entered a phase 2 clinical trial for non-small cell lung cancer. 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 preclinical studies and clinical trials currently in process or that we may initiate in the future. 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 any of our 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. 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. 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.

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We, the FDA, other 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 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.

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*Even if we receive regulatory approval for any of our product candidates, we will be subject to ongoing FDA requirements 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 jurisdictions or by the FDA. The foreign regulatory approval process may include all of the risks associated with obtaining FDA 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.

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**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.*

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 September 30, 2010, we had an accumulated deficit of \$226.2 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, and the continued clinical development of our phase 2 product candidate, AV-299, to which we recently regained rights from Merck.

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.

*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, preclinical and clinical development of our product candidates. In particular, we are currently conducting a phase 3 clinical trial of tivozanib and a phase 2 clinical trial of AV-299, which will require substantial funds to complete. We believe that we will continue to expend substantial resources for the foreseeable future developing tivozanib, AV-299 and other new and existing antibody product candidates. These expenditures will include costs associated with research and development, acquiring new 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 our existing cash and cash equivalents (including the proceeds received from our sale of common stock in November 2010), 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 first half 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;

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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, stockholders will be diluted, and the terms may include liquidation or other preferences that adversely affect stockholders' rights. 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 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 Pharmaceuticals 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 and 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 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.

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For a discussion of additional risks that we face with respect to our strategic partnership agreements, see [Item 1](#). 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 21.

### ***Fluctuations in our quarterly operating losses could adversely affect the price of our common stock.***

Our quarterly operating losses may fluctuate significantly. Some of the factors that may cause our operating losses to fluctuate on a period-to-period basis include:

the status of our preclinical and clinical development programs;

the level of expenses incurred in connection with our preclinical and clinical development programs;

any intellectual property infringement lawsuit in which we may become involved;

the implementation or termination of collaboration, licensing, manufacturing or other material agreements with third parties, and non-recurring revenue or expenses under any such agreement; and

compliance with regulatory requirements.

Period-to-period comparisons of our historical and future financial results may not be meaningful, and investors should not rely on them as an indication of future performance. Our fluctuating losses may fail to meet the expectations of securities analysts or investors. Our failure to meet these expectations may cause the price of our common stock to decline.

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

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 current adverse economic conditions 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 September 30, 2010, we had \$87.0 million of cash, cash equivalents and marketable securities consisting of money market funds, U.S. treasuries, U.S. government agency securities, corporate debt and commercial paper. 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. However, 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:

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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;

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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 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, Michael Bailey, our Chief Commercial Officer, and Jenő 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, Michael Bailey and Jenő 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.



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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.

### ***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;

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.

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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.

***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.

Where appropriate, we may elect in the future to utilize strategic partners or contract sales forces to assist in the commercialization of tivozanib, AV-299 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 the product candidate, as demonstrated in clinical trials;



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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;

with respect to tivozanib, the results obtained in our phase 3 clinical trial 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 over alternative treatments, including, with respect to tivozanib, advantages over Avastin, Nexavar, Sutent or Votrient;

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.

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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 any products we may develop or commercialize 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. Any products that we may develop or commercialize may not be considered cost-effective, and coverage and reimbursement may not be available or sufficient to allow us to sell our products on a profitable basis.

***Foreign 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 countries 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 could hinder or prevent our product candidates' commercial success.***

The U.S. government and other governments have shown significant interest in pursuing healthcare reform. Any government-adopted reform measures could adversely impact the pricing of healthcare products and services in the U.S. or internationally and the amount of reimbursement available from governmental agencies or other third party payors. The continuing efforts of the U.S. and foreign governments, insurance companies, managed care organizations and other payors of health care services to contain or reduce health care costs may adversely affect our ability to set prices which we believe are fair for any products we may develop and commercialize, and our ability to generate revenues and achieve and maintain profitability.

New laws, regulations and judicial decisions, or new interpretations of existing laws, regulations and decisions, that relate to healthcare availability, methods of delivery or payment for products and services, or sales, marketing or pricing, may limit our potential revenue, and we may need to revise our research and development programs. The pricing and reimbursement environment may change in the future and become more challenging due to several reasons, including policies advanced by the U.S. government, new healthcare legislation or fiscal challenges faced by government health administration authorities. Specifically, in both the U.S. and some foreign jurisdictions, there have been a number of legislative and regulatory proposals and initiatives to change the health care system in ways that could affect our ability to sell any products we may develop and commercialize profitably. Some of these proposed and implemented reforms could result in reduced reimbursement rates for our potential products, which would adversely affect our business strategy, operations and financial results. For example, in March 2010, President Obama signed into law a legislative overhaul of the U.S. healthcare system, known as the Patient Protection and Affordable Care Act of 2010, as amended by the Healthcare and Education Affordability Reconciliation Act of 2010, or the PPACA, which may have far reaching consequences for life science companies like us. As a result of this new legislation, substantial changes could be made to the current system for paying for healthcare in the United States, including changes made in order to extend medical benefits to those who currently lack insurance coverage. Extending coverage to a large population could substantially change the structure of the health insurance system and the methodology for reimbursing medical services, drugs and devices. These structural changes could entail modifications to the existing system of private payors and government programs, such as Medicare and Medicaid, creation of a government-sponsored healthcare insurance source, or some combination of both, as well as other changes. Restructuring the coverage of medical care in the United States could impact the reimbursement for prescribed drugs, biopharmaceuticals, medical devices, or our product candidates. If reimbursement for our approved product candidates, if any, is substantially less than we expect in the future, or rebate obligations associated with them are substantially increased, our business could be materially and adversely impacted.





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Further federal and state proposals and health care reforms could limit the prices that can be charged for the product candidates that we develop and may further limit our commercial opportunity. Our results of operations could be materially adversely affected by the PPACA, by Medicare prescription drug coverage legislation, by the possible effect of such current or future legislation on amounts that private insurers will pay and by other health care reforms that may be enacted or adopted in the future.

### **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 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.

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.

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.

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

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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 recently terminated its collaboration agreement with us related to AV-299 effective December 27, 2010, at which point we will assume responsibility for research and clinical development, manufacturing and future commercialization of AV-299. 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 enter into one or more transactions with third parties, including a merger, consolidation, reorganization, sale of a substantial amount of its assets, sale of a substantial amount of its 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 OSI Pharmaceuticals prior to it being acquired by Astellas Pharma, Inc. or Astellas. Although the effect of the acquisition of OSI on our strategic partnership is unknown, Astellas' management could determine to reduce the efforts and resources that it will apply to its strategic partnership with us. In addition, the third-party in such a transaction with our strategic partner 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 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 OSI Pharmaceuticals breaches or terminates its arrangement 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 partners 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 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.



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*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.

Multiple batches of drug substance were produced to support clinical trials of AV-299 through at least phase 2 clinical trials. As of December 27, 2010, the effective date of the termination of our collaboration with Merck, we will be responsible for manufacturing future batches of AV-299 for additional clinical trials or for commercial use. If we are unsuccessful in engaging a third party to manufacture AV-299 on terms acceptable to us, future clinical trials and any commercial production of AV-299 could be adversely affected.



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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.

***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.

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The third parties on whom we rely generally may terminate their engagements with us at any time. If we are required to enter into alternative arrangements because of any such termination the introduction of our product candidates to market could be delayed.

If these third parties do not successfully carry out their duties under their agreements with us, if the quality or accuracy of the data they obtain 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 and our reputation could be harmed.

### **Risks Related to Our Intellectual Property Rights**

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

We cannot be certain that patents will be issued or granted with respect to applications that are currently pending, or that issued or granted patents will not later be found to be invalid and/or unenforceable. The patent position of biotechnology and pharmaceutical companies is generally uncertain because it involves complex legal and factual considerations. The standards applied by the United States Patent and Trademark Office and foreign patent offices in granting patents are not always applied uniformly or predictably. For example, there is no uniform worldwide policy regarding patentable subject matter or the scope of claims allowable in biotechnology and pharmaceutical patents. Consequently, patents may not issue from our pending patent applications. As such, we do not know the degree of future protection that we will have on our proprietary products and technology. The scope of patent protection that the U.S. Patent and Trademark Office will grant with respect to 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.

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

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

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

With regard to 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 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.



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### ***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 aspects of our technology platform, or barred from developing and commercializing related products. Prohibitions against using specified technologies, or prohibitions against commercializing specified products, could be imposed by a court or by a settlement agreement between us and a plaintiff. In addition, if we are unsuccessful in defending against allegations of patent infringement or misappropriation of trade secrets, we may be forced to pay substantial damage awards to the plaintiff. There is inevitable uncertainty in any litigation, including intellectual property litigation. There can be no assurance that we would prevail in any intellectual property litigation, even if the case against us is weak or flawed. If litigation leads to an outcome unfavorable to us, we may be required to obtain a license from the patent owner in order to continue our research and development programs or 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 specified products, or both.

Most of our competitors are larger than we are and have substantially greater resources. They are, therefore, likely to be able to sustain the costs of complex patent litigation longer than we could. In addition, the uncertainties associated with litigation could have a material adverse effect on our ability to raise the funds necessary to continue our clinical trials, 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.

### ***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 our market share in the markets for any of our approved products 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.

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***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, development and business activities, we often rely on confidentiality agreements to protect our proprietary information. Such confidentiality agreements are used, for example, when we talk to 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 we seek to carefully draft our confidentiality agreements 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.



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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 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 specified circumstances or weakening the rights of patent owners in specified 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 Ownership of Our Common Stock**

***The market price of our common stock has been, and may continue to be, highly volatile, and could fall below the price you paid.***

The trading price of our common stock is likely to continue 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;

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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;

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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.

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.***

To our knowledge, as of November 3, 2010, our executive officers, directors and principal stockholders, together with their respective affiliates, owned approximately 24% of our common stock, including shares subject to outstanding options and warrants that are exercisable within 60 days after November 3, 2010. Accordingly, 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 control of our company 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.***

As of November 3, 2010, there were 35,509,967 shares of our common stock outstanding, a substantial portion of which are currently freely tradable. Of these, 4.5 million shares of common stock may be sold in this offering by the selling stockholders. In addition, as of November 3, 2010, we had outstanding options to purchase an aggregate of 3,621,971 shares of common stock that, if exercised, will result in the additional shares underlying these options becoming available for sale. A large portion of our shares and options are held by a small number of persons and investment funds. Sales by these stockholders or optionholders of a substantial number of shares could significantly reduce the market price of our common stock. Moreover, certain holders of our common stock and warrants to purchase shares of common stock, including the selling stockholders, have rights, subject to certain conditions, to require us to file registration statements covering the shares they currently hold, or to include these shares in registration statements that we may file for ourselves or other stockholders.

We have also registered for resale all common stock that we may issue under our 2010 Stock Incentive Plan, 2002 Stock Incentive Plan, and 2010 Employee Stock Purchase Plan. As of November 3, 2010, an aggregate of 1,512,103 shares of our common stock has been reserved for future issuance under the 2010 Stock Incentive Plan, plus any shares reserved and unissued under our 2002 Stock Incentive Plan, and an aggregate of 250,000 shares has been reserved for future issuance under our 2010 Employee Stock Purchase Plan. These shares can be freely sold in the public market upon issuance, subject to restrictions imposed on our affiliates under Rule 144 and any lock-up or other contractual restrictions that may exist from time to time with respect to these shares.



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If a large number of shares of our common stock are sold in the public market, such sales could reduce the trading price of our common stock.

***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 a stockholder could receive a premium for shares of our common stock held by a stockholder in an acquisition.

***Our business could be negatively affected as a result of the actions of activist shareholders.***

Proxy contests have been waged against many companies in the biopharmaceutical industry over the last few years. If faced with a proxy contest, we may not be able to successfully respond to the contest, which would be disruptive to our business. Even if we are successful, our business could be adversely affected by a proxy contest because:

responding to proxy contests and other actions by activist shareholders may be costly and time-consuming, and may disrupt our operations and divert the attention of management and our employees;

perceived uncertainties as to the potential outcome of any proxy contest may result in our inability to consummate potential acquisitions, collaborations or in-licensing opportunities and may make it more difficult to attract and retain qualified personnel and business partners; and



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if individuals that have a specific agenda different from that of our management or other members of our board of directors are elected to our board as a result of any proxy contest, such an election may adversely affect our ability to effectively and timely implement our strategic plan and create additional value for our stockholders.

***We have limited experience complying with public company obligations.***

We face increased legal, accounting, administrative and other costs and expenses as a public company. Compliance with the Sarbanes-Oxley Act of 2002, the federal securities laws, as well as other rules of the SEC and NASDAQ, will result in significant initial cost to us as well as ongoing increases in our legal, audit and financial compliance costs.

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***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.***

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 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 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.

***Our management has broad discretion over the use of the cash available for our operations and working capital requirements and might not spend available cash in ways that increase the value of your investment.***

Our management has broad discretion on where and how to use our cash and you will be relying on the judgment of our management regarding the application of our available cash to fund our operations. Our management might not apply our cash in ways that increase the value of your investment. We expect to use a substantial portion of our cash 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, which may in the future include investments in, or acquisitions of, complementary businesses, joint ventures, partnerships, services or technologies. Our management might not be able to yield a significant return, if any, on any investment of this cash. You will not have the opportunity to influence our decisions on how to use our cash reserves.

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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, and 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, AV-299 and our other product candidates;

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.

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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 are filing the registration statement of which this prospectus is a part to permit holders of the shares of our common stock described in the section entitled "Selling Stockholders" to resell such shares. We will not receive any proceeds from the resale of shares by the selling stockholders.

The selling stockholders will pay any underwriting discounts and commissions and expenses incurred by such selling stockholders for brokerage, accounting, tax or legal services or any other expenses incurred by such selling stockholders in disposing of the shares. We will bear all other costs, fees and expenses incurred in effecting the registration of the shares covered by this prospectus, including, without limitation, all registration and filing fees, NASDAQ Global Market listing fees and fees and expenses of our counsel and our auditors.

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**SELLING STOCKHOLDERS**

On November 3, 2010, we sold 4.5 million shares of our common stock in a private placement to accredited and institutional accredited investors in connection with our execution of a securities purchase agreement with such parties, which we refer to herein as the securities purchase agreement. The table below sets forth, to our knowledge, information about the selling stockholders as of November 3, 2010.

We do not know when or in what amounts the selling stockholders may offer shares for sale. The selling stockholders might not sell any or all of the shares offered by this prospectus. Because the selling stockholders may offer all or some of the shares pursuant to this offering and because there are currently no agreements or understandings with respect to the sale of any shares, we cannot estimate the number of shares that will be held by the selling stockholders after completion of this offering. However, for purposes of this table, we have assumed that, after completion of this offering, none of the shares covered by this prospectus will be held by the selling stockholders.

Beneficial ownership is determined in accordance with the rules of the SEC and includes voting or investment power with respect to shares of our common stock. Unless otherwise indicated below, to our knowledge, the selling stockholders named in the table have sole voting and investment power with respect to the shares of common stock beneficially owned by them. The number of shares of common stock beneficially owned prior to the offering for each selling stockholder includes (i) all shares of our common stock held by such selling stockholder prior to the private placement, plus (ii) all shares of our common stock purchased by such selling stockholder pursuant to the private placement and being offered pursuant to the prospectus, as well as (iii) all options or other derivative securities held by such selling stockholder, which are exercisable within 60 days of November 3, 2010. The percentages of shares owned after the offering are based on 35,509,967 shares of our common stock outstanding as of November 3, 2010, which includes the outstanding shares of common stock offered by this prospectus. The inclusion of any shares in this table does not constitute an admission of beneficial ownership by the person named below.

Throughout this prospectus, when we refer to the shares of our common stock being offered by this prospectus on behalf of the selling stockholders, we are referring to the shares of our common stock sold in the private placement, unless otherwise indicated.

The selling stockholders may have sold or transferred, in transactions exempt from the registration requirements of the Securities Act, some or all of their shares of common stock since the date on which the information in the table below is presented. Information about the selling stockholders may change over time.

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| Name of Selling Stockholders   | Shares of Common Stock Beneficially Owned Prior to Offering |                | Number of Shares of Common Stock Being Offered | Shares of Common Stock to be Beneficially Owned After Offering |                |
|--|---|----------------|--|--|----------------|
|  | Number  | Percentage (%) |  | Number   | Percentage (%) |
| Variable Insurance Products Fund II: Contrafund Portfolio <sup>(1)</sup>                         | 625,140   | 1.76%          | 107,096  | 518,044  | 1.46%          |
| Fidelity Advisor Series I: Fidelity Advisor Balanced Fund <sup>(1)</sup>                         | 22,447  | *              | 3,908  | 18,539   | *              |
| Fidelity Devonshire Trust: Fidelity Series All-Sector Equity Fund <sup>(1)</sup>                 | 362,552   | 1.02%          | 61,752   | 300,800  | *              |
| Fidelity Puritan Trust: Fidelity Balanced Fund <sup>(1)</sup>                                    | 431,444   | 1.21%          | 77,244   | 354,200  | 1.00%          |
| Fidelity Destiny Portfolios: Fidelity Advisor Capital Development Fund <sup>(1)</sup>            | 404,600   | 1.14%          | 404,600  | 0  | *              |
| Fidelity Securities Fund: Fidelity Dividend Growth Fund <sup>(1)</sup>                           | 1,063,609   | 3.00%          | 290,609  | 773,000  | 2.18%          |
| Fidelity Advisor Series I: Fidelity Advisor Dividend Growth Fund <sup>(1)</sup>                  | 99,352  | *              | 27,497   | 71,855   | *              |
| Fidelity Advisor Series VII: Fidelity Advisor Health Care Fund <sup>(1)</sup>                    | 57,566  | *              | 28,715   | 28,851   | *              |
| Variable Insurance Products Fund IV: Health Care Portfolio <sup>(1)</sup>                        | 8,876   | *              | 4,421  | 4,455  | *              |
| Fidelity Central Investment Portfolios LLC: Fidelity Health Care Central Fund <sup>(1)</sup>     | 102,992   | *              | 51,392   | 51,600   | *              |
| Variable Insurance Products Fund III: Balanced Portfolio <sup>(1)</sup>                          | 140,563   | *              | 39,037   | 101,526  | *              |
| Fidelity Select Portfolios: Health Care Portfolio <sup>(1)</sup>                                 | 234,832   | *              | 117,323  | 117,509  | *              |
| Janus Investment Fund on behalf of its series Janus Global Life Sciences Fund <sup>(2)</sup>     | 380,050   | 1.07%          | 78,609   | 301,441  | *              |
| Janus Capital Funds plc on behalf of its sub-fund Janus Global Life Sciences Fund <sup>(2)</sup> | 36,312  | *              | 7,797  | 28,515   | *              |
| HealthCor, L.P. <sup>(3)</sup>   | 113,346   | *              | 113,346  | 0  | *              |
| HealthCor Offshore Master Fund, L.P. <sup>(3)</sup>  | 230,170   | *              | 230,170  | 0  | *              |
| HealthCor Hybrid Offshore Master Fund, L.P. <sup>(3)</sup>                                       | 56,484  | *              | 56,484   | 0  | *              |
| Alyeska Master Fund, L.P. <sup>(4)</sup>   | 498,247   | 1.40%          | 428,571  | 69,676   | *              |
| Deutsche Bank AG London <sup>(5)</sup>   | 199,299   | *              | 171,429  | 27,870   | *              |
| Baupost Group Securities, L.L.C. <sup>(6)</sup>  | 2,000,000   | 5.63%          | 2,000,000                                      | 0  | *              |
| Plutus Holdings 2 LTD <sup>(7)</sup>   | 1,043,696   | 2.94%          | 200,000  | 843,696  | 2.38%          |
| <b>Total</b>   | <b>8,111,577</b>  | <b>22.8%</b>   | <b>4,500,000</b>                               | <b>3,611,577</b>   | <b>10.2%</b>   |

\* Less than one percent

- (1) Fidelity Management & Research Company ( Fidelity ), a wholly-owned subsidiary of FMR LLC and an investment adviser registered under Section 203 of the Investment Advisers Act of 1940, is the beneficial owner of such shares as a result of acting as investment adviser to various investment companies (the Fidelity Funds ) registered under Section 8 of the Investment Company Act of 1940. Each of Edward C. Johnson III and FMR LLC, through its control of Fidelity and the Fidelity Funds has power to dispose of the shares owned by the Fidelity Funds. Through their ownership of voting common shares and a shareholders' voting agreement, members of the Johnson family may be deemed to form a controlling group with respect to FMR LLC. Neither FMR LLC nor Edward C. Johnson III, Chairman of FMR LLC, has the sole power to vote or direct the voting of the shares owned directly by the Fidelity Funds, which power resides with the Fidelity Funds' Boards of Trustees. Fidelity carries out the voting of the shares under written guidelines established by the Fidelity Funds' Boards of Trustees.





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- (2) Andrew Acker, portfolio manager for Janus Capital Management LLC ( Janus ), may be deemed to have discretionary investment authority with respect to such shares. Mr. Acker or any authorized officer of Janus may be deemed to share discretionary voting authority with respect to such shares.
- (3) The partners of HealthCor Management, L.P. may be deemed to share voting and investment power with respect to such shares.
- (4) Alyeska Investment Group, L.P., which is the investment manager of Alyeska Master Fund, L.P., may be deemed to have voting and investment power with respect to such shares.
- (5) Alyeska Investment Group, L.P., which is the subadvisor to DB Alternative Strategies Limited, which is the advisor to Deutsche Bank AG London, may be deemed to have voting and investment power with respect to such shares.
- (6) The Baupost Group, L.L.C., ( Baupost ), manager to Baupost Group Securities, L.L.C., and each of SAK Corp., the manager of Baupost, and Seth A. Klarman, the director of SAK Corp., may be deemed to share voting and investment power with respect to such shares.
- (7) Herve Benzakein, director of Senebier Ltd, acting as director of Plutus Holdings 2 LTD, may be deemed to have voting and investment power with respect to such shares.

**Relationships with the Selling Stockholders**

Certain funds registered under Section 8 of the Investment Company Act of 1940 and beneficially owned by Fidelity Management & Research Company, a wholly-owned subsidiary of FMR LLC, beneficially owned approximately 12.3% of our voting securities prior to purchasing shares of our common stock in the private placement.

In connection with the sale of shares to the selling stockholders, we entered into a securities purchase agreement and a registration rights agreement with the selling stockholders. The registration statement of which this prospectus is a part has been filed in accordance with the registration rights agreement and securities purchase agreement.

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**PLAN OF DISTRIBUTION**

The selling stockholders, which as used herein includes donees, pledgees, transferees or other successors-in-interest selling shares of common stock or interests in shares of common stock received after the date of this prospectus from a selling stockholder as a gift, pledge, partnership distribution or other transfer, may, from time to time, sell, transfer or otherwise dispose of any or all of their shares of common stock or interests in shares of common stock on any stock exchange, market or trading facility on which the shares are traded or in private transactions. These dispositions may be at fixed prices, at prevailing market prices at the time of sale, at prices related to the prevailing market price, at varying prices determined at the time of sale, or at negotiated prices.

The selling stockholders may use any one or more of the following methods when disposing of shares or interests therein:

ordinary brokerage transactions and transactions in which the broker-dealer solicits purchasers;

block trades in which the broker-dealer will attempt to sell the shares as agent, but may position and resell a portion of the block as principal to facilitate the transaction;

purchases by a broker-dealer as principal and resale by the broker-dealer for its account;

an exchange distribution in accordance with the rules of the applicable exchange;

privately negotiated transactions;

short sales effected after the date the registration statement of which this prospectus is a part is declared effective by the SEC;

through the writing or settlement of options or other hedging transactions, whether through an options exchange or otherwise;

broker-dealers may agree with the selling stockholders to sell a specified number of such shares at a stipulated price per share;

a combination of any such methods of sale; and

any other method permitted by applicable law.

The selling stockholders may, from time to time, pledge or grant a security interest in some or all of the shares of common stock owned by them and, if they default in the performance of their secured obligations, the pledgees or secured parties may offer and sell the shares of common stock, from time to time, under this prospectus, or under an amendment to this prospectus under Rule 424(b)(3) or other applicable provision of the Securities Act amending the list of selling stockholders to include the pledgee, transferee or other successors in interest as selling stockholders under this prospectus. The selling stockholders also may transfer the shares of common stock in other circumstances, in which case the transferees, pledgees or other successors in interest will be the selling beneficial owners for purposes of this prospectus.

In connection with the sale of our common stock or interests therein, the selling stockholders may enter into hedging transactions with broker-dealers or other financial institutions, which may in turn engage in short sales of the common stock in the course of hedging the positions

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they assume. The selling stockholders may also sell shares of our common stock short and deliver these securities to close out their short positions, or loan or pledge the common stock to broker-dealers that in turn may sell these securities. The selling stockholders may also enter into option or other transactions with broker-dealers or other financial institutions or the creation of one or more derivative securities which require the delivery to such broker-dealer or other financial institution of shares offered by this prospectus, which shares such broker-dealer or other financial institution may resell pursuant to this prospectus (as supplemented or amended to reflect such transaction).

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The aggregate proceeds to the selling stockholders from the sale of the common stock offered by them will be the purchase price of the common stock less discounts or commissions, if any. Each of the selling stockholders reserves the right to accept and, together with their agents from time to time, to reject, in whole or in part, any proposed purchase of common stock to be made directly or through agents. We will not receive any of the proceeds from this offering.

The selling stockholders also may resell all or a portion of the shares in open market transactions in reliance upon Rule 144 under the Securities Act of 1933, provided that they meet the criteria and conform to the requirements of that rule.

The selling stockholders and any underwriters, broker-dealers or agents that participate in the sale of the common stock or interests therein may be underwriters within the meaning of Section 2(11) of the Securities Act. Any discounts, commissions, concessions or profit they earn on any resale of the shares may be underwriting discounts and commissions under the Securities Act. Selling stockholders who are underwriters within the meaning of Section 2(11) of the Securities Act will be subject to the prospectus delivery requirements of the Securities Act.

To the extent required, the shares of our common stock to be sold, the names of the selling stockholders, the respective purchase prices and public offering prices, the names of any agents, dealer or underwriter, any applicable commissions or discounts with respect to a particular offer will be set forth in an accompanying prospectus supplement or, if appropriate, a post-effective amendment to the registration statement that includes this prospectus.

In order to comply with the securities laws of some states, if applicable, the common stock may be sold in these jurisdictions only through registered or licensed brokers or dealers. In addition, in some states the common stock may not be sold unless it has been registered or qualified for sale or an exemption from registration or qualification requirements is available and is complied with.

We have advised the selling stockholders that the anti-manipulation rules of Regulation M under the Exchange Act may apply to sales of shares in the market and to the activities of the selling stockholders and their affiliates. In addition, to the extent applicable, we will make copies of this prospectus (as it may be supplemented or amended from time to time) available to the selling stockholders for the purpose of satisfying the prospectus delivery requirements of the Securities Act. The selling stockholders may indemnify any broker-dealer that participates in transactions involving the sale of the shares against certain liabilities, including liabilities arising under the Securities Act.

We have agreed to indemnify the selling stockholders against liabilities, including liabilities under the Securities Act and state securities laws, relating to the registration of the shares offered by this prospectus.

We have agreed with the selling stockholders to keep the registration statement of which this prospectus constitutes a part effective until the earlier of (1) such time as all of the shares covered by this prospectus have been disposed of pursuant to and in accordance with such registration statement or (2) the date on which all of the shares may be sold without restriction pursuant to Rule 144 of the Securities Act.

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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 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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**Table of Contents****MARKET PRICE INFORMATION**

Our common stock began trading on the NASDAQ Global Market on March 12, 2010 under the symbol AVEO . Prior to that time, there was no established public trading market for our common stock. The following table sets forth the high and low sale prices per share for our common stock on the NASDAQ Global Market for the period indicated:

|   | <b>High</b> | <b>Low</b> |
|---|-------------|------------|
| <b>2010</b>                               |             |            |
| First Quarter (beginning March 12, 2010)  | \$ 9.02     | \$ 8.16    |
| Second Quarter                            | \$ 9.91     | \$ 6.90    |
| Third Quarter                             | \$ 11.23    | \$ 6.01    |
| Fourth Quarter (through November 9, 2010) | \$ 17.72    | \$ 11.24   |

On November 9, 2010, the last reported sale price of our common stock on the NASDAQ Global Market was \$16.45 per share.

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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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**DILUTION**

This offering is for sales of common stock by the selling stockholders on a continuous or delayed basis in the future. Sales of common stock by the selling stockholders will not result in a change to the net tangible book value per share before and after the distribution of shares by such selling stockholders.

There will be no change in net tangible book value per share attributable to cash payments made by purchasers of the shares being offered. Prospective investors should be aware, however, that the price of shares of common stock may not bear any rational relationship to net tangible book value per share of the common stock.



**Table of Contents****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 interim consolidated financial data from our unaudited interim consolidated financial statements 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 unaudited interim consolidated financial statements have been prepared on the same basis as the annual consolidated financial statements and include all adjustments, which include only normal recurring adjustments, necessary for the fair presentation of the information set forth therein.

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.

|  | 2005                                  | 2006        | Years Ended<br>December 31,<br>2007 | 2008        | 2009        | Nine Months Ended<br>September 30,<br>2009 | 2010<br>(in thousands, except |
|--|---------------------------------------|-------------|-------------------------------------|-------------|-------------|--|-------------------------------|
|  | (in thousands, except per share data) |             |                                     |             |             | per share data<br>(unaudited) (unaudited)  |                               |
| <b>Statement of operations data:</b>   |                                       |             |                                     |             |             |  |                               |
| Revenue  | \$ 6,213                              | \$ 7,783    | \$ 11,034                           | \$ 19,660   | \$ 20,719   | \$ 14,683                                  | \$ 32,725                     |
| <b>Operating expenses:</b>   |                                       |             |                                     |             |             |  |                               |
| Research and development   | 17,758                                | 26,845      | 29,248                              | 41,821      | 51,792      | 38,326                                     | 68,867                        |
| General and administrative   | 4,783                                 | 5,161       | 6,502                               | 9,164       | 10,120      | 7,504                                      | 10,199                        |
| <b>Total operating expenses</b>  | 22,541                                | 32,006      | 35,750                              | 50,985      | 61,912      | 45,830                                     | 79,066                        |
| <b>Income (loss) from operations</b>   | (16,328)                              | (24,223)    | (24,716)                            | (31,325)    | (41,193)    | (31,147)                                   | (46,341)                      |
| <b>Other income and expense:</b>   |                                       |             |                                     |             |             |  |                               |
| Other income (expense), net  | 7                                     |             |                                     | 18          | (333)       | (273)                                      | 722                           |
| Loss on loan extinguishment  |                                       |             |                                     | (248)       |             |  | (582)                         |
| Interest expense   | (635)                                 | (1,591)     | (2,437)                             | (2,086)     | (2,811)     | (2,141)                                    | (2,361)                       |
| Interest income  | 859                                   | 909         | 2,171                               | 1,168       | 144         | 121  | 87                            |
| <b>Other income (expense), net</b>   | 231                                   | (682)       | (266)                               | (1,148)     | (3,000)     | (2,293)                                    | (2,134)                       |
| Net loss before taxes  | (16,097)                              | (24,905)    | (24,982)                            | (32,473)    | (44,193)    | (33,440)                                   | (48,475)                      |
| <b>Tax benefit</b>   |                                       |             |                                     |             | 100         | 63   |                               |
| <b>Net loss</b>  | \$ (16,097)                           | \$ (24,905) | \$ (24,982)                         | \$ (32,473) | \$ (44,093) | \$ (33,377)                                | \$ (48,475)                   |
| <b>Net loss per share applicable to common stockholders-basic and diluted</b>                            | \$ (12.35)                            | \$ (18.73)  | \$ (17.89)                          | \$ (21.08)  | \$ (27.43)  | \$ (20.87)                                 | \$ (2.13)                     |
| <b>Weighted average number of common shares used in net loss per share calculation basic and diluted</b> | 1,303                                 | 1,330       | 1,396                               | 1,541       | 1,607       | 1,599                                      | 22,773                        |



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|   | 2005      | 2006      | As of December 31,<br>2007 |           | 2008      | 2009      | As of<br>September 30,<br>2010<br>(in<br>thousands)<br>(unaudited) |
|---|-----------|-----------|----------------------------|-----------|-----------|-----------|--|
|   |           |           | (in thousands)             |           |           |           |  |
| <b>Balance sheet data:</b>                                |           |           |                            |           |           |           |  |
| Cash, cash equivalents, and marketable securities         | \$ 25,991 | \$ 16,748 | \$ 61,742                  | \$ 32,364 | \$ 51,301 | \$ 87,022 |  |
| Working capital   | 17,087    | 3,674     | 42,542                     | 16,073    | 18,789    | 57,325    |  |
| Total assets  | 33,074    | 22,448    | 67,654                     | 40,087    | 59,844    | 96,512    |  |
| Loans payable, including current portion, net of discount | 7,076     | 19,365    | 15,078                     | 21,055    | 19,745    | 23,140    |  |
| 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) | (226,200) |  |
| Total stockholders' equity (deficit)                      | (49,817)  | (74,547)  | (98,458)                   | (128,688) | (170,291) | 23,411    |  |

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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, and in any amendments or supplements we may make to 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, 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 phase 2 clinical 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 August 2010, we completed enrollment of our 517-patient phase 3 clinical trial of tivozanib in patients with advanced RCC, which we refer to as the TIVO-1 study. 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.

In addition to the TIVO-1 study, 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 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.

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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 recently initiated a phase 2 clinical trial for non-small cell lung cancer. In 2007, we entered into an agreement with Merck & Co., Inc. (formerly Schering-Plough Corporation), or Merck, under which we granted Merck exclusive worldwide rights to co-develop and commercialize AV-299 and under which Merck funded all development and manufacturing expenses, subject to an agreed-upon budget. On September 28, 2010, we received notice from Merck of termination of the collaboration agreement effective as of December 27, 2010 at which point we will be responsible for funding all future development manufacturing and commercialization costs for the AV-299 program.

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 into 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.

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.

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 September 30, 2010, have principally funded our operations through:

\$118.1 million of non-dilutive capital in the form of license fees, milestone payments and research and development funding received from our strategic partners;

\$169.6 million of funding from the sale of convertible preferred stock to our investors, including \$77.5 million of equity sales to our strategic partners;

\$89.7 million of gross proceeds from the sale of common stock in connection with the completion of our initial public offering in March 2010; and

\$25.0 million of loan proceeds in connection with the loan agreement with Hercules Technology II, L.P. and Hercules Technology III, L.P.

We have never been profitable and, as of September 30, 2010, we had an accumulated deficit of \$226.2 million. We incurred net losses of approximately \$25.0 million, \$32.5 million and \$44.1 million during the years ended December 31, 2007, 2008 and 2009, respectively. We incurred net losses of approximately \$33.4 million and \$48.5 million during the nine months ended September 30, 2009 and 2010, 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.

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### **Recent Financing**

On October 28, 2010, we entered into a definitive agreement with respect to the private placement of 4.5 million shares of our unregistered common stock at \$13.50 per share to a group of institutional and accredited investors. We completed the private placement on November 3, 2010, resulting in approximately \$56.6 million in net proceeds to us.

### **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, 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 also made a \$10.0 milestone payment to Kyowa Hakko Kirin in March 2010 in connection with the initial dosing of patients in our phase 3 clinical trial of tivozanib. 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. (a wholly-owned subsidiary of Astellas US Holding Inc., a holding company owned by Astellas Pharma 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, \$25.0 million.

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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 shares of our 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 connection with the initial public offering we consummated in March 2010 and the related 1:4 reverse stock split of our common stock, each four shares of outstanding series C convertible preferred stock were converted into one share of common stock.

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 our 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. In connection with the initial public offering we consummated in March 2010 and the related 1:4 reverse stock split of our common stock, each four shares of outstanding series E convertible preferred stock were converted into one share of common stock.

Under the amended 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.

***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 up-front cash payment of \$5.0 million in March 2009, which will be amortized over our period of substantial involvement, defined as the twenty-year patent life of the development candidate. 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 connection with the initial public offering we consummated in March 2010 and the related 1:4 reverse stock split of our common stock, each four shares of outstanding series E convertible preferred stock were converted into one share of common stock.



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In June 2009, we received a \$5.0 million milestone payment for achievement of the first pre-clinical discovery milestone under the agreement. 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 also earned a second \$5.0 million milestone payment upon selection of a development candidate in March 2010. This milestone was considered substantive and at risk and has been included in revenue for the quarter ended March 31, 2010. We could also receive (i) a \$5.0 million 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.

### ***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. We also are using our Human Response Platform to conduct translational research to guide the clinical development of AV-299. Prior to Merck's termination of its collaboration agreements with us, Merck was responsible for all costs related to the clinical development of AV-299 and clinical and commercial manufacturing. On September 28, 2010, we received notice from Merck of termination of the collaboration agreement effective as of December 27, 2010, at which point we will be responsible for funding all future development, manufacturing and commercialization costs for the AV-299 program.

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, which was initially estimated to be through completion of the first phase 2 proof-of-concept trial for AV-299 (which was expected to be the first half of 2012), but has been adjusted to reflect the termination of the agreement effective as of December 27, 2010. In addition, Merck purchased 4,000,000 shares of our 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. In connection with the initial public offering we consummated in March 2010, and the related 1:4 reverse stock split of our common stock, each four shares of outstanding series D convertible preferred stock were converted into one share of common stock.

In June 2010, we earned and received an \$8.5 million milestone payment from Merck in connection with the enrollment of patients in our phase 2 clinical trial of AV-299 under the agreement. Since the \$8.5 million milestone payment earned in June 2010 was considered substantive and at risk, it has been included in revenue for the nine months ended September 30, 2010.

## **Financial 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.

**Table of Contents*****Research and Development Expense***

Research and development expenses consist 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. Non-refundable advance payments for goods and services that will be used in future research and development activities are expensed when the activity has been performed or when the goods have been received rather than when the payment is made.

Conducting a significant amount of research and development is central to our business model. Product candidates in later 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 later 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 the AV-299 program and our earlier-stage research and development projects.

We track external development expenses and personnel expense on a program-by-program basis and allocate 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, and the nine months ended September 30, 2009 and 2010:

|           | Years Ended December 31, |           |           | Nine Months Ended         |           |
|-----------|--------------------------|-----------|-----------|---------------------------|-----------|
|           | 2007                     | 2008      | 2009      | 2009                      | 2010      |
|           | (in thousands)           |           |           | (unaudited, in thousands) |           |
| Tivozanib | \$ 5,810                 | \$ 14,231 | \$ 23,399 | \$ 17,315                 | \$ 43,980 |
| AV-299    | 4,101                    | 5,671     | 6,498     | 4,579                     | 7,336     |

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|   |           |           |           |           |           |
|---|-----------|-----------|-----------|-----------|-----------|
| AV-203 program                          |           | 992       | 1,763     | 1,294     | 2,102     |
| Platform collaborations                 | 2,025     | 2,836     | 2,960     | 2,139     | 2,339     |
| Antibody pipeline                       | 4,660     | 5,176     | 5,523     | 4,094     | 4,473     |
| Other research and development          | 5,010     | 3,437     | 2,358     | 1,892     | 1,109     |
| Overhead                                | 7,642     | 9,478     | 9,291     | 7,013     | 7,528     |
| Total research and development expenses | \$ 29,248 | \$ 41,821 | \$ 51,792 | \$ 38,326 | \$ 68,867 |

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### *Tivozanib*

We have completed a phase 2 clinical trial for tivozanib and in August 2010 completed enrollment of our 517-patient phase 3 clinical trial for tivozanib in advanced RCC. We are also conducting phase 1 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, such as additional trials in combination with other drugs, the timing of the regulatory process, and the success of the ongoing phase 3 clinical trial. Our current estimate for the cost of the phase 3 clinical trial, including the cost of the comparator drug, Nexavar, is approximately \$67.0 million. In the first quarter of 2010, we paid Kyowa Hakko Kirin a \$10.0 million milestone in connection with the initial dosing of patients in our phase 3 clinical trial of tivozanib. We may also be required to make up to an aggregate of \$50.0 million in 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 entered into a license agreement related to AV-299 with Merck (formerly Schering-Plough) pursuant to which Merck was responsible for all expenses relating to development of AV-299 in accordance with an agreed-upon budget prior to Merck's termination of the agreement. We recorded revenue and expenses on a gross basis under this arrangement. We completed a phase 1 clinical trial of AV-299 and initiated a phase 2 clinical trial of AV-299 in the second quarter of 2010, for which we earned an \$8.5 million milestone payment from Merck. On September 28, 2010, we received notice from Merck of termination of the agreement effective as of December 27, 2010, at which point we will be responsible for funding all future development, manufacturing and commercialization costs for the AV-299 program. Due to the unpredictable nature of preclinical and clinical development, we are unable to estimate with certainty the costs we will incur in the future development of AV-299.

### *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 certainty the costs we will incur in the future development of any candidate identified from this program. We selected a development candidate in the first quarter of 2010 for which we earned a \$5.0 million milestone payment from Biogen Idec. We commenced process development for manufacturing of this candidate in September 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 Pharmaceuticals 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.

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*Other Research and Development*

Other research and development includes expenses related to AV-412, a product candidate for which we 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.

*Uncertainties of Estimates Related to Research and Development Expenses*

The process of conducting preclinical studies and clinical trials necessary to obtain FDA approval for each of our product candidates is costly and time consuming. The probability of success for each product candidate and clinical trial may be affected by a variety of factors, including, among others, the 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.

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 (except for the estimates we have made for the cost of our phase 3 clinical trial of tivozanib) or when, or to what extent, we will generate revenues from the commercialization and sale of any of our product candidates (except for our expectation related to the earliest we might generate revenue from product sales under *Financial Overview* *Revenue* above). 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 commercialization of tivozanib and to fund the development of the AV-299 program and our other product candidates.

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### ***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 directors and officers 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 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 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.

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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.

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We typically receive up-front, non-refundable 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 up-front, non-refundable 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 non-refundable 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 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 September 30, 2010, 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 \$275,000.





**Table of Contents****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. We utilized a weighted average method of using our own data for the quarters that we have been public, along with data we obtained from our 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 and for all periods thereafter, 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.

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

|                          | Years Ended December 31, |             |               | Nine Months Ended |
|--------------------------|--------------------------|-------------|---------------|-------------------|
|                          | 2007                     | 2008        | 2009          | September 30,     |
|                          |                          |             |               | 2010              |
|                          |                          |             |               | (unaudited)       |
| Volatility               | 68.16%                   | 68.70%      | 70.35%-72.04% | 63.92%-66.80%     |
| Expected Term (in years) | 5.58                     | 5.61        | 5.50-6.25     | 5.50-6.25         |
| Risk-Free Interest Rates | 3.49%-5.03%              | 1.55%-3.34% | 1.98%-3.04%   | 1.59%-2.92%       |

**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. We recognized stock-based compensation expense of approximately \$1.7 million and \$2.9 million for the nine months ended September 30, 2009 and 2010, respectively in accordance with ASC 718. As of September 30, 2010, we had approximately \$5.1 million of total unrecognized compensation expense, net of related forfeiture estimates which we expect to recognize over a weighted-average period of approximately 2.0 years.

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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. Prior to our initial public offering in March 2010, the fair value of our common stock was determined by our board of directors, with input from management, as there was no public market for our common stock at that time. Prior to our initial public offering, our board of directors had 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 through the date of our initial public offering:

| 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                              |
| <b>Total</b>      | <b>991,857</b>                              |                |  |                                  |

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;

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.

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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.

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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 *S&P 500 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 *S&P 500 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      |
| <b>Probabilities</b>   |          |          |          |          |          |          |          |
| 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  |
| 1 <sup>st</sup> IPO date   | 12/31/09 | 12/31/09 | 3/31/10  | 3/31/10  | 3/31/10  | 3/31/10  | 3/31/10  |
| 2 <sup>nd</sup> 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;

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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.

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 up-front payment;

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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 anticipated that data would 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 up-front 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 for our IPO determined the range for the IPO. 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 then 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 noted that, as is typical in initial public offerings, the 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 this 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 range and management's determination of the estimated fair value of our common stock on January 22, 2010 is 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 its initial public offering, which we believed demonstrated a significant improvement in the market for initial public offerings in the U.S. in the biopharmaceutical industry. We noted, 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 for our IPO 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.

The initial public offering price of our common stock was \$9.00 per share. The difference between the estimated fair value of our common stock of \$12.24 per share in January 2010 and the initial public offering price took into account several factors considered by our board of directors and underwriters, including:

an analysis of the typical valuation ranges seen in initial public offerings for companies in our industry with similar market capitalization;

a deterioration in financial markets with accompanying decrease in market capitalization of companies comparable to ours;

increased difficulty in raising equity financing with accompanying financing uncertainty;

a review of the then current market conditions and the results of operations, competitive position and the stock performance of our competitors; and

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consideration of our history as a private company and previous valuation reports received by independent valuation firms. As of September 30, 2010, 3,481,141 shares of our common stock were issuable upon exercise of stock options.

**Table of Contents****Results of Operations***Comparison of Nine Months Ended September 30, 2009 and 2010*

|                             | Nine Months Ended<br>September 30, |                                   | Increase/<br>(decrease) | %      |
|-----------------------------|------------------------------------|-----------------------------------|-------------------------|--------|
|                             | 2009                               | 2010<br>(unaudited, in thousands) |                         |        |
| Revenue                     | \$ 14,683                          | \$ 32,725                         | \$ 18,042               | 123%   |
| Operating expenses:         |                                    |                                   |                         |        |
| Research and development    | 38,326                             | 68,867                            | 30,541                  | 80%    |
| General and administrative  | 7,504                              | 10,199                            | 2,695                   | 36%    |
| Total operating expenses    | 45,830                             | 79,066                            | 33,326                  | 73%    |
| Loss from operations        | (31,147)                           | (46,341)                          | (15,194)                | 49%    |
| Other income (expense), net | (273)                              | 140                               | 413                     | (151)% |
| Interest expense            | (2,141)                            | (2,361)                           | (220)                   | 10%    |
| Interest income             | 121                                | 87                                | (34)                    | (28)%  |
| Tax benefit                 | 63                                 |                                   | (63)                    | (100)% |
| Net loss                    | \$ (33,377)                        | \$ (48,475)                       | \$ (15,098)             | 45%    |

| Revenue             | Nine Months Ended<br>September 30, |                                   | Increase/<br>(decrease) | %    |
|---------------------|------------------------------------|-----------------------------------|-------------------------|------|
|                     | 2009                               | 2010<br>(unaudited, in thousands) |                         |      |
| Strategic Partner:  |                                    |                                   |                         |      |
| Merck               | \$ 7,986                           | \$ 17,709                         | \$ 9,723                | 122% |
| OSI Pharmaceuticals | 6,619                              | 9,313                             | 2,694                   | 41%  |
| Biogen Idec         |                                    | 5,530                             | 5,530                   | 100% |
| Other               | 78                                 | 173                               | 95                      | 122% |
|                     | \$ 14,683                          | \$ 32,725                         | \$ 18,042               | 123% |

**Revenue.** Revenue for the nine months ended September 30, 2010 was \$32.7 million compared to \$14.7 million for the nine months ended September 30, 2009, an increase of approximately \$18.0 million or 123%. The increase is attributable to a \$8.5 million milestone payment from Merck earned in May 2010 for enrollment of patients in our phase 2 clinical trial of AV-299; a \$5.0 million milestone payment from Biogen Idec earned in March 2010 for selection of the development candidate for our AV-203 program; additional research and development funding from Merck related to the AV-299 program in the amount of \$1.9 million; an increase in amortization of deferred revenue associated with the amended OSI Pharmaceuticals agreement in the amount of \$1.7 million; an increase in research revenue earned under the OSI Pharmaceuticals agreement of \$1.0 million; and an increase of \$0.5 million associated with amortization of previously deferred Biogen Idec license revenue

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which began in the first quarter of 2010. These increases were partially offset by a decrease of \$0.7 million in amortization of the deferred revenue under the Merck agreement due to the expiration of the research plan, and related funding, in March 2010.

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**Research and Development.** Research and development expenses for the nine months ended September 30, 2010 were \$68.9 million compared to \$38.3 million for the nine months ended September 30, 2009, an increase of \$30.5 million or 80%. The increase is primarily attributable to an increase in clinical trial costs of \$15.7 million resulting primarily from an increase in costs due to the phase 3 clinical trial of tivozanib, including a \$11.6 million purchase of Nexavar, the comparator drug, for the clinical trial, partially offset by a reduction in costs of the phase 2 clinical trial of tivozanib as it winds down; a \$10.0 million milestone payment to Kyowa Hakko Kirin in connection with the initial dosing of patients in our phase 3 clinical trial of tivozanib; a \$2.8 million increase in development costs related to AV-299, which were reimbursed by Merck but recorded on a gross basis; a \$2.6 million increase in salaries and benefits mainly due to an increase in personnel primarily supporting development activities for tivozanib; a \$1.0 million increase in contract manufacturing for tivozanib to support an increasing number of clinical trials; and a \$0.4 million increase in stock compensation expense. These increases were partially offset by a decrease of \$1.3 million for preclinical studies as we wind down certain preclinical activities primarily related to toxicology; a decrease of \$0.4 million for outsourcing costs due to timing of work performed on certain projects; and a decrease in scientific advisory board fees of \$0.4 million.

Included in research and development expenses were stock-based compensation charges of approximately \$1.3 million and \$910,000 for the nine months ended September 30, 2010 and 2009, respectively.

**General and Administrative.** General and administrative expenses for the nine months ended September 30, 2010 were \$10.2 million compared to \$7.5 million for the nine months ended September 30, 2009, an increase of \$2.7 million or 36%. The increase is primarily the result of an increase of \$0.8 million for costs related to being a public company such as directors and officers liability insurance premiums, public relations, audit services, and an increase in board of directors compensation; a \$0.8 million increase in stock-based compensation expense principally related to grants of annual individual performance options and milestone-based options to our officers in February 2010; a \$0.8 million increase in costs related to market development for tivozanib; and an increase in recruiting and relocation costs of \$0.3 million due to our hiring of additional personnel.

Included in general and administrative expenses were stock-based compensation charges of approximately \$1.6 million and \$0.8 million for the nine months ended September 30, 2010 and 2009, respectively.

**Other Income (Expense), Net.** Other income (expense), net for the nine months ended September 30, 2010 was \$140,000 compared to \$(273,000) for the nine months ended September 30, 2009, an increase of \$413,000. The increase for the nine months ended September 30, 2010 is largely a result of a decrease in the value of warrants to purchase preferred stock resulting from a decrease in value of the underlying stock, partially offset by the loss on the loan extinguishment related to the refinancing of our outstanding debt with Hercules Technology Growth Capital and Comerica Bank on May 28, 2010 (see footnote 5 of the notes to our unaudited condensed consolidated financial statements).

**Interest Expense.** Interest expense for the nine months ended September 30, 2010 was \$2.4 million compared to \$2.1 million for the nine months ended September 30, 2009, an increase of \$0.2 million or 10%. The increase is due to the overall debt increasing in 2010 due to the refinancing of our outstanding debt with Hercules Technology Growth Capital and Comerica Bank on May 28, 2010.

**Interest Income.** Interest income for the nine months ended September 30, 2010 was \$87,000 compared to \$121,000 for the nine months ended September 30, 2009, a decrease of \$34,000 or 28%. Although average cash balances were higher for the nine months ended September 30, 2010 compared to the same period in 2009, interest rates decreased to only slightly above 0% in 2010, causing the decrease in interest income.

**Table of Contents***Comparison of Years Ended December 31, 2008 and 2009*

|                                 | Years Ended<br>December 31, |                    | Increase/<br>(decrease) | %          |
|---------------------------------|-----------------------------|--------------------|-------------------------|------------|
|                                 | 2008                        | 2009               |                         |            |
|                                 | (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%        |
| <b>Total operating expenses</b> | <b>50,985</b>               | <b>61,912</b>      | <b>10,927</b>           | <b>21%</b> |
| Loss from operations            | (31,325)                    | (41,193)           | (9,868)                 | 32%        |
| Other income (expense), net     | 18                          | (333)              | (351)                   | (1,950)%   |
| Loss on loan extinguishment     | (248)                       |                    | 248                     | (100)%     |
| Interest income                 | 1,168                       | 144                | (1,024)                 | (88)%      |
| Interest expense                | (2,086)                     | (2,811)            | (725)                   | 35%        |
| <b>Loss before taxes</b>        | <b>(32,473)</b>             | <b>(44,193)</b>    | <b>(11,720)</b>         | <b>36%</b> |
| Taxes                           |                             | 100                | 100                     |            |
| <b>Net loss</b>                 | <b>\$ (32,473)</b>          | <b>\$ (44,093)</b> | <b>\$ (11,620)</b>      | <b>36%</b> |

|                         | Years Ended<br>December 31, |           | Increase/<br>(decrease) | %      |
|-------------------------|-----------------------------|-----------|-------------------------|--------|
|                         | 2008                        | 2009      |                         |        |
|                         | (in thousands)              |           |                         |        |
| <b>Revenue</b>          |                             |           |                         |        |
| 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 which is 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 were 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.



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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 Debtors 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.

**Table of Contents***Comparison of Years Ended December 31, 2007 and 2008*

|                             | Years Ended<br>December 31, |                        | Increase/<br>(decrease) | %     |
|-----------------------------|-----------------------------|------------------------|-------------------------|-------|
|                             | 2007                        | 2008<br>(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<br>December 31, |                        | Increase/<br>(decrease) | %      |
|-------------------------|-----------------------------|------------------------|-------------------------|--------|
|                         | 2007                        | 2008<br>(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 up-front 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 up-front 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 partially 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 were fully reimbursed by Schering-Plough (now Merck) but are recorded on a gross basis; an increase in licensing costs of \$0.8 million as

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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.

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.

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**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 million increase in travel costs; and a \$0.1 million 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.

**Selected Quarterly Financial Data (unaudited)**

The following tables set forth our unaudited consolidated quarterly operating results for each of the eight quarters in the two-year period ended December 31, 2009 and the three quarters in the period ended September 30, 2010. This information is derived from our unaudited financial statements, which in the opinion of management contain all adjustments consisting of only normal recurring adjustments, that we consider necessary for a fair statement of such financial data. Operating results for the period ended September 30, 2010 are not necessarily indicative of the operating results for a full year. Historical results are not necessarily indicative of the results to be expected in future periods. You should read this data together with our consolidated financial statements and the related notes included elsewhere in this prospectus.

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|   | Three Months Ended                                   |                  |                       |
|---|--|------------------|-----------------------|
|   | March 31,<br>2010                                    | June 30,<br>2010 | September 30,<br>2010 |
|   | (in thousands, except per share data)<br>(unaudited) |                  |                       |
| Collaboration revenue   | \$ 10,881  | \$ 15,622        | \$ 6,222              |
| Operating expenses:   |  |                  |                       |
| Research and development  | 22,618   | 25,997           | 20,252                |
| General and administrative  | 2,753  | 3,835            | 3,611                 |
|   | 25,371   | 29,832           | 23,863                |
| Loss from operations  | (14,490)   | (14,210)         | (17,641)              |
| Other income and expense:   |  |                  |                       |
| Other income (expense), net   | 712  | (582)            | 10                    |
| Interest expense  | (607)  | (725)            | (1,029)               |
| Interest income   | 7  | 28               | 52                    |
| Other income (expense), net   | 112  | (1,279)          | (967)                 |
| Net loss before benefit for income taxes  | (14,378)   | (15,489)         | (18,608)              |
| Benefit for income taxes  |  |                  |                       |
| Net Loss  | \$ (14,378)  | \$ (15,489)      | \$ (18,608)           |
| Net loss per share basic and diluted  | \$ (2.27)  | \$ (0.50)        | \$ (0.60)             |
| Weighted-average number of common shares used in net loss per share basic and diluted | 6,340  | 30,822           | 30,889                |

|                             | Three Months Ended                                   |                  |                       |                      |
|-----------------------------|--|------------------|-----------------------|----------------------|
|                             | March 31,<br>2009                                    | June 30,<br>2009 | September 30,<br>2009 | December 31,<br>2009 |
|                             | (in thousands, except per share data)<br>(unaudited) |                  |                       |                      |
| Collaboration revenue       | \$ 3,670   | \$ 5,096         | \$ 5,917              | \$ 6,036             |
| Operating expenses:         |  |                  |                       |                      |
| Research and development    | 9,729  | 12,071           | 16,526                | 13,466               |
| General and administrative  | 2,571  | 2,424            | 2,509                 | 2,616                |
|                             | 12,300   | 14,495           | 19,035                | 16,082               |
| Loss from operations        | (8,630)  | (9,399)          | (13,118)              | (10,046)             |
| Other income and expense:   |  |                  |                       |                      |
| Other income (expense), net | (62)   | (155)            | (56)                  | (60)                 |
| Interest expense            | (743)  | (720)            | (678)                 | (670)                |
| Interest income             | 28   | 39               | 54                    | 23                   |
| Other income (expense), net | (777)  | (836)            | (680)                 | (707)                |

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|   |            |             |             |             |
|---|------------|-------------|-------------|-------------|
| Net loss before benefit for income taxes  | (9,407)    | (10,235)    | (13,798)    | (10,753)    |
| Benefit for income taxes  |            |             | 63          | 37          |
| Net Loss  | \$ (9,407) | \$ (10,235) | \$ (13,735) | \$ (10,716) |
| Net loss per share basic and diluted  | \$ (5.92)  | \$ (6.41)   | \$ (8.53)   | \$ (6.57)   |
| Weighted-average number of common shares used in net loss per share basic and diluted | 1,590      | 1,596       | 1,611       | 1,630       |

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|   | March 31,<br>2008 | Three Months Ended |                       |                      |
|---|-------------------|--------------------|-----------------------|----------------------|
|   |                   | June 30,<br>2008   | September 30,<br>2008 | December 31,<br>2008 |
| (in thousands, except per share data)<br>(unaudited)                                  |                   |                    |                       |                      |
| Collaboration revenue   | \$ 3,656          | \$ 3,964           | \$ 7,432              | \$ 4,608             |
| Operating expenses:   |                   |                    |                       |                      |
| Research and development  | 9,619             | 10,973             | 10,820                | 10,408               |
| General and administrative  | 2,953             | 2,011              | 2,086                 | 2,115                |
|   | 12,572            | 12,984             | 12,906                | 12,523               |
| Loss from operations  | (8,916)           | (9,020)            | (5,474)               | (7,915)              |
| Other income and expense:   |                   |                    |                       |                      |
| Other income (expense), net   | 74                | (196)              | (101)                 | (8)                  |
| Interest expense  | (446)             | (418)              | (458)                 | (764)                |
| Interest income   | 576               | 335                | 193                   | 65                   |
| Other income (expense), net   | 204               | (279)              | (366)                 | (707)                |
| Net loss before taxes   | (8,712)           | (9,299)            | (5,840)               | (8,622)              |
| Tax benefit   |                   |                    |                       |                      |
| Net loss  | \$ (8,712)        | \$ (9,299)         | \$ (5,840)            | \$ (8,622)           |
| Net loss per share basic and diluted  | \$ (5.93)         | \$ (5.90)          | \$ (3.69)             | \$ (5.44)            |
| Weighted-average number of common shares used in net loss per share basic and diluted | 1,470             | 1,575              | 1,583                 | 1,586                |

**Liquidity and Capital Resources**

We have funded our operations principally through the sale of equity securities sold in connection with our initial public offering, the private placement of equity securities, revenue from strategic partnerships, debt financing and interest income. As of September 30, 2010, we have received gross proceeds of \$89.7 million from the sale of common stock in our initial public offering and \$169.6 million from the sale of convertible preferred stock, including \$32.9 million from the sale of 11,250,000 shares of series E convertible preferred stock in 2009. As of September 30, 2010, we had received an aggregate of \$118.1 million in cash from our three agreements with Merck and our agreements with OSI Pharmaceuticals, Biogen Idec, and Eli Lilly, and \$25.0 million in funding from our debt financing with Hercules Technology Growth Capital and certain of its affiliates. As of September 30, 2010, we had cash, cash equivalents and marketable securities of approximately \$87.0 million. Currently, our funds are invested in money market funds, U.S. government agency securities and commercial paper. The following table sets forth the primary sources and uses of cash for each of the periods set forth below:

|   | 2007       | Years Ended          |            | Nine Months Ended     |             |
|---|------------|----------------------|------------|-----------------------|-------------|
|   |            | December 31,<br>2008 | 2009       | September 30,<br>2009 | 2010        |
| (in thousands)<br>(unaudited, in thousands)         |            |                      |            |                       |             |
| Net cash used in operating activities               | \$ (8,605) | \$ (35,301)          | \$ (9,973) | \$ (344)              | \$ (48,198) |
| Net cash provided by (used in) investing activities | (39,894)   | 28,151               | 3,414      | (11,988)              | (42,349)    |
| Net cash provided by financing activities           | 52,834     | 6,881                | 31,035     | 31,702                | 85,303      |

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|  |          |          |           |           |            |
|--|----------|----------|-----------|-----------|------------|
| Net increase (decrease) in cash and cash equivalents | \$ 4,335 | \$ (269) | \$ 24,476 | \$ 19,370 | \$ (5,244) |
|--|----------|----------|-----------|-----------|------------|

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 up-front 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 up-front 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.



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For the nine months ended September 30, 2009 and 2010, our operating activities used cash of \$0.3 million, and \$48.2 million, respectively. The cash used in operations for the nine months ended September 30, 2010 was due primarily to our net loss adjusted for non-cash items as well as a \$2.3 million increase in prepaid expenses primarily associated with advance payments for our clinical trials, and a decrease in deferred revenue of \$6.4 million related to the recognition of previously deferred revenue. The cash used in operating activities for the nine months ended September 30, 2009 was primarily the result of our net loss adjusted for non-cash items and an increase in deferred revenue of \$23.9 million related to up-front license payments, near term milestones and equity premiums from our agreements with Biogen Idec and OSI Pharmaceuticals completed in 2009 and an increase in accrued clinical expenses of \$4.1 million primarily related to our phase 2 clinical trial of tivozanib and costs in preparation for our phase 3 clinical trial of tivozanib.

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.

For the nine months ended September 30, 2009 and 2010, our investing activities used cash of \$12.0 million, and \$42.3 million, respectively. The cash used by investing activities for the nine months ended September 30, 2009 and 2010 was primarily the net result of purchases of marketable securities partially offset by maturities and sales, in addition to purchases of property and equipment of \$1.2 million and \$1.3 million, respectively.

During 2007, 2008 and 2009, our financing activities provided cash of \$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 by financing activities 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.

For the nine months ended September 30, 2009 and 2010, our financing activities provided cash of \$31.7 million and \$85.3 million, respectively. The cash provided by financing activities during the first nine months of 2010 was due to the sale and issuance of 9,000,000 shares of common stock at a price of \$9.00 per share in our initial public offering with net proceeds of \$72.2 million, the exercise of the option to purchase an additional 968,539 shares by the underwriters in the initial public offering resulting in net proceeds of \$8.1 million, stock option exercises of \$0.7 million, and net proceeds of \$7.6 million from the refinancing of loans payable from our loan agreement entered in to with affiliates of Hercules Technology Growth Capital, offset partially by principal payments on loans payable in the amount of \$3.3 million. The cash provided by financing activities during the first nine months of 2009 was due to the sale of 11,250,000 shares of series E convertible preferred stock with net proceeds of \$32.9 million, offset partially by the principal payments on loans payable of \$1.2 million.

**Credit Facilities.** On March 29, 2006, we entered into a \$15.0 million financing agreement with Hercules Technology Growth Capital 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 Technology Growth Capital and Comerica Bank, which we refer to as the 2008 loan. The full amount of the 2008 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 2008 loan was repayable over 48 months beginning June 2008, with the first 18 payments representing interest only. The 2008 loan also called for a deferred charge of 5.95% to be paid upon maturity. The deferred charge of \$1.3 million was recorded as a loan discount and was 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 was not contingent on any future event. Interest was payable at a fixed interest rate of 9.75%. The 2008 loan was 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.

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On May 28, 2010, we entered into a new loan and security agreement with Hercules Technology II, L.P. and Hercules Technology III, L.P., affiliates of Hercules Technology Growth Capital, referred to as the 2010 loan, pursuant to which we received a loan in the aggregate principal amount of \$25.0 million. In connection with the 2010 loan, we paid off the remaining outstanding principal and interest of \$17.4 million under the 2008 loan. We are required to repay the aggregate principal balance that is outstanding under the 2010 loan in 30 equal monthly installments of principal starting on April 1, 2011, provided, however, that such date will be extended under certain circumstances specified in the 2010 loan. The 2010 loan requires a deferred charge of \$1.25 million to be paid in May 2012 related to the termination of the 2008 loan. The 2010 loan also includes an obligation to pay an additional deferred charge of \$1.24 million due upon the maturity of the loan which has been recorded as a loan discount and is being amortized to interest expense over the term of the 2010 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. Per annum interest is payable at the greater of 11.9% and an amount equal to 11.9% plus the prime rate of interest minus 4.75%, provided however, that the per annum interest shall not exceed 15.0%. We must make interest payments on the loan each month following the date of borrowing under the 2010 loan. The entire principal balance and all accrued but unpaid interest, plus the end of term payment in the amount of approximately \$1.24 million, will be due and payable on September 1, 2013, provided, however, such amounts will be due and payable on a later date under certain circumstances specified in the 2010 loan.

The 2010 loan is secured by a lien on all of our personal property, as of, or acquired after, the date of the 2010 loan agreement, except for intellectual property. As of September 30, 2010, the principal balance outstanding was \$25.0 million.

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 were repayable over 54 months, the first six of which were 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 aggregate principal outstanding under the equipment line and the refinancing line was fully paid in June 2010. There is no remaining ability to borrow under the equipment line and refinancing line with General Electric Capital Corporation.

***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. We believe that our existing cash and cash equivalents, including the proceeds received from our sale of common stock in the private placement in November 2010, marketable securities, and 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 first half of 2012.

If our available cash and cash equivalents are insufficient to satisfy our liquidity requirements, or if we identify 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 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.

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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 September 30, 2010:

|   | Total          | Less than<br>1 Year | 1 to 3<br>Years | 4 to 5<br>Years | After 5<br>Years |
|---|----------------|---------------------|-----------------|-----------------|------------------|
|   | (in thousands) |                     |                 |                 |                  |
| Short and long-term debt (including interest) | \$ 33,094      | \$ 7,301            | \$ 25,793       | \$              | \$               |
| Operating lease obligations                   | 7,930          | 2,453               | 4,557           | 920             |                  |
| Other License Agreements <sup>(1)</sup>       | 925            | 525                 | 350             | 50              |                  |
| Total contractual cash obligations            | \$ 41,949      | \$ 10,279           | \$ 30,700       | \$ 970          | \$               |

- (1) As discussed in Note 7 to our audited consolidated financial statements, we have executed license agreements for patented technology and other technology related to research projects, including technology to humanize AV-299 and other antibody product candidates. The license agreements required us to pay non-refundable 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

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maximum of \$475,000 per year. We have included one milestone payment of \$50,000 in the table above, but have not included any additional milestone payments 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.

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### **New Accounting Pronouncements**

In October 2009, the FASB issued Accounting Standards Update ( ASU ) 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 we 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.

In February 2010, the FASB issued amended guidance on subsequent events. Under this amended guidance, SEC filers are no longer required to disclose the date through which subsequent events have been evaluated in originally issued and revised financial statements. This guidance was effective immediately and we adopted these new requirements upon issuance of this guidance.

In April 2010, the FASB issued ASU No. 2010-17, *Revenue Recognition Milestone Method* (ASU 2010-017). ASU 2010-017 provides guidance in applying the milestone method of revenue recognition to research or development arrangements. This guidance concludes that the milestone method is a valid application of the proportional performance model when applied to research or development arrangements. Accordingly, an entity can make an accounting policy election to recognize a payment that is contingent upon the achievement of a substantive milestone in its entirety in the period in which the milestone is achieved. The guidance is effective for fiscal years, and interim periods within those years, beginning on or after June 15, 2010. The adoption of this accounting standard is not expected to impact our financial position or results of operations.

### **Quantitative and Qualitative Disclosures About Market Risks**

We are exposed to market risk related to changes in interest rates. As of September 30, 2010 and December 31, 2009, we had cash and cash equivalents and marketable securities of \$87.0 million and \$51.3 million, respectively, consisting of money market funds, U.S. Treasuries, U.S. government agency securities, corporate debt 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 bears interest at variable rates. In May 2010, we entered into a new loan agreement with affiliates of Hercules Technology Growth Capital pursuant to which we received a loan in the aggregate principal amount of \$25.0 million. Per annum interest is payable at the greater of 11.9% and 11.9% plus the prime rate of interest minus 4.75%, not to exceed 15%. As a result of the 15% maximum per annum interest rate under the new loan agreement, we have limited exposure to changes in interest rates on these borrowings under this loan. For every 1% increase in prime over 4.75% on the outstanding debt amount as of September 30, 2010, we would have a decrease in future annual cash flows of approximately \$235,000 over the next twelve month period.

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**Table of Contents****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 phase 2 clinical 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 August 2010, we completed enrollment of our 517-patient phase 3 clinical trial of tivozanib in patients with advanced RCC, which we refer to as the TIVO-1 study. 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.

In addition to the TIVO-1 study, 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 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.

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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 recently initiated a phase 2 clinical trial for non-small cell lung cancer. In 2007, we entered into an agreement with Merck (formerly Schering-Plough Corporation) under which we granted Merck exclusive worldwide rights to co-develop and commercialize AV-299 and under which Merck funded all development and manufacturing expenses, subject to an agreed-upon budget. On September 28, 2010, we received notice from Merck of termination of the collaboration agreement effective as of December 27, 2010 at which point we will be responsible for funding all future development, manufacturing and commercialization costs for the AV-299 program.

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.

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.

**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.



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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 \$7 billion worldwide in 2009, based on 2009 annual reports made publicly available by companies marketing such drugs. According to EvaluatePharma<sup>®</sup> 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.

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

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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.

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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 the highest grade (Grade 3) of 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 gastrointestinal 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 completed a 272-patient phase 2 clinical trial of tivozanib in advanced RCC in August of 2010. 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 August 2010, we completed enrollment of our 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. We anticipate receiving topline data from this registration trial in mid-2011. 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 58,240 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 2009 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.

**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.



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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 received tivozanib for over two years 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 (version 1.0), 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  $\geq 25\%$  tumor regression continued on tivozanib for the next 12 weeks 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  $\geq 25\%$  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 after the initial 16 week treatment period 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.

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). Progression-free survival was significantly higher among patients with clear cell RCC (12.5 months) compared to patients with non clear cell RCC (6.7 months). Within the group of 176 patients with clear cell histology and prior nephrectomy, Progression-free survival was similar between those patients who were treatment naïve (14.3 months), and those who had received prior therapy with cytokines and/or chemotherapy (15.8 months). Based on preliminary data as of June 7, 2010, 33 patients had remained on therapy for more than 2 years.

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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)

| Adverse Event              | Severity         |                  |                  |                  | Total<br># (%) |
|----------------------------|------------------|------------------|------------------|------------------|----------------|
|                            | Grade 1<br># (%) | Grade 2<br># (%) | Grade 3<br># (%) | Grade 4<br># (%) |                |
| 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 European Medicines Agency, or EMA, we initiated a phase 3 clinical trial in patients with advanced RCC in December 2009. We completed enrollment in this clinical trial in August 2010. We refer to the phase 3 clinical trial as our TIVO-1 study. The TIVO-1 study has enrolled 517 patients 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 in which 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 was 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 EMA, we have set the number of patients to be enrolled in the clinical trial based on standard statistical assumptions and an assumed 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-alpha 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-alpha or interleukin-2. Because the TIVO-1 study allowed 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 EMA indicated that Nexavar is an acceptable choice as the active comparator in the TIVO-1 study.

Enrollment into the TIVO-1 study was completed in August 2010. In the TIVO-1 study, patients have been randomized in approximately equal numbers to treatment with tivozanib or Nexavar. Patients randomized to the tivozanib treatment arm 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 receive the approved dose of Nexavar, which is 400 mg twice a day. Patients randomized to the tivozanib treatment arm who develop documented disease progression will be discontinued from the clinical trial. Patients randomized to the Nexavar treatment arm who develop 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.

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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.

### *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 results presented at the ASCO Annual Meeting in 2010 for the ATROVA trial, which tested the combination of Avastin and Torisel in patients with RCC, showed substantial toxicity with this combination.

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 September 15, 2010, with a median duration of treatment of 21.1 weeks, no dose-limiting toxicities have been reported. As of September 15, 2010, preliminary results of this ongoing study show tumor shrinkage in 22 out of 28 patients in all dose groups evaluated, and eight 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 October 1, 2010, 29 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 with pancreatic cancer, and two patients with esophageal 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 has been 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.

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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 October 1, 2010, 18 patients were enrolled in this trial, of whom 5 patients have demonstrated a confirmed partial response. We have completed enrollment in this clinical trial. The maximal tolerated dose has been defined as full dose of 1.5 mg of tivozanib in combination with full dose paclitaxel chemotherapy (90 mg/m<sup>2</sup>) administered weekly.

*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. In this clinical trial we are testing a continuous dosing regimen of tivozanib and expect that the trial will also provide preliminary 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.

### **Orphan Drug Designation.**

In June of 2010, the EMA granted orphan medicinal product designation for tivozanib for RCC. According to the EMA, tivozanib was awarded the designation based on the prevalence of RCC among people in the European Union; the life-threatening nature of the disease, particularly for those with advanced or metastatic RCC; and the assumption that tivozanib may provide significant benefit for patients with RCC, and may be more potent and specific than existing treatments with similar mechanism of action as supported by preliminary clinical results. Companies granted orphan medicinal product designation by the EMA receive, among several other benefits, market exclusivity in the European Union for ten years following market authorization. Demonstration of quality, safety and efficacy is necessary before a designated orphan medicinal product can be granted a marketing authorization.

### ***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 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.

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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, and to determine the safety, tolerability, and maximum tolerated dose of AV-299 in combination with Tarceva, an approved EGFR inhibitor. 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. 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 metastatic tumors.

Preclinical and clinical observations suggest that increased HGF and/or c-Met receptor amplification may confer resistance to EGFR inhibitors. Recently, encouraging Phase 2 clinical data were reported at the 2010 ASCO Annual Meeting with a small molecule c-Met inhibitor in combination with an epidermal growth factor receptor (EGFR) tyrosine kinase inhibitor (TKI) in patients with advanced, refractory NSCLC. Additionally, phase 2 clinical data were reported at the 2010 35th Congress of the European Society for Medical Oncology (ESMO) with an antibody to the c-Met receptor in combination with an EGFR TKI in patients with advanced, refractory NSCLC. This phase 2 clinical data demonstrated encouraging trends in progression-free survival and overall survival for a subset of patients treated with this antibody. Collectively, these data signal the potential patient benefit from combination therapy of an EGFR TKI and an inhibitor of the HGF/c-Met pathway.

In June 2010, we commenced a phase 2 clinical trial testing a combination of AV-299 with Iressa (gefitinib), an EGFR inhibitor, versus Iressa alone in patients with newly diagnosed non-small-cell lung cancer. Patients are randomized 1:1 to receive AV-299 in combination with Iressa or Iressa monotherapy. Patients who demonstrate disease progression during treatment with Iressa alone will have the opportunity to be treated with AV-299 in combination with Iressa provided that safety is maintained and the patient continues to meet trial eligibility criteria. This 170-patient, randomized clinical trial, which is being conducted in Asia, will study response rate and progression-free survival in two distinct patient subsets: those with activating EGFR mutations and those with wild-type EGFR. We expect to receive topline efficacy data from the phase 2 trial in late 2012.

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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.

In March 2007, we entered into a collaboration agreement with Merck under which we granted Merck worldwide rights to develop and commercialize AV-299. Pursuant to the terms of the collaboration agreement, Merck funded all development and manufacturing expenses, subject to an agreed-upon budget, was responsible for manufacturing AV-299 for clinical use and was required to pay us development milestones and royalties on the sale of AV-299. On September 28, 2010, we received notice from Merck of termination of the collaboration agreement effective as of December 27, 2010 at which point we will be responsible for all future development, manufacturing and commercialization funding for the AV-299 program.

### ***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.

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. We selected a development candidate in March 2010 and recently commenced process development for 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.





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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.

*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.

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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.

*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.

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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 and OSI 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 gene mutations. Oncogene activating mutations function to promote cell growth. By analogy to driving a car, oncogene activating mutations act much like 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 xenograft 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.

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### ***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 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 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.

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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 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.

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### ***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.

### ***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.

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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 useful for identifying candidate biomarkers. We have two issued United States patents on different biomarker tests for identifying patients likely to be sensitive or resistant to treatment with tivozanib. 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 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 2009 sales in excess of \$7.0 billion worldwide, based on 2009 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.



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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), Abbott's ABT-869 (linifanib), AstraZeneca plc's AZD2171 (Recentin, cediranib) and AZD6474 (Zactima, vandetanib), Bayer AG's BAY-73-4506 (regorafenib), Boehringer Ingelheim International GmbH's BIBF-1120, Bristol-Myers Squibb Company's BMS-582664 (brivanib alaninate), Exelixis Inc.'s XL-184, ImClone LLC's IMC-1121b (ramucirumab), Onco Therapy Science Inc.'s OTS-102 (elpamotide) 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 (rilatumumab), currently in phase 2 clinical trials, and Takeda's TAK-701 (HuL2G7, under license from Galaxy Biotech, LLC), currently in phase 1 clinical trials.

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), Incyte Corp.'s and Novartis' INCB-028060, Pfizer's PF-2341066 (crizotinib) and Exelixis' 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, which is currently in phase 2 clinical development, and Daiichi Sankyo's and Amgen's U3-1287 / AMG-888, which is 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 up-front payments, equity investments, research and development funding, payments upon achievement of specified milestones, and potential royalties from product sales.

Pursuant to the following strategic partnerships, 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 September 30, 2010 <sup>(1)</sup> |
| Kyowa Hakko Kirin   | December 2006             | Tivozanib <sup>(2)</sup>            | N/A  |
| OSI Pharmaceuticals | September 2007            | Target and Biomarker Identification | \$48.1 million                                   |
| Biogen Idec         | March 2009                | AV-203                              | \$55.0 million <sup>(3)</sup>                    |
| Merck               | November 2003             | Target Identification               | \$22.3 million                                   |
| Merck               | August 2005               | Biomarker Identification            | \$6.5 million                                    |

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- (1) Includes up-front 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.

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**Table of Contents*****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 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 March 2010, we made a one-time cash payment in the amount of \$10.0 million in connection with the initial dosing of patients in the TIVO-1 study. In addition, we are required to make certain milestone payments which could total, in the aggregate, \$50.0 million, 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.

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**Table of Contents*****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;

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, \$25.0 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

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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.

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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.

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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 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 each of June 2009 and April 2010, we received a \$5.0 million milestone payment for achievement of the first two pre-clinical discovery milestone under the agreement. We could also receive (i) additional pre-clinical discovery and development milestone payments of \$5.0 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 ErbB3 antibody product in the applicable country, and (2) any regulatory exclusivity applicable to the ErbB3 antibody product in that country.

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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 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.



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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 September 30, 2010, 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: 5 issued; 1 pending; expirations ranging from 2018 to 2030

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 applications: 2 pending; expirations ranging from 2029 to 2030

our antibody product pipeline and related technologies

U.S. patents: 3 issued; 8 pending; expirations ranging from 2027 to 2031

European patents: none granted; 2 pending; expirations 2027

International applications: 2 pending; expirations 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 2025 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 are two of our own issued U.S. patents that cover different biomarker tests for identifying human patients likely to respond to treatment with tivozanib, and a pending application on a method of using tivozanib in combination with temsirolimus.

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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, ErbB3 antibodies, FGFR2 antibodies, EGFR antibodies, RON antibodies, Notch1 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.

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 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.

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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.

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*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 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.

Prior to Merck's termination of its collaboration agreement with us, multiple batches of drug substance were produced by Merck to support clinical trials of AV-299 through phase 2 clinical trials. As of December 27, 2010, the effective date of the termination of our collaboration with Merck, we will be responsible for the all process development and all manufacturing of AV-299 for future development and commercialization.

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.



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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 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.

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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 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.

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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.

### ***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.

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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.

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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 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.

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The EMA 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 EMA is typically provided based on questions concerning, for example, quality (chemistry, manufacturing and controls testing), nonclinical testing and clinical studies, and 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 EMA'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.

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

### *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 EMA 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 EMA 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 EMA, 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.



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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, EMA ensures that the opinion of the CHMP is given within 150 days.

### ***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.

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### ***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/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 November 1, 2010, we had 138 full-time employees, including a total of 33 employees with M.D. or Ph.D. degrees. Of our workforce, 113 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.

**Table of Contents****MANAGEMENT**

The following table sets forth the name, age and position of each of our executive officers and directors as of September 30, 2010.

| <b>Name</b>                                | <b>Age</b> | <b>Position</b>                                  |
|--|------------|--|
| <b>Executive Officers</b>                  |            |  |
| Tuan Ha-Ngoc                               | 58         | Chief Executive Officer, President and Director  |
| David Johnston                             | 55         | Chief Financial Officer                          |
| Elan Ezickson                              | 47         | Executive Vice President, Chief Business Officer |
| William Slichenmyer, M.D., Sc.M.           | 52         | Chief Medical Officer                            |
| Michael P. Bailey                          | 45         | Chief Commercial Officer                         |
| Jeno Gyuris, Ph.D.                         | 50         | Senior Vice President, Head of Research          |
| <b>Directors</b>                           |            |  |
| Kenneth M. Bate <sup>(1)(2)</sup>          | 60         | Director   |
| Douglas G. Cole, M.D. <sup>(1)</sup>       | 50         | Director   |
| Ronald A. DePinho, M.D.                    | 55         | Director   |
| Anthony B. Evnin, Ph.D. <sup>(1)(3)</sup>  | 69         | Director (Chairman of the Board)                 |
| Nicholas G. Galakatos <sup>(2)</sup>       | 53         | Director   |
| Russell Hirsch, M.D., Ph.D. <sup>(2)</sup> | 48         | Director   |
| Raju Kucherlapati, Ph.D. <sup>(3)</sup>    | 67         | Director   |
| Kenneth E. Weg                             | 72         | Director   |
| Robert C. Young, M.D. <sup>(3)</sup>       | 70         | 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. Mr. Ha-Ngoc served on the Board of Directors of ArQule, Inc., from 2002 until 2006. He holds an M.B.A. from INSEAD and an M.A. in pharmacy from the University of Paris, France. We believe that Mr. Ha-Ngoc's qualifications to serve on our Board of Directors include his position as our chief executive officer and his significant experience in the cancer research field and corporate strategy development, including his executive leadership roles at global pharmaceutical companies, and his experiences in commercializing potential drug candidates, including his commercialization experience in North America, Europe and Japan.

**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.

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**Elan Ezickson** was named Executive Vice President effective as of July 1, 2010 and 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 and the Board of Trustees of the Commonwealth Covenant Fund. Mr. Ezickson holds a B.A in Political Science from Yale University and a J.D. from the Columbia University School of Law.

**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 Sc.M. in clinical investigation from Johns Hopkins Oncology Center.

**Michael P. Bailey** has served as our Chief Commercial Officer since September 2010. Prior to joining our company, Mr. Bailey served as Senior Vice President, Business Development and Chief Commercial Officer at Synta Pharmaceuticals from 2008 to September 2010. From 1999 to 2008, Mr. Bailey worked at ImClone, leading their commercial organization, most recently as Senior Vice President of Commercial Operations. Prior to his role at ImClone, Mr. Bailey managed the cardiovascular development portfolio at Genentech, Inc. from 1997 to 1999. Mr. Bailey started his career in the pharmaceutical industry as part of Smith-Kline Beecham's Executive Marketing Development Program, where he held a variety of commercial roles from 1992 to 1997, including sales, strategic planning, and product management. Mr. Bailey received a B.S. in psychology from St. Lawrence University and an M.B.A. in international marketing from the University of Notre Dame Graduate School of Business.

**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**

We believe that our Board of Directors should be composed of individuals with sophistication and experience in many substantive areas that will help us achieve our goals of delivering beneficial medicines to patients and generating value for our stockholders. The common qualifications possessed by all our board members include a commitment to represent both the short- and long-term interests of our stockholders; strong personal and professional ethics, integrity and values; strong business acumen; and achievement in the pharmaceutical and life science industry. These areas are in addition to the personal qualifications described in each of our directors' biographies set forth below. We believe that all current members of our board of directors possess the professional and personal qualifications necessary to serve on our board of 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., BioMarin Pharmaceutical, Inc. and Archemix Corp. During the last five years, Mr. Bate has served as a director of NitroMed, Inc. and Coley Pharmaceutical Group, Inc. He holds a B.A. in Chemistry from Williams College and an M.B.A. from The Wharton School of the University of Pennsylvania. We believe Mr. Bate's qualifications to serve on our Board of Directors include his operating, finance, commercial, transactional and senior management experience in the industry, such as his experience as Chief Executive Officer of Archemix Corp. and NitroMed, Inc., and Head of Commercial Operations and Chief Financial Officer at Millennium Pharmaceuticals, Inc., as well as his experience serving on the boards of directors of other public companies in the life sciences industry, such as Cubist Pharmaceuticals, Inc. and BioMarin Pharmaceutical, Inc.

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**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, Tetrphase Pharmaceuticals, Inc., Concert Pharmaceuticals, Inc., Quanterix Corporation, Agios Pharmaceuticals, Inc., Selecta Biosciences, Inc., Avedro, Inc., Resolvix Pharmaceuticals, Inc., Receptos, Inc., and Seventh Sense Biosystems, Inc. In the past five years Dr. Cole has served on the board of Zalicus, Inc. (formerly CombinatoRx). 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. We believe Dr. Cole's qualifications to sit on our Board of Directors include his substantial experience as an investor in early stage biopharmaceutical and life sciences companies, as well as his experience of serving on the board of directors for several biopharmaceutical companies, including Ensemble Discovery Corporation, Tetrphase Pharmaceuticals, Inc., Concert Pharmaceuticals, Inc., Quanterix Corporation, Agios Pharmaceuticals, Inc., Selecta Biosciences, Inc., Avedro, Inc., Resolvix Pharmaceuticals, Inc., Receptos, Inc., and Seventh Sense Biosystems, Inc.

**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. He currently serves on the Board of Directors at Karyopharm Therapeutics, Inc. 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. During the last five years, Dr. DePinho has served as Chair of the NIH Human Cancer Genome (TCGA) External Advisory Board and NCI Mouse Models of Human Cancer Consortium. He is a member of the Institute of Medicine of the National Academies and Fellow of the American Academy of Arts and Sciences. 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. We believe Dr. DePinho is qualified to sit on our Board of Directors given his role as a scientific founder of our company's tumor maintenance, gene discovery and human response platform. His qualifications also include his leadership in the field of cancer modeling and cancer genetics, his extensive experience in the research, development and treatment of oncological diseases, which are the focus of our research and development programs, as well as his practical experience as a physician.

**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., Altea Therapeutics Corporation, Celladon Corporation, Constellation Pharmaceuticals, Inc., and Metabolex, Inc. During the last five years, Dr. Evnin served as a director of Memory Pharmaceuticals Corp., Sunesis, Inc., Renovis, Inc., and Coley Pharmaceuticals Group, 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. We believe Dr. Evnin's qualifications to sit on our Board of Directors include his substantial experience as an investor in, and director of, early stage biopharmaceutical companies, including Icagen, Inc. and Infinity Pharmaceuticals, Inc., as well as his expertise in corporate strategy at a publicly traded biopharmaceutical company.

**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. From 1997 to 2000 Dr. Galakatos served as Vice President, New Business at Millennium Pharmaceuticals, Inc. He is a founder of TransForm Pharmaceuticals and Millennium Predictive Medicine. He serves on the boards of a number of private companies, including Aerovance Inc., Link Medicine Corporation, Nanostring Technologies, Inc., Ophthotech, Inc. Portola Pharmaceuticals, Inc. and Taligen Therapeutics, Inc. During the last five years, Dr. Galakatos has served as a member of the board of directors of Cornerstone Therapeutics, Inc. (formerly Critical Therapeutics, Inc.) and Affyamx, Inc. where he was the Lead Director. He holds a B.A. in chemistry from Reed College and a Ph.D. in organic chemistry from the Massachusetts Institute of Technology. We believe Dr. Galakatos' qualifications to sit on our Board of Directors include his substantial experience as an investor in, and director of, early stage biopharmaceutical companies such as TransForm Pharmaceuticals and Affymax, Inc., as well as his expertise in corporate strategy in a public biopharmaceutical company, particularly as Vice President, New Business at Millennium Pharmaceuticals.

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**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. and serves or has served on the boards of a number of private companies, including Portola Pharmaceuticals, Inc., Visiogen, Inc., DFine, Inc., Baxano, Inc., SentreHEART, Inc., Nine Point Medical, Inc. and Opus Medical, Inc. 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. We believe Dr. Hirsch's qualifications to sit on our Board of Directors include his medical background, his substantial experience in the development and direction of early stage biopharmaceutical companies as well as his service on the board of directors at Hansen Medical, Inc.

**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. During the last five years Dr. Kucherlapati has served as a member of the Board of Directors at Millennium Pharmaceuticals and Abgenix, Inc. 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. We believe Dr. Kucherlapati is qualified to sit on our Board of Directors given his role as a scientific founder of our company's human response platform. In addition, we believe Dr. Kucherlapati's qualifications to sit on our Board of Directors include his substantial experience in the development and growth of early stage biopharmaceutical companies such as Cell Genesys, Inc., Abgenix, Inc. and at large global pharmaceutical companies such as Millennium Pharmaceuticals, Inc. and his service as a member of the board of directors at publicly traded life sciences companies such as Enlight Millennium Pharmaceuticals, Inc. and Abgenix, Inc.

**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. During the last five years Mr. Weg has served as a member of the board of directors at Millennium Pharmaceuticals, Inc. He is also a founder and chairman 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. We believe Mr. Weg's qualifications to sit on our Board of Directors include his extensive leadership experience in the global pharmaceutical industry, including his extensive executive leadership at Bristol-Myers Squibb Company and his service as a member of the board of directors of Millennium Pharmaceuticals, Inc.

**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 (ASCO), the American Cancer Society and the International Gynecologic Cancer Society and past Chairman of the Board of Scientific Advisors of the National Cancer Institute and is past Chairman of the Comprehensive Cancer Network. Dr. Young serves as Chairman of the editorial board of Oncology Times. He also serves on the Boards of Directors of West Pharmaceutical Services, Inc. and Human Genome Sciences, Inc. During the last five years Dr. Young has served as a member of the scientific advisory boards of the Dana Farber Cancer Center, the Huntsman Cancer Center and the Ohio State Cancer Center. 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. We believe that Dr. Young's qualifications to serve on our Board of Directors include his substantial experience in cancer research as head of the Fox Chase Cancer Center and as Chairman of the Board of Scientific Advisors of the National Cancer Institute as well as his prior role with the National Cancer Policy Board at the Institute of Medicine, his service as a member of the board of directors at publicly traded life sciences companies West Pharmaceutical Services, Inc. and Human Genome Sciences, Inc., as well as his accomplished background as a board-certified physician.

**Table of Contents****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.

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:

| <b>Name</b>               | <b>Professional Affiliation</b>   |
|---------------------------|---|
| 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 |

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| <b>Name</b>               | <b>Professional Affiliation</b>  |
|---------------------------|--|
| 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 ten members, although we are authorized under our certificate of incorporation and bylaws to elect up to 11 members. 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 determined that none of Kenneth Bate, Douglas Cole, Anthony Evnin, Nicholas Galakatos, Russell Hirsch, Raju Kucherlapati, 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.



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### **Board Committees**

Our board of directors has established an audit committee, a compensation committee and a nominating and governance committee. Each committee operates under a charter approved by our board. A copy of each committee's charter is posted on the Corporate Governance section of our website, [www.aveopharma.com](http://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. Our audit committee's responsibilities 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.

#### ***Compensation Committee***

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The members of our compensation committee are Nicholas Galakatos, Kenneth Bate and Russell Hirsch. Nicholas Galakatos chairs the compensation committee. Our compensation committee's responsibilities include:

annually reviewing and approving corporate goals and objectives relevant to Chief Executive Officer compensation;

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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 Evin, Robert Young and Raju Kucherlapati. Anthony Evin chairs the nominating and governance committee. Our nominating and governance committee's responsibilities 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***

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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. A current copy of the code is posted on the Corporate Governance section of our website, [www.aveopharma.com](http://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, Executive Vice President, 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

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

***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.

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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.

Upon approval by our compensation committee, we have engaged Ms. Arnosti to review our non-executive bonus program for market competitiveness and overall design. In addition, she has advised us on stock option grants for new hires and annual awards for existing employees. In the past we have worked with Ms. Arnosti to review the competitiveness and design of all of our non-executive compensation programs including base salary, bonus and equity.



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Our compensation committee has particularly relied on data from the annual life science compensation survey of Radford Biotechnology Surveys. Specifically, in establishing 2009 and 2010 compensation, 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.

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.

### ***Risk Considerations in our Compensation Program***

We have reviewed our compensation policies and practices with our compensation and audit committees and have concluded that any risks arising from our policies and programs are not reasonably likely to have a material adverse effect on our company or business.

### ***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.

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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.

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.

In July 2010, Mr. Ezickson received an additional increase in salary of 5% over his 2010 base salary in connection with his promotion to Executive Vice President.

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                      | 2010                      |
|---------------------|---------------------------|---------------------------|
|                     | Annual<br>Base Salary(\$) | Annual<br>Base Salary(\$) |
| Tuan Ha-Ngoc        | \$ 412,000                | \$ 422,300                |
| David Johnston      | \$ 289,823                | \$ 297,070                |
| Elan Ezickson       | \$ 305,138                | \$ 328,404 <sup>(1)</sup> |
| Jeno Gyuris         | \$ 256,174                | \$ 285,634                |
| William Slichenmyer | \$ 340,000 <sup>(2)</sup> | \$ 342,833                |

- (1) Mr. Ezickson's 2010 annual base salary was \$312,766 until his promotion to Executive Vice President on July 1, 2010, at which time his salary was increased to \$328,404.



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- (2) 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.

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:

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

- (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.



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(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 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.

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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 <sup>(1)</sup>                     | \$ 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               |
| <b>Total</b>  | <b>100%</b>      |

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 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.

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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.



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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<br>Base<br>Salary (\$) | Target<br>Percentage of<br>2010 Annual<br>Base<br>Salary<br>(%) | Target<br>2010 Annual<br>Cash<br>Incentive<br>Award (\$) |
|---------------------|------------------------------------|---|--|
| Tuan Ha-Ngoc        | \$ 422,300                         | 50%   | \$ 211,150   |
| David Johnston      | \$ 297,070                         | 30%   | \$ 89,121  |
| Elan Ezickson       | \$ 328,404 <sup>(1)</sup>          | 40% <sup>(2)</sup>  | \$ 112,596 <sup>(3)</sup>                                |
| Jeno Gyuris         | \$ 285,634                         | 30%   | \$ 85,690  |
| William Slichenmyer | \$ 342,833                         | 40%   | \$ 137,133   |

- (1) Mr. Ezickson's annual base salary was \$312,766 until his promotion to Executive Vice President on July 1, 2010 when his salary was increased to \$328,404.
- (2) In connection with and effective upon his promotion on July 1, 2010, Mr. Ezickson's target bonus as a percentage of base salary was increased from 30% to 40%.
- (3) In connection with Mr. Ezickson's promotion on July 1, 2010, his target 2010 annual cash incentive award will be calculated on a prorated basis with the first six months of 2010 at 30% of \$312,766, his annual base salary prior to his promotion, and last six months of 2010 at 40% of \$328,404, his annual base salary after his promotion.

*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

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the amount and percentage of total equity on a diluted basis held by our executives.

All historical stock option grants prior to our initial public offering 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<br>Shares of<br>Common<br>Stock<br>Underlying<br>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 granted these stock options 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.

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| Name                | Number of Shares<br>of Common<br>Stock<br>Underlying<br>Annual<br>Performance<br>Option(1) | Number of Shares<br>of Common<br>Stock<br>Underlying<br>Milestone-Based<br>Option(2) | Total Number<br>of Shares of<br>Common<br>Stock<br>Underlying<br>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  |

- (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.

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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 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 (\$) <sup>(2)</sup> | Non-Equity Incentive                  |  | Total (\$)   |
|---|------|-------------|---------------------------|-----------------------------------|---------------------------------------|--|--------------|
|   |      |             |                           |                                   | Plan Compensation (\$) <sup>(3)</sup> | All Other Compensation (\$) <sup>(4)</sup> |              |
| Tuan Ha-Ngoc,<br>Chief Executive Officer                              | 2009 | \$ 411,572  |                           | \$ 362,940                        | \$ 185,400                            | \$ 9,737                                   | \$ 969,649   |
|   | 2008 | \$ 400,000  |                           | \$ 232,325                        | \$ 180,000                            | \$ 9,362                                   | \$ 821,687   |
| David Johnston,<br>Chief Financial Officer                            | 2009 | \$ 289,509  |                           | \$ 78,900                         | \$ 80,861                             | \$ 7,580                                   | \$ 456,850   |
|   | 2008 | \$ 280,000  | \$ 100,000 <sup>(1)</sup> |                                   | \$ 75,600                             | \$ 7,157                                   | \$ 462,757   |
| Elan Ezickson,<br>Executive Vice President,<br>Chief Business Officer | 2009 | \$ 304,907  |                           | \$ 94,680                         | \$ 86,507                             | \$ 7,130                                   | \$ 493,224   |
|   | 2008 | \$ 296,250  |                           | \$ 139,935                        | \$ 79,988                             | \$ 6,726                                   | \$ 522,899   |
| Jeno Gyuris,<br>Senior Vice President, Head of Research               | 2009 | \$ 255,981  |                           | \$ 78,900                         | \$ 71,473                             | \$ 6,954                                   | \$ 413,308   |
|   | 2008 | \$ 248,713  |                           | \$ 111,516                        | \$ 55,960                             | \$ 6,555                                   | \$ 422,744   |
| William Slichenmyer,<br>Chief Medical Officer                         | 2009 | \$ 102,137  | \$ 20,000 <sup>(5)</sup>  | \$ 1,305,675                      | \$ 42,160                             | \$ 2,213                                   | \$ 1,472,185 |

(1)

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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.

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- (2) The assumptions we used in valuing options are described under the caption "Stock-Based Compensation" in Note 14 to our audited financial statements included in this prospectus. This column reflects the aggregate grant date fair value as calculated in accordance with ASC 718 for the indicated year in connection with options we granted in the indicated year, adjusted to disregard the effects of any estimate of forfeitures related to service-based vesting.
- (3) Our compensation committee determined to pay Tuan Ha-Ngoc, David Johnston, Elan Ezickson, Jenó 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<br>401(k)<br>Contribution<br>(\$) | Group Life<br>Insurance<br>(\$) | Total<br>(\$) |
|--|------|---|---------------------------------|---------------|
| Tuan Ha-Ngoc,<br>Chief Executive Officer                           | 2009 | \$ 6,125                                  | \$ 3,612                        | \$ 9,737      |
|  | 2008 | \$ 5,750                                  | \$ 3,612                        | \$ 9,362      |
| David Johnston,<br>Chief Financial Officer                         | 2009 | \$ 6,125                                  | \$ 1,455                        | \$ 7,580      |
|  | 2008 | \$ 5,750                                  | \$ 1,407                        | \$ 7,157      |
| Elan Ezickson,<br>Executive Vice President, Chief Business Officer | 2009 | \$ 6,125                                  | \$ 1,005                        | \$ 7,130      |
|  | 2008 | \$ 5,750                                  | \$ 976                          | \$ 6,726      |
| Jeno Gyuris,<br>Senior Vice President, Head of Research            | 2009 | \$ 6,125                                  | \$ 829                          | \$ 6,954      |
|  | 2008 | \$ 5,750                                  | \$ 805                          | \$ 6,555      |
| William Slichenmyer,<br>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<br>Future<br>Payouts<br>Under Non-<br>Equity<br>Incentive<br>Plan<br>Awards <sup>(1)</sup><br>Target<br>(\$) | All Other<br>Option<br>Awards:<br>Number of<br>Securities<br>Underlying<br>Options<br>(#) <sup>(2)</sup> | Exercise or<br>Base<br>Price<br>of Option<br>Awards<br>(\$/sh) <sup>(3)</sup> | Grant Date<br>Fair Value of<br>Stock and<br>Option<br>Awards <sup>(4)</sup><br>(\$) |
|---------------------|------------|--|--|---|---|
| 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  |

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- (1) Represents the target payout levels under the annual cash incentive program. Target payouts for Tuan Ha-Ngoc, David Johnston, Elan Ezickson, Jenő 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. 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.

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- (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 audited 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.

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





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- (2) These options vest in equal monthly installments through January 1, 2013.
- (3) These options vested as to 25% of the shares on September 14, 2010 and vest 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 vested 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 vest as to an additional 1/48 of the shares per month thereafter. Pursuant to the terms of the option agreements, these options vested as to an additional aggregate 37,500 shares upon successful completion of our initial public offering.
- (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.

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*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.

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, Jenő Gyuris and William Slichenmyer, each such named 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 contendere 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;



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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;

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);

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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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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.

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

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|  |  |                           |                           |
|--|--|---------------------------|---------------------------|
| William Slichenmyer<br>Chief Medical Officer | Base Salary  | \$ 340,000 <sup>(1)</sup> | \$ 340,000 <sup>(5)</sup> |
|  | Bonus  | \$ 45,333 <sup>(2)</sup>  | \$ 181,333 <sup>(6)</sup> |
|  | Healthcare Benefits  | \$ 15,778 <sup>(3)</sup>  | \$ 15,778 <sup>(7)</sup>  |
|  | Market Value of Awards Vesting on Termination <sup>(4)</sup> | \$                        | \$ 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 vested as to an additional aggregate 37,500 shares upon the successful completion of our initial public offering.

**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.

As of September 30, 2010, there were options to purchase 3,265,083 shares of common stock outstanding under the 2002 stock plan at a weighted average exercise price of \$5.72 per share, 598,893 shares of common stock had been issued pursuant to the exercise of options granted under the 2002 stock plan and 345,000 shares of common stock (net of forfeitures) had been issued pursuant to restricted stock awards granted under the plan. As of September 30, 2010, there were no more shares of common stock reserved for grant under the 2002 stock plan.

Upon the effective date of the 2010 Stock Incentive Plan described below, all shares of common stock reserved for issuance under the 2002 stock plan that remained available for issuance were rolled into the 2010 Stock Incentive Plan. 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 will also be rolled into the 2010 Stock Incentive Plan, up to a specified number of shares.

The 2002 stock plan provided for the grant of incentive stock options, nonstatutory stock options, restricted stock and other stock-based awards. Our employees, officers, directors, consultants and advisors were eligible to receive awards under the 2002 stock plan; however, incentive stock options could 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, administered the 2002 stock plan and, subject to any limitations in the 2002 stock plan, selected the recipients of awards and determined:

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

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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 2002 stock plan also permitted 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 would 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 could 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 could 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.

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***2010 Stock Incentive Plan***

Our 2010 Stock Incentive Plan, which we refer to as the 2010 stock plan was adopted by our board of directors on February 2, 2010 and approved by our stockholders on February 11, 2010 and became effective upon the closing of our initial public offering on March 17, 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 are reserved for issuance under the 2010 stock plan are the number of shares of our common stock reserved for issuance under the 2002 stock plan that remained available for grant under the 2002 stock plan immediately prior to the closing of our initial public 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.

As of September 30, 2010, there were options to purchase 216,058 shares of common stock outstanding under the 2010 stock plan at a weighted average exercise price of \$7.87 per share and no shares of common stock had been issued pursuant to the exercise of options granted under the 2010 stock plan. As of September 30, 2010, there were 1,719,028 shares of common stock reserved but not granted under the 2010 stock plan.

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 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.

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 are 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.

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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 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.

The commencement date of our first purchase plan period was 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.

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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 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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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 (\$) <sup>(1)</sup> | Option Awards (\$) <sup>(2)</sup> | All Other Compensation (\$) <sup>(3)</sup> | Total (\$) |
|--------------------------------------|---|-----------------------------------|--|------------|
| Kenneth Bate <sup>(4)(5)</sup>       | \$ 21,500                                       | \$ 39,200                         |  | \$ 45,966  |
| Douglas Cole <sup>(4)(5)</sup>       |   | \$ 65,880                         |  | \$ 32,940  |
| Ronald DePinho <sup>(4)(5)</sup>     | \$ 9,500  | \$ 65,880                         | \$ 100,000                                 | \$ 142,440 |
| Anthony Evnin <sup>(4)(5)</sup>      |   | \$ 65,880                         |  | \$ 32,940  |
| Nicholas Galakatos <sup>(4)(5)</sup> |   | \$ 65,880                         |  | \$ 32,940  |
| Robert Higgins <sup>(4)(5)</sup>     |   | \$ 65,880                         |  | \$ 32,940  |
| Russell Hirsch <sup>(4)(5)</sup>     |   | \$ 65,880                         |  | \$ 32,940  |
| Raju Kucherlapati <sup>(4)(5)</sup>  | \$ 9,500  | \$ 65,880                         | \$ 23,000                                  | \$ 65,440  |
| Kenneth Weg <sup>(4)(5)</sup>        |   | \$ 65,880                         |  | \$ 32,940  |
| Robert Young <sup>(4)(5)</sup>       | \$ 9,500  | \$ 65,608                         |  | \$ 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 audited financial statements included in this prospectus. This column reflects the aggregate grant date fair value as calculated in accordance with ASC 718 for the indicated year in connection with options we granted in the indicated year, 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.
- (4) 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.

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.



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- (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 <sup>(1)</sup>       | 20,000        |
| Douglas Cole <sup>(2)</sup>       | 10,000        |
| Ronald DePinho <sup>(3)</sup>     | 20,000        |
| Anthony Evnin <sup>(2)</sup>      | 10,000        |
| Nicholas Galakatos <sup>(2)</sup> | 10,000        |
| Robert Higgins <sup>(4)</sup>     | 4,166         |
| Russell Hirsch <sup>(2)</sup>     | 10,000        |
| Raju Kucherlapati <sup>(5)</sup>  | 7,709         |
| Kenneth Weg <sup>(2)</sup>        | 10,000        |
| Robert Young <sup>(6)</sup>       | 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.

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.



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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 and which became effective upon the consummation of our initial public offering. This policy superseded the policy approved in June 2009. Under this new policy, our non-employee directors are 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.

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 is also 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.

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**Consulting Agreement with Dr. Ronald DePinho.** We entered into a consulting arrangement with Dr. DePinho effective as of January 1, 2010, 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. To date, Dr. DePinho has received \$75,000 for consulting services provided under this agreement. In 2009, Dr. DePinho received \$100,000 for consulting services provided under a similar consulting agreement with Dr. DePinho dated as of January 1, 2008.

**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 provided scientific and business advice as well as attended meetings of our scientific advisory board. The consulting agreement expired December 31, 2009. In 2009, Dr. Kucherlapati received \$23,000 for consulting services provided under this agreement for attendance of certain scientific advisory board meetings.

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**Limitation of Liability and Indemnification**

Our certificate of incorporation 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.

**Table of Contents****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. These shares converted into shares of our common stock upon the closing of our initial public offering.

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 our initial public offering, these shares converted 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<br>Convertible Preferred<br>Stock | Aggregate<br>Purchase<br>Price (\$) |
|---|--|-------------------------------------|
| Affiliates of MPM BioVentures <sup>(1)</sup>                  | 776,307  | \$ 1,940,767.50                     |
| Affiliates of Highland Capital Partners <sup>(2)</sup>        | 2,005,155  | \$ 5,012,887.50                     |
| Affiliates of Venrock <sup>(3)</sup>                          | 802,062  | \$ 2,005,155.00                     |
| Affiliates of Prospect Venture Partners II, LP <sup>(4)</sup> | 661,781  | \$ 1,654,452.50                     |
| Affiliates of Flagship Ventures <sup>(5)</sup>                | 400,981  | \$ 1,002,452.50                     |
| Kenneth E. Weg <sup>(6)</sup>                                 | 165,969  | \$ 414,922.50                       |
| Heidrich Community Property Trust UDT 8/84 <sup>(7)</sup>     | 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 Member of Prospect Management Company II, LLC, or PMC II, the respective General Partner of PVP II and PA II. The Managing Members of PMC 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.
- (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.



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(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 [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 Merck (formerly Schering-Plough Corporation). On September 28, 2010, we received notice from Merck of termination of the agreement effective as of December 27, 2010. Please see [Management's Discussion and Analysis of Financial Condition and Results of Operations Strategic Partnerships Schering-Plough \(now Merck\)](#) for information on our agreement with Merck.

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 of \$5,500,002. Upon the closing of our initial public offering, these shares converted 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 and further amended. 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. Mr. Clark has received \$7,500 pursuant to this consulting agreement during our fiscal year 2010.

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 September 30, 2010, Dr. Chin received \$311,500 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 our initial public offering, these shares converted 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 our initial public offering, these shares converted 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.

On November 3, 2010, we sold 4.5 million shares of our common stock to accredited investors in a private placement at a purchase price of \$13.50 per share for total gross proceeds of \$60.75 million. Upon the closing of the private placement, Baupost Group Securities, L.L.C. became a beneficial owner of more than 5% of our voting securities and certain funds registered under Section 8 of the Investment Company Act of 1940 and beneficially owned by Fidelity Management & Research Company, a wholly-owned subsidiary of FMR LLC, also known as Fidelity Investments, which, prior to the sale of the shares of our common stock in the private placement, beneficially owned approximately 12.3% of our voting securities, became a beneficial owner of more than 14% of our voting securities. The table below sets forth the number of shares of our common stock sold to our stockholders that beneficially own more than 5% of our voting securities and their affiliates and immediate family members in connection with the private placement:

| Name   | Shares of<br>Common Stock | Aggregate<br>Purchase<br>Price (\$) |
|--|---------------------------|-------------------------------------|
| Variable Insurance Products Fund II: Contrafund Portfolio(1)                     | 107,096                   | \$ 1,445,796.00                     |
| Fidelity Advisor Series I: Fidelity Advisor Balanced Fund(1)                     | 3,908                     | \$ 52,758.00                        |
| Fidelity Devonshire Trust: Fidelity Series All-Sector Equity Fund(1)             | 61,752                    | \$ 833,652.00                       |
| Fidelity Puritan Trust: Fidelity Balanced Fund(1)                                | 77,244                    | \$ 1,042,794.00                     |
| Fidelity Destiny Portfolios: Fidelity Advisor Capital Development Fund(1)        | 404,600                   | \$ 5,462,100.00                     |
| Fidelity Securities Fund: Fidelity Dividend Growth Fund(1)                       | 290,609                   | \$ 3,923,221.50                     |
| Fidelity Advisor Series I: Fidelity Advisor Dividend Growth Fund(1)              | 27,497                    | \$ 371,209.50                       |
| Fidelity Advisor Series VII: Fidelity Advisor Health Care Fund(1)                | 28,715                    | \$ 387,652.50                       |
| Variable Insurance Products Fund IV: Health Care Portfolio(1)                    | 4,421                     | \$ 59,683.50                        |
| Fidelity Central Investment Portfolios LLC: Fidelity Health Care Central Fund(1) | 51,392                    | \$ 693,792.00                       |
| Variable Insurance Products Fund III: Balanced Portfolio(1)                      | 39,037                    | \$ 526,999.50                       |
| Fidelity Select Portfolios: Health Care Portfolio(1)                             | 117,323                   | \$ 1,583,860.50                     |
| Baupost Group Securities, L.L.C.   | 2,000,000                 | \$ 27,000,000.00                    |
| <b>Total</b>   | <b>3,213,594</b>          | <b>\$ 43,383,519.00</b>             |

(1) Stockholder is affiliated with Fidelity Investments.

**Agreements With Our Stockholders**

We previously entered into an investor rights agreement with holders of registrable securities (as such term is defined in our investor rights agreement) and warrants to purchase shares of such registrable securities. The investor rights agreement provides, among other things, that such holders 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.

In connection with the sale of shares to the selling stockholders, we entered into a securities purchase agreement and a registration rights agreement on October 28, 2010 with the selling stockholders.

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### **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 our consulting arrangement with Dr. DePinho. From January 1, 2007 to September 30, 2010, Dr. DePinho has received \$375,000 under his consulting arrangement with us. Additionally, since January 1, 2007, Dr. Kucherlapati has received \$77,000 under a consulting agreement, which expired in December 2009.

### **Policies and Procedures for Related Person Transactions**

In March 2010, our board of directors 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.

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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.



**Table of Contents****PRINCIPAL STOCKHOLDERS**

The following table sets forth information with respect to the beneficial ownership of our common stock as of November 3, 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 November 3, 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 such 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 35,509,967 shares of our common stock outstanding as of November 3, 2010. The column **Percentage of Shares Beneficially Owned After the Offering** assumes the selling stockholders have sold all shares offered hereby.

Except as otherwise set forth below, the address of each 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 Before the Offering |   |   | Total Securities Beneficially Owned | Shares Beneficially Owned After the Offering | Percentage of Shares Beneficially Owned |                    |
|--|---|---|---|-------------------------------------|--|---|--------------------|
|  | Number of Shares Owned                        | + Underlying Options Exercisable Within 60 Days | = |                                     |  | Before the Offering                     | After the Offering |
| <b>Holders of more than 5% of our voting securities</b>                    |   |   |   |                                     |  |   |                    |
| Entities affiliated with FMR LLC <sup>(1)</sup>                            | 5,024,348                                     | 0   |   | 5,024,348                           | 3,810,754                                    | 14.1%                                   | 10.7%              |
| Biogen Idec Inc. <sup>(2)</sup>  | 2,877,700                                     | 0   |   | 2,877,700                           | 2,877,700                                    | 8.1%                                    | 8.1%               |
| Entities affiliated with MPM Capital <sup>(3)</sup>                        | 2,208,961                                     | 16,250  |   | 2,225,211                           | 2,225,211                                    | 6.3%                                    | 6.3%               |
| Entities affiliated with Highland Capital Partners <sup>(4)</sup>          | 2,039,748                                     | 0   |   | 2,039,748                           | 2,039,748                                    | 5.7%                                    | 5.7%               |
| Entities affiliated with The Baupost Group, L.L.C. <sup>(5)</sup>          | 2,000,000                                     | 0   |   | 2,000,000                           | 0  | 5.6%                                    | *                  |
| Entities affiliated with Venrock <sup>(6)</sup>                            | 1,147,068                                     | 16,250  |   | 1,163,318                           | 1,163,318                                    | 3.3%                                    | 3.3%               |
| Entities affiliated with Prospect Venture Partners II, L.P. <sup>(7)</sup> | 1,611,891                                     | 0   |   | 1,611,891                           | 1,611,891                                    | 4.5%                                    | 4.5%               |
| <b>Directors and Named Executive Officers</b>                              |   |   |   |                                     |  |   |                    |
| Kenneth M. Bate  | 3,750   | 26,250  |   | 30,000                              | 30,000                                       | *                                       | *                  |
| Douglas C. Cole <sup>(8)</sup>   | 919,033                                       | 16,250  |   | 935,283                             | 935,283                                      | 2.6%                                    | 2.6%               |
| Ronald A. DePinho <sup>(9)</sup>   | 592,524                                       | 35,208  |   | 627,732                             | 627,732                                      | 1.8%                                    | 1.8%               |
| Anthony B. Evnin <sup>(10)</sup>   | 1,152,052                                     | 16,250  |   | 1,168,302                           | 1,168,302                                    | 3.3%                                    | 3.3%               |
| Nicholas G. Galakatos <sup>(11)</sup>                                      | 2,208,961                                     | 16,250  |   | 2,225,211                           | 2,225,211                                    | 6.3%                                    | 6.3%               |
| Tuan Ha-Ngoc <sup>(12)</sup>   | 227,624                                       | 742,497   |   | 970,121                             | 970,121                                      | 2.7%                                    | 2.7%               |

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|   |           |             |             |           |       |       |
|---|-----------|-------------|-------------|-----------|-------|-------|
| Russell Hirsch <sup>(13)</sup>  | 1,611,891 | 16,250      | 1,628,141   | 1,628,141 | 4.6%  | 4.6%  |
| Raju Kucherlapati <sup>(14)</sup>                                       | 160,415   | 10,835      | 171,250     | 171,250   | *     | *     |
| Kenneth E. Weg <sup>(15)</sup>  | 600,595   | 16,250      | 616,845     | 616,845   | 1.7%  | 1.7%  |
| Robert C. Young <sup>(16)</sup>   | 2,250     | 13,000      | 15,250      | 15,250    | *     | *     |
| Elan Ezickson   | 45,000    | 173,436     | 218,436     | 218,436   | *     | *     |
| Jeno Gyuris   | 0         | 199,998     | 199,998     | 199,998   | *     | *     |
| David Johnston  | 0         | 173,393     | 173,393     | 173,393   | *     | *     |
| William Slichenmyer   | 0         | 61,842      | 61,842      | 61,842    | *     | *     |
| All current executive officers and directors as a group<br>(15 persons) | 7,524,095 | + 1,517,709 | = 9,041,804 | 9,041,804 | 24.4% | 24.4% |

\* Represents beneficial ownership of less than one percent of our outstanding common stock.

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- (1) Fidelity Management & Research Company ( Fidelity ), a wholly-owned subsidiary of FMR LLC and an investment adviser registered under Section 203 of the Investment Advisers Act of 1940, is the beneficial owner of 5,024,348 shares of common stock as a result of acting as investment adviser to various investment companies (the Fidelity Funds ) registered under Section 8 of the Investment Company Act of 1940. Each of Edward C. Johnson III and FMR LLC, through its control of Fidelity and the Fidelity Funds has power to dispose of the shares owned by the Fidelity Funds. Through their ownership of voting common shares and a shareholders voting agreement, members of the Johnson family may be deemed to form a controlling group with respect to FMR LLC. Neither FMR LLC nor Edward C. Johnson III, Chairman of FMR LLC, has the sole power to vote or direct the voting of the shares owned directly by the Fidelity Funds, which power resides with the Fidelity Funds Boards of Trustees. Fidelity carries out the voting of the shares under written guidelines established by the Fidelity Funds Boards of Trustees. Fidelity s address is 82 Devonshire Street, Boston, Massachusetts 02109.
- (2) Consists of 2,877,700 shares of common stock held by Biogen Idec Inc. Biogen Idec Inc. is a publicly-traded corporation. Its address is 14 Cambridge Center, Cambridge, Massachusetts 02142.
- (3) Consists of (a) 1,493,260 shares of common stock held by MPM Bioventures II-QP, L.P., or BV2QP, (b)164,567 shares of common stock held by MPM Bioventures II L.P., or BV2LP, (c) 25,402 shares of common stock held by MPM Asset Management Investors 2002 BVII LLC, or INV02 (d) 525,732 shares of common stock held by MPM BioVentures GmbH &Co. Parallel-Beteiligungs KG, or BV2KG and (e) 16,250 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 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 options are held by Dr. Galakatos for the benefit of MPM Capital and may only be exercised at the discretion 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.
- (4) Consists of (a) 1,276,821 shares of common stock held by Highland Capital Partners VI Limited Partnership, or Highland Capital VI, (b) 699,696 shares of common stock held by Highland Capital Partners VI-B Limited Partnership, or Highland Capital VI-B and (c) 63,231 shares of common stock held by Highland Entrepreneurs Fund VI Limited Partnership, or Highland Entrepreneurs Fund. Highland Management Partners 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. Nova, 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.
- (5) The Baupost Group, L.L.C., ( Baupost ) manager to Baupost Group Securities, L.L.C., and each of SAK Corp., the manager of Baupost, and Seth A. Klarman, the director of SAK Corp., may be deemed to share voting and investment power with respect to such shares.
- (6) Consists of (a) 917,569 shares of common stock held by Venrock Associates III, L.P., or VA3, (b) 206,452 shares of common stock held by Venrock Associates, L.P., or VA, (c) 22,938 shares of common stock held by Venrock Entrepreneurs Fund III, L.P., or VEF3, (d) 109 shares of common stock held by VEF Management III, LLC, or VEFM3, (e) 16,250 shares of common stock issuable upon exercise of a stock option held by Anthony B. Evnin and (f) 4,984 shares of common stock held by Dr. Evnin. Venrock Management III, LLC, or VM3 and VEFM3 are the sole general partners of VA3 and VEF3, respectively, may be deemed to beneficially own all shares held by VA3 and VEF3, respectively, and disclaim beneficial ownership of these shares except to the extent of their pecuniary interest therein. Dr. Evnin is a member of our board of directors and a limited partner of VA and VA3, a general partner of VA, and a member of VM3 and VEFM3. Dr. Evnin may be deemed to beneficially own all shares held by VA, VA3, VEF3, VN3, and VEFM3 and expressly disclaims beneficial ownership over these shares, except to the extent of his indirect pecuniary interest therein. The stock options 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 VA, VA3, VEF3, VM3 and VEFM3. 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.



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- (7) Consists of (a) 1,587,714 shares of common stock held by Prospect Ventures Partners II, L.P., or PVP II and (b) 24,177 shares of common stock held by Prospect Associates II, L.P., or PA II. 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.
- (8) Consists of (a) 49,559 shares of common stock held by AGTC Advisors Fund, L.P., or AGTC, (b) 869,474 shares of common stock held by Applied Genomic Technology Capital Fund, L.P., or AGTC Fund and (c) 16,250 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.
- (9) 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 A. DePinho and Lynda Chin Family Trust, (d) 242,512 shares of common stock held by Dr. Chin, Dr. DePinho's wife, (e) 31,250 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. 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.
- (10) Consists of (a) 1,147,068 shares of common stock held by entities affiliated with Venrock, (b) 4,984 shares of common stock and (c) 16,250 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.
- (11) Consists of (a) 2,208,961 shares of common stock held by entities affiliated with MPM Capital and (b) 16,250 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.
- (12) Consists of (a) 170,329 shares of common stock held by Gabriel Schmergel, Trustee, or his successors in trust, of the Tuan Ha-Ngoc 2009 GRAT, (b) 57,295 shares of common stock and (c) 742,497 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.
- (13) Consists of (a) 1,587,714 and 24,177 shares of common stock held by PVP II and PA II, respectively and (b) 16,250 shares of common stock issuable upon exercise of stock options. Dr. Hirsch is a Managing Member of Prospect Management Company II, LLC, the respective General Partner of PVP II and PA II. 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.
- (14) Consists of (a) 45,511 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) 10,835 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.

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- (15) Consists of (a) 41,592 shares of common stock, (b) 559,003 shares of common stock held by The Weg Family Limited Partnership, and (c) 16,250 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 disclaims beneficial ownership over shares held of record by The Weg Family Limited Partnership except to the extent of his pecuniary interest therein.
- (16) Consists of (a) 1,250 shares of common stock, (b) 13,000 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.

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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 our certificate of incorporation and our by-laws, which are filed as exhibits to the registration statement of which this prospectus forms a part and to applicable provisions of the Delaware General Corporation Law.

Our authorized capital stock consists of 100,000,000 shares of common stock, par value \$0.001 per share, and 5,000,000 shares of preferred stock, par value \$0.001 per share, all of which preferred stock are undesignated.

#### **Common Stock**

As of November 3, 2010, there were 35,509,967 shares of our common stock outstanding and held of record by 138 stockholders.

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 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**

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. As of September 30, 2010, there are no shares of preferred stock outstanding, and we have no present plans to issue any shares of preferred stock.

#### **Options and Warrants**

As of September 30, 2010, options to purchase 3,481,141 shares of common stock at a weighted average exercise price of \$5.85 per share were outstanding and warrants to purchase an aggregate of 338,841 shares of common stock at a weighted average exercise price of \$8.81 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

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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. This provision may discourage or prevent unsolicited tender offers for our outstanding common stock.

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### ***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.

### ***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**

Certain holders of our common stock and holders of warrants to purchase shares of our common stock have the right to require us to register these shares of common stock under the Securities Act under specified circumstances pursuant to the terms of an investor rights agreement with such stockholders.

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Subject to specified limitations, these stockholders may require that we register all or part of their shares of common stock 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.

Furthermore, we have granted our lenders, Hercules Technology II, L.P. and Hercules Technology III, L.P., an option to acquire, subject our written consent, not to be unreasonably withheld, either with cash or through conversion of outstanding principal under our loan agreement, up to \$2,000,000 of the same equity securities sold by us in any sale of equity securities resulting in at least \$10,000,000 in net cash proceeds to us, subject to certain exceptions. If our lenders exercise their option, we have agreed to register the underlying shares on a Form S-3 when we are eligible to use this form.

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. We have granted substantially similar rights to our lenders with respect to the 156,641 shares of common stock underlying warrants they hold.

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 is traded on the NASDAQ Global Market under the symbol **AVEO**.

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**LEGAL MATTERS**

The validity of the issuance of the common stock offered by this prospectus is being passed upon for us by Wilmer Cutler Pickering Hale and Dorr LLP, Boston, Massachusetts.

**EXPERTS**

Ernst & Young LLP, independent registered public accounting firm, has audited our consolidated financial statements at December 31, 2009 and 2008, and for each of the three years in the period ended December 31, 2009, as set forth in their report. We have included our financial statements in the prospectus and elsewhere in the registration statement in reliance on Ernst & Young LLP's report, given on their authority as experts in accounting and auditing.

**WHERE YOU CAN FIND MORE INFORMATION**

We file reports and other information with the SEC as required by the Exchange Act. You can find, copy and inspect information we file at the SEC's public reference room, which is located at 100 F Street, N.E., Room 1580, Washington, DC 20549. Please call the SEC at 1-800-SEC-0330 for more information about the operation of the SEC's public reference room. You can review our electronically filed reports and other information that we file with the SEC on the SEC's web site at <http://www.sec.gov> or on our web site at <http://www.aveopharma.com>.

This prospectus is part of a registration statement that we filed with the SEC. The registration statement contains more information than this prospectus regarding us and the securities, including exhibits and schedules. You can obtain a copy of the registration statement from the SEC at any address listed above or from the SEC's web site.

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**AVEO Pharmaceuticals, Inc.**

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**REPORT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM**

The Board of Directors and Stockholders of

AVEO Pharmaceuticals, Inc.

We have audited the accompanying consolidated balance sheets of AVEO Pharmaceuticals, Inc. as of December 31, 2008 and 2009, and the related consolidated statements of operations, stockholders' deficit, and cash flows for each of the three years in the period ended December 31, 2009. These consolidated financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on these consolidated financial statements based on our audits.

We conducted our audits in accordance with the standards of the Public Company Accounting Oversight Board (United States). Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the financial statements are free of material misstatement. We were not engaged to perform an audit of the Company's internal control over financial reporting. Our audits included consideration of internal control over financial reporting as a basis for designing audit procedures that are appropriate in the circumstances, but not for the purpose of expressing an opinion on the effectiveness of the Company's internal control over financial reporting. Accordingly, we express no such opinion. An audit also includes examining, on a test basis, evidence supporting the amounts and disclosures in the financial statements, assessing the accounting principles used and significant estimates made by management, and evaluating the overall financial statement presentation. We believe that our audits provide a reasonable basis for our opinion.

In our opinion, the financial statements referred to above present fairly, in all material respects, the consolidated financial position of AVEO Pharmaceuticals, Inc. at December 31, 2008 and 2009, and the consolidated results of its operations and its cash flows for each of the three years in the period ended December 31, 2009 in conformity with U.S. generally accepted accounting principles.

The accompanying financial statements have been prepared assuming that the Company will continue as a going concern. As more fully described in Note 1, the Company has incurred operating losses and negative cash flows from operations since inception and will be required to obtain additional financing, alternative means of financial support or both prior to December 31, 2010 in order to continue to fund its operations. These factors raise substantial doubt about its ability to continue as a going concern. Management's plans in regard to these matters are also described in Note 1. The consolidated financial statements do not include any adjustments to reflect the possible future effects on the recoverability and classification of assets or the amounts and classifications of liabilities that may result from the outcome of this uncertainty.

/s/ Ernst & Young LLP

Boston, Massachusetts

February 8, 2010, except for the matters disclosed

in Notes 11 and 16, as to which the date is February 18, 2010

**Table of Contents****AVEO Pharmaceuticals, Inc.****Consolidated Balance Sheets**

|  | December 31,         |                      |                          |
|--|----------------------|----------------------|--------------------------|
|  | 2008                 | 2009                 | Pro forma<br>(unaudited) |
| <b>Assets</b>  |                      |                      |                          |
| Current assets:  |                      |                      |                          |
| Cash and cash equivalents  | \$ 20,813,812        | \$ 45,289,482        | \$ 45,289,482            |
| Marketable securities  | 11,550,405           | 6,011,350            | 6,011,350                |
| Accounts receivable  | 2,080,809            | 486,797              | 486,797                  |
| Prepaid expenses and other current assets  | 1,161,501            | 1,306,242            | 1,306,242                |
| <b>Total current assets</b>  | <b>35,606,527</b>    | <b>53,093,871</b>    | <b>53,093,871</b>        |
| Property and equipment, net  | 3,752,440            | 4,197,475            | 4,197,475                |
| Other assets   | 120,995              | 1,945,614            | 1,945,614                |
| Restricted cash  | 607,392              | 607,392              | 607,392                  |
| <b>Total assets</b>  | <b>\$ 40,087,354</b> | <b>\$ 59,844,352</b> | <b>\$ 59,844,352</b>     |
| <b>Liabilities and stockholders deficit</b>  |                      |                      |                          |
| Current liabilities:   |                      |                      |                          |
| Accounts payable   | \$ 3,854,301         | \$ 7,490,425         | \$ 7,490,425             |
| Accrued expenses (Note 5)  | 3,408,524            | 7,389,133            | 7,389,133                |
| Loans payable, net of discount   | 5,037,442            | 7,466,973            | 7,466,973                |
| Deferred revenue   | 7,092,117            | 11,781,903           | 11,781,903               |
| Deferred rent  | 141,074              | 176,081              | 176,081                  |
| <b>Total current liabilities</b>   | <b>19,533,458</b>    | <b>34,304,515</b>    | <b>34,304,515</b>        |
| Loans payable, net of current portion and discount   | 16,017,808           | 12,277,786           | 12,277,786               |
| Deferred revenue, net of current portion   | 6,048,079            | 23,320,483           | 23,320,483               |
| Deferred rent, net of current portion  | 995,401              | 819,320              | 819,320                  |
| Other liabilities  | 1,249,500            | 1,249,500            | 1,249,500                |
| Warrants to purchase convertible preferred stock   | 1,211,002            | 1,458,528            |                          |
| Commitments and contingencies (Note 9)   |                      |                      |                          |
| Convertible preferred stock, \$.001 par value: 80,624,363 and no shares authorized (actual and pro forma); 64,638,532 and 75,916,730 shares issued and outstanding at December 31, 2008 and 2009 (actual), respectively and no shares at December 31, 2009 (pro forma), (at liquidation value) (Note 11) | 123,719,937          | 156,704,937          |                          |
| Stockholders deficit:  |                      |                      |                          |
| Common stock, \$.001 par value: 25,500,000 and 100,000,000 shares authorized (actual and pro forma); 1,586,468 and 1,640,714 shares issued and outstanding at December 31, 2008 and 2009 (actual), respectively and 20,619,869 shares at December 31, 2009 (pro forma)                                   | 1,587                | 1,641                | 20,620                   |
| Additional paid-in capital   | 4,924,268            | 7,432,422            | 165,576,908              |
| Accumulated other comprehensive income   | 17,568               | (138)                | (138)                    |
| Accumulated deficit  | (133,631,254)        | (177,724,642)        | (177,724,642)            |

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|   |               |               |               |
|---|---------------|---------------|---------------|
| Total stockholders' deficit                 | (128,687,831) | (170,290,717) | (12,127,252)  |
| Total liabilities and stockholders' deficit | \$ 40,087,354 | \$ 59,844,352 | \$ 59,844,352 |

See accompanying notes

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**Table of Contents**

**AVEO Pharmaceuticals, Inc.**  
**Consolidated Statements of Operations**

|   | Year Ended December 31, |                 |                 |
|---|-------------------------|-----------------|-----------------|
|   | 2007                    | 2008            | 2009            |
| Collaboration revenue   | \$ 11,034,138           | \$ 19,660,210   | \$ 20,718,532   |
| Operating expenses:   |                         |                 |                 |
| Research and development  | 29,248,014              | 41,820,505      | 51,791,943      |
| General and administrative  | 6,501,915               | 9,164,718       | 10,120,360      |
|   | 35,749,929              | 50,985,223      | 61,912,303      |
| Loss from operations  | (24,715,791)            | (31,325,013)    | (41,193,771)    |
| Other income and expense:   |                         |                 |                 |
| Other income (expense), net   |                         | 18,039          | (332,966)       |
| Loss on loan extinguishment   |                         | (248,586)       |                 |
| Interest expense  | (2,437,330)             | (2,085,917)     | (2,810,965)     |
| Interest income   | 2,171,301               | 1,168,353       | 144,258         |
| Other income (expense), net   | (266,029)               | (1,148,111)     | (2,999,673)     |
| Net loss before benefit for income taxes  | (24,981,820)            | (32,473,124)    | (44,193,444)    |
| Benefit for income taxes  |                         |                 | 100,056         |
| Net loss  | \$ (24,981,820)         | \$ (32,473,124) | \$ (44,093,388) |
| Net loss per share basic and diluted  | \$ (17.89)              | \$ (21.08)      | \$ (27.43)      |
| Weighted-average number of common shares used in net loss per share basic and diluted | 1,396,323               | 1,540,575       | 1,607,329       |
| 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)   |                         |                 | 19,768,082      |

See accompanying notes

**Table of Contents****AVEO Pharmaceuticals, Inc.****Statements of Convertible Preferred Stock and Stockholders Deficit**

| Transaction   | Series A - E<br>Convertible<br>Preferred Stock |               | Common Shares<br>Shares | Par<br>Value | Additional<br>Paid-in<br>Capital | Accumulated<br>Other<br>Comprehensive<br>Loss | Accumulated<br>Deficit | Total<br>Stockholders<br>Deficit | Comprehensive<br>Loss |
|---|--|---------------|-------------------------|--------------|----------------------------------|---|------------------------|----------------------------------|-----------------------|
|   | Shares   | Amount        |                         |              |                                  |   |                        |                                  |                       |
| Balance at<br>December 31, 2006   | 41,639,688                                     | \$ 66,222,827 | 1,361,588               | \$ 1,362     | \$ 1,627,722                     | \$  | \$ (76,176,310)        | \$ (74,547,226)                  |                       |
| Issuance of Series D<br>Convertible Preferred<br>Stock, net of offering<br>costs of \$97,996                                    | 21,165,510                                     | 52,913,775    |                         |              | (97,996)                         |   |                        | (97,996)                         |                       |
| Issuance of Series C<br>Convertible Preferred<br>Stock, net of offering<br>costs of \$22,557                                    | 1,833,334                                      | 4,583,335     |                         |              | (22,557)                         |   |                        | (22,557)                         |                       |
| Exercise of stock<br>options  |  |               | 72,084                  | 72           | 77,435                           |   |                        | 77,507                           |                       |
| Stock-based<br>compensation<br>expense related to<br>stock options granted<br>to employees                                      |  |               |                         |              | 745,729                          |   |                        | 745,729                          |                       |
| Stock-based<br>compensation<br>expense related to<br>restricted common<br>stock and stock<br>options granted to<br>nonemployees |  |               |                         |              | 42,588                           |   |                        | 42,588                           |                       |
| Vesting of restricted<br>stock  |  |               |                         |              | 2,062                            |   |                        | 2,062                            |                       |
| Beneficial conversion<br>feature-loan payable   |  |               |                         |              | 208,360                          |   |                        | 208,360                          |                       |
| Change in unrealized<br>gain/loss on<br>investments   |  |               |                         |              |                                  | 115,218                                       |                        | 115,218                          | \$ 115,218            |
| Net loss  |  |               |                         |              |                                  |   | (24,981,820)           | (24,981,820)                     | (24,981,820)          |
| Comprehensive loss  |  |               |                         |              |                                  |   |                        |                                  | \$ (24,866,602)       |

**Table of Contents****AVEO Pharmaceuticals, Inc.****Statements of Convertible Preferred Stock and Stockholders Deficit (Continued)**

| Transaction   | Series A - E<br>Convertible<br>Preferred Stock |                | Common Shares |              | Additional<br>Paid-in<br>Capital | Accumulated<br>Other<br>Comprehensive<br>Loss | Accumulated<br>Deficit | Total<br>Stockholders<br>Deficit | Comprehensive<br>Loss |
|---|--|----------------|---------------|--------------|----------------------------------|---|------------------------|----------------------------------|-----------------------|
|   | Shares   | Amount         | Shares        | Par<br>Value |                                  |   |                        |                                  |                       |
| Balance at<br>December 31,<br>2007  | 64,638,532                                     | 123,719,937    | 1,433,672     | 1,434        | 2,583,343                        | 115,218                                       | (101,158,130)          | (98,458,135)                     |                       |
| Exercise of<br>stock options  |  |                | 27,796        | 28           | 33,045                           |   |                        | 33,073                           |                       |
| Issuance of<br>common stock   |  |                | 125,000       | 125          | 804,875                          |   |                        | 805,000                          |                       |
| Stock-based<br>compensation<br>expense related<br>to stock<br>options granted<br>to employees   |  |                |               |              | 1,368,671                        |   |                        | 1,368,671                        |                       |
| Stock-based<br>compensation<br>expense related<br>to restricted<br>common stock<br>and stock<br>options granted<br>to<br>nonemployees |  |                |               |              | 132,443                          |   |                        | 132,443                          |                       |
| Vesting of<br>restricted stock  |  |                |               |              | 1,891                            |   |                        | 1,891                            |                       |
| Change in<br>unrealized<br>gain/loss on<br>investments  |  |                |               |              |                                  | (97,650)                                      |                        | (97,650)                         | \$ (97,650)           |
| Net loss  |  |                |               |              |                                  |   | (32,473,124)           | (32,473,124)                     | (32,473,124)          |
| Comprehensive<br>loss   |  |                |               |              |                                  |   |                        |                                  | \$ (32,570,774)       |
| Balance at<br>December 31,<br>2008  | 64,638,532                                     | \$ 123,719,937 | 1,586,468     | \$ 1,587     | \$ 4,924,268                     | \$ 17,568                                     | \$ (133,631,254)       | \$ (128,687,831)                 |                       |
| Issuance of<br>Series E<br>Convertible<br>Preferred<br>Stock, net of<br>offering costs<br>of \$63,363                                 | 11,250,000                                     | 32,925,000     |               |              | (63,363)                         |   |                        | (63,363)                         |                       |
| Exercise of<br>Series A<br>warrants   | 28,198   | 60,000         |               |              | 25,440                           |   |                        | 25,440                           |                       |
| Exercise of<br>stock options  |  |                | 54,246        | 54           | 159,095                          |   |                        | 159,149                          |                       |
| Stock-based<br>compensation<br>expense related<br>to stock  |  |                |               |              | 2,120,369                        |   |                        | 2,120,369                        |                       |

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|   |  |  |  |  |          |              |  |              |              |
|---|--|--|--|--|----------|--------------|--|--------------|--------------|
| options granted to employees  |  |  |  |  |          |              |  |              |              |
| Stock-based compensation expense related to stock options granted to nonemployees |  |  |  |  | 266,613  |              |  | 266,613      |              |
| Change in unrealized gain/loss on investments                                     |  |  |  |  | (17,706) |              |  | (17,706)     | \$ (17,706)  |
| Net loss  |  |  |  |  |          | (44,093,388) |  | (44,093,388) | (44,093,388) |

Comprehensive loss \$ (44,111,094)

|                              |            |                |           |          |              |          |                  |                  |
|------------------------------|------------|----------------|-----------|----------|--------------|----------|------------------|------------------|
| Balance at December 31, 2009 | 75,916,730 | \$ 156,704,937 | 1,640,714 | \$ 1,641 | \$ 7,432,422 | \$ (138) | \$ (177,724,642) | \$ (170,290,717) |
|------------------------------|------------|----------------|-----------|----------|--------------|----------|------------------|------------------|

|   |              |               |            |        |             |  |  |             |
|---|--------------|---------------|------------|--------|-------------|--|--|-------------|
| Conversion of convertible preferred stock into common stock | (75,916,730) | (156,704,937) | 18,979,155 | 18,979 | 156,685,958 |  |  | 156,704,937 |
|---|--------------|---------------|------------|--------|-------------|--|--|-------------|

|  |  |  |  |  |           |  |  |           |
|--|--|--|--|--|-----------|--|--|-----------|
| Conversion of warrants to purchase preferred stock into common stock |  |  |  |  | 1,458,528 |  |  | 1,458,528 |
|--|--|--|--|--|-----------|--|--|-----------|

|  |    |  |            |           |                |          |                  |                 |
|--|----|--|------------|-----------|----------------|----------|------------------|-----------------|
| Pro forma at December 31, 2009 (Unaudited) | \$ |  | 20,619,869 | \$ 20,620 | \$ 165,576,908 | \$ (138) | \$ (177,724,642) | \$ (12,127,252) |
|--|----|--|------------|-----------|----------------|----------|------------------|-----------------|

See accompanying notes

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**AVEO Pharmaceuticals, Inc.**  
**Consolidated Statements of Cash Flows**

|   | Years Ended December 31, |                 |                 |
|---|--------------------------|-----------------|-----------------|
|   | 2007                     | 2008            | 2009            |
| <b>Operating activities</b>   |                          |                 |                 |
| Net loss  | \$ (24,981,820)          | \$ (32,473,124) | \$ (44,093,388) |
| Adjustments to reconcile net loss to net cash used in operating activities:         |                          |                 |                 |
| Depreciation and amortization   | 1,334,239                | 1,320,754       | 1,288,886       |
| Stock-based compensation  | 788,317                  | 2,305,615       | 2,386,982       |
| Noncash interest expense  | 540,530                  | 476,162         | 686,002         |
| Loss on loan extinguishment   |                          | 248,586         |                 |
| Loss on disposal of property and equipment  |                          | 10,240          |                 |
| Remeasurement of warrants to purchase convertible preferred stock                   |                          | (7,430)         | 332,966         |
| Amortization of (premium) discount on investments                                   | (1,024,740)              | (496,417)       | 373,067         |
| Changes in operating assets and liabilities:  |                          |                 |                 |
| Accounts receivable   | (621,056)                | (1,459,753)     | 1,594,012       |
| Prepaid expenses and other current assets   | (521,942)                | (211,488)       | (155,229)       |
| Other noncurrent assets   | (27,405)                 | (146,048)       | (1,824,619)     |
| Accounts payable  | 1,284,965                | 1,436,841       | 3,636,124       |
| Accrued expenses  | 1,437,193                | 417,220         | 3,980,609       |
| License fee payable   | (5,000,000)              |                 |                 |
| Deferred rent   | (141,939)                | (116,021)       | (141,074)       |
| Deferred revenue  | 18,329,178               | (6,606,523)     | 21,962,190      |
| Net cash used in operating activities   | (8,604,480)              | (35,301,386)    | (9,973,472)     |
| <b>Investing activities</b>   |                          |                 |                 |
| Purchases of property and equipment   | (375,400)                | (1,356,502)     | (1,733,921)     |
| Purchases of marketable securities  | (73,019,015)             | (28,644,995)    | (35,926,719)    |
| Proceeds from maturities and sales of marketable securities                         | 33,500,000               | 58,152,331      | 41,075,000      |
| Net cash (used in) provided by investing activities                                 | (39,894,415)             | 28,150,834      | 3,414,360       |
| <b>Financing activities</b>   |                          |                 |                 |
| Proceeds from issuance of convertible preferred stock, net of issuance costs        | 57,376,557               |                 | 32,861,637      |
| Proceeds from exercise of stock options and issuance of common and restricted stock | 77,507                   | 33,572          | 159,149         |
| Net proceeds from issuance of loans payable   |                          | 20,795,370      |                 |
| Extinguishment of loan  |                          | (10,139,906)    |                 |
| Principal payments on loans payable   | (4,619,766)              | (3,807,772)     | (1,986,004)     |
| Net cash provided by financing activities   | 52,834,298               | 6,881,264       | 31,034,782      |
| Net (decrease) increase in cash and cash equivalents                                | 4,335,403                | (269,288)       | 24,475,670      |
| Cash and cash equivalents at beginning of period                                    | 16,747,697               | 21,083,100      | 20,813,812      |
| Cash and cash equivalents at end of period  | \$ 21,083,100            | \$ 20,813,812   | \$ 45,289,482   |

**Supplemental cash flow and noncash investing and financing activities**



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|   |    |           |              |              |
|---|----|-----------|--------------|--------------|
| Issuance of warrants in conjunction with loan | \$ |           | \$ 313,671   | \$           |
| Cash paid for interest                        | \$ | 1,925,313 | \$ 1,559,141 | \$ 2,124,963 |
| Cash paid for income taxes                    | \$ | 456       | \$ 456       | \$ 456       |
| Vesting of restricted common stock            | \$ | 2,062     | \$ 1,891     | \$           |

See accompanying notes

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**AVEO Pharmaceuticals, Inc.**

**Notes to Consolidated Financial Statements**

**December 31, 2009**

**1. Nature of Business and Organization**

AVEO Pharmaceuticals, Inc. (the Company) was incorporated in the state of Delaware on October 18, 2001, under the name of GenPath Pharmaceuticals, Inc. and commenced operations in January 2002. In September 2004, the Company changed its name to AVEO Pharmaceuticals, Inc. The Company operates as a single segment and is a Cambridge, Massachusetts-based clinical stage biopharmaceutical company focused on the discovery and development of novel, targeted cancer therapeutics. The Company's product candidates are targeted against important mechanisms known or believed to be involved in cancer. Tivozanib, the Company's lead product candidate, is a highly potent and selective oral inhibitor of the vascular endothelial growth factor (VEGF) receptors 1, 2 and 3. The Company's clinical trials to date have demonstrated a favorable safety and efficacy profile for tivozanib. The Company has completed a 272-patient phase 2 clinical trial of tivozanib in patients with advanced renal cell cancer (RCC). The overall median progression-free survival of patients in the phase 2 clinical trial was 11.8 months. The Company initiated patient screening for a phase 3 clinical trial of tivozanib in patients with advanced RCC in December 2009, in which the Company plans to enroll 500 patients. The Company is also conducting phase 1b clinical trials of tivozanib in various combinations and dosing regimens in advanced RCC and additional solid tumor indications, including breast cancer and colorectal cancer. In addition to tivozanib, the Company has a pipeline of monoclonal antibodies derived from its Human Response Platform, a novel method of building preclinical models of human cancer, which are intended to more accurately represent cancer biology in patients. The Company's first product candidate derived from its Human Response Platform, AV-299, is expected to enter a phase 2 clinical trial for non-small cell lung cancer in the first of half of 2010.

*Subsequent events*

The Company has evaluated subsequent events after the balance sheet date of December 31, 2009 through February 8, 2010, the date of the filing of the consolidated financial statements.

*Liquidity*

The Company has incurred operating losses and negative cash flows from operations since inception, incurred a net loss of approximately \$44.1 million during the year ended December 31, 2009, and has an accumulated deficit of approximately \$177.7 million as of December 31, 2009. The Company has primarily funded these losses through revenue from collaborations and equity and debt financings. To date, the Company has no product revenue and management expects operating losses to continue until any of its product candidates are approved and commercialized. The Company believes that its existing cash, cash equivalents and marketable securities as of December 31, 2009 and committed research and development funding and milestone payments that the Company expects to receive under its strategic partnership and license agreements, will not be sufficient to allow it to fund its operating plan through the end of 2010. As a result, the Company will be required to obtain additional financing, alternative means of financial support, or both, in order to continue to fund its operations. These factors raise substantial doubt about the Company's ability to continue as a going concern.

The Company's board of directors has approved the filing of a registration statement on Form S-1 with respect to a proposed initial public offering of its common stock. The Company may raise additional funds through equity or debt financings or generate revenues from collaborative partners through a combination of upfront license payments, milestone payments, research funding, and cost reimbursement. There can be no assurance that the Company will be able to obtain additional debt or equity financing or generate revenues from collaborative partners, on terms acceptable to the Company, or at all. The failure of the Company to obtain sufficient funds on acceptable terms when needed could have a material adverse effect on the Company's business, results of operations and financial condition.

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**AVEO Pharmaceuticals, Inc.**

**Notes to Consolidated Financial Statements (Continued)**

**December 31, 2009**

**1. Nature of Business and Organization (Continued)**

The accompanying consolidated financial statements have been prepared assuming that the Company will continue as a going concern, which contemplates the realization of assets and the settlement of liabilities and commitments in the normal course of business. The financial statements for the year ended December 31, 2009 do not include any adjustments to reflect the possible future effects on the recoverability and classification of assets or the amounts and classification of liabilities that may result from uncertainty related to the Company's ability to continue as a going concern.

**2. Significant Accounting Policies**

*Unaudited Pro Forma Balance Sheet and Pro Forma Net Loss per Common Share*

In November 2009, the Company's Board of Directors authorized management of the Company to file a registration statement with the SEC permitting the Company to sell shares of its common stock to the public. The unaudited pro forma balance sheet as of December 31, 2009 and statement of stockholders deficit as of December 31, 2009 reflects the conversion of all Series A, Series B, Series C, Series D and Series E convertible preferred stock outstanding as of that date into 18,979,155 shares of common stock, such event to occur immediately prior to the closing of the Company's proposed initial public offering. In addition, the unaudited pro forma balance sheet as of December 31, 2009 reflects the impact of the reclassification of the preferred stock warrant liability into additional paid-in capital as a result of the conversion of warrants to purchase convertible preferred stock into warrants to purchase common stock immediately prior to the closing of the Company's proposed initial public offering.

Unaudited pro forma net loss per share is computed using the weighted-average number of common shares outstanding after giving effect to the conversion of all convertible preferred stock into shares of the Company's common stock as if such conversion had occurred at the beginning of the period presented, or the date of original issuance, if later.

*Revenue Recognition*

The Company's revenue is generated primarily through collaborative research and development and licensing agreements. The terms of these agreements typically include payment to the Company of one or more of the following: nonrefundable, up-front license fees; premiums on the sale of convertible preferred stock; milestone payments; and royalties on product sales. In addition, the Company generates revenue through agreements that generally provide for fees for research and development services rendered. These service agreements also contemplate royalty payments to the Company on future sales of its customers' products. To date the Company has earned several milestones but has not earned royalty revenue as a result of product sales.

For arrangements that include multiple deliverables, the Company identifies separate units of accounting if certain criteria are met. Accordingly, revenues from licensing and collaboration agreements are recognized based on the performance requirements of the agreement.

Nonrefundable up-front fees, where the Company has ongoing involvement or performance obligations, are recorded as deferred revenue in the balance sheet and amortized on a straight-line basis into collaboration revenue in the statements of operations over the term of the performance obligations.

Payments or reimbursements resulting from the Company's research and development efforts are recognized as the services are performed and are presented on a gross basis in accordance with the accounting guidance, *Overall Considerations of Reporting Revenue Gross as a Principal*,

so long as there is persuasive

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**AVEO Pharmaceuticals, Inc.**

**Notes to Consolidated Financial Statements (Continued)**

**December 31, 2009**

**2. Significant Accounting Policies (Continued)**

evidence of an arrangement, the fee is fixed or determinable, and collection of the related receivable is reasonably assured.

At the inception of each agreement that includes milestone payments, the Company evaluates whether each milestone is substantive and at risk to both parties on the basis of the contingent nature of the milestone, specifically reviewing factors such as the scientific and other risks that must be overcome to achieve the milestone, as well as the level of effort and investment required. Revenues from milestones, if they are nonrefundable and deemed substantive, are recognized upon successful accomplishment of the milestones. Milestones that are not considered substantive are accounted for as license payments and recognized on a straight-line basis over the remaining period of performance.

Amounts received prior to satisfying the above revenue recognition criteria are recorded as deferred revenue in the accompanying balance sheets.

*Principles of Consolidation*

The Company's consolidated financial statements include the Company's accounts and the accounts of the Company's wholly owned subsidiary, AVEO Pharma Limited. All intercompany transactions have been eliminated.

*Research and Development Expenses*

Research and development expenses are charged to expense as incurred. Research and development costs comprise costs incurred in performing research and development activities, including personnel-related costs, stock-based compensation, facilities, research related overhead, clinical trial costs, contracted services, license fees, and other external costs.

On January 1, 2008, the Company adopted the provisions of Accounting Standards Codification (ASC) 730-20-25-13, which requires that nonrefundable advance payments for goods and services that will be used in future research and development activities be expensed when the activity has been performed or when the goods have been received rather than when the payment is made.

*Cash and Cash Equivalents*

The Company considers highly liquid investments with a maturity of three months or less when purchased to be cash equivalents. Cash equivalents at December 31, 2008 and 2009 consist of money market funds and commercial paper.

*Marketable Securities*

On January 1, 2008, the Company adopted Financial Accounting Standards Board (FASB) ASC Topic 820, *Fair Value Measurements and Disclosures* (formerly FASB Statement No. 157, *Fair Value Measurements*), which provides guidance for using fair value to measure assets and liabilities. ASC 820 applies whenever other standards require (or permit) assets or liabilities to be measured at fair value but does not expand the use of fair value in any new circumstances. ASC 820 also requires expanded disclosure of the effect on earnings for items measured using unobservable data, establishes a fair value hierarchy that prioritizes the information used to develop those assumptions and requires separate disclosure by level within the fair value hierarchy.

**Table of Contents****AVEO Pharmaceuticals, Inc.****Notes to Consolidated Financial Statements (Continued)****December 31, 2009****2. Significant Accounting Policies (Continued)**

The Company records marketable securities at fair value. ASC 820 establishes a fair value hierarchy for those instruments measured at fair value that distinguishes between assumptions based on market data (observable inputs) and the Company's own assumptions (unobservable inputs). The hierarchy consists of three levels:

Level 1 Quoted market prices in active markets for identical assets or liabilities. Assets utilizing Level 1 inputs include U.S. government securities.

Level 2 Inputs other than Level 1 inputs that are either directly or indirectly observable, such as quoted market prices, interest rates and yield curves. Assets utilizing Level 2 inputs include U.S. agency securities, including direct issuance bonds and corporate bonds.

Level 3 Unobservable inputs developed using estimates and assumptions developed by the Company, which reflect those that a market participant would use. The Company currently has no assets or liabilities valued with Level 3 inputs.

The following tables summarize the financial instruments measured at fair value on a recurring basis in the accompanying consolidated balance sheet as of December 31, 2008 and 2009.

|                       | Fair Value Measurement as of December 31, 2008 |              |         |               |
|-----------------------|--|--------------|---------|---------------|
|                       | Level 1  | Level 2      | Level 3 | Total         |
| Cash equivalents      | \$   | \$ 498,274   | \$      | \$ 498,274    |
| Marketable securities | 9,550,695                                      | 1,999,710    |         | 11,550,405    |
|                       | \$ 9,550,695                                   | \$ 2,497,984 | \$      | \$ 12,048,679 |

|                       | Fair Value Measurement as of December 31, 2009 |         |         |              |
|-----------------------|--|---------|---------|--------------|
|                       | Level 1  | Level 2 | Level 3 | Total        |
| Marketable securities | \$ 6,011,350                                   | \$      | \$      | \$ 6,011,350 |

The Company's Level 2 securities in 2008 include commercial paper issuances and are valued using third-party pricing sources. These sources generally use interest rates and yield curves observable at commonly quoted intervals of similar assets as observable inputs for pricing.

Marketable securities primarily consist of U.S. Treasuries, U.S. government agencies and corporate debt maintained by an investment manager. Credit risk is minimized as a result of the Company's policy to limit the amount invested in any one issue. Marketable securities consist primarily of investments which have original maturities at the date of purchase in excess of three months, but not longer than 24 months. The Company classifies these investments as available-for-sale. Unrealized gains and losses are included in other comprehensive loss as a component of stockholders' deficit until realized. The cost of securities sold is based on the specific identification method. The Company sold one security in

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2008 and recognized a gain of \$20,800. There were no realized gains or losses recognized on the sale or maturity of securities during 2007 or 2009.

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**Table of Contents****AVEO Pharmaceuticals, Inc.****Notes to Consolidated Financial Statements (Continued)****December 31, 2009****2. Significant Accounting Policies (Continued)**

Available-for-sale securities at December 31, 2008 and 2009 consist of the following:

|                              | Amortized<br>Cost | Unrealized<br>Gains | Unrealized<br>Losses | Fair<br>Value |
|------------------------------|-------------------|---------------------|----------------------|---------------|
| <b>December 31, 2008:</b>    |                   |                     |                      |               |
| U.S. Treasuries              | \$ 7,529,444      | \$ 6,251            | \$                   | \$ 7,535,695  |
| Government agency securities | 2,013,049         | 1,951               |                      | 2,015,000     |
| Corporate debt securities    | 1,990,344         | 9,366               |                      | 1,999,710     |
|                              | \$ 11,532,837     | \$ 17,568           | \$                   | \$ 11,550,405 |
| <b>December 31, 2009:</b>    |                   |                     |                      |               |
| U.S. Treasuries              | \$ 2,002,852      | \$ 48               | \$                   | \$ 2,002,900  |
| Government agency securities | 4,008,636         | 227                 | (413)                | 4,008,450     |
|                              | \$ 6,011,488      | \$ 275              | \$ (413)             | \$ 6,011,350  |

All marketable securities at December 31, 2008 and 2009 had maturities of one year or less. At December 31, 2009 there was one marketable security in an unrealized loss position for less than one year. The unrealized loss was caused by fluctuations in interest rates. The Company reviewed its investment with an unrealized loss and concluded that no other than temporary impairment existed at December 31, 2009 as the Company had the ability and intent to hold to maturity.

Marketable Security in unrealized loss position at December 31, 2009:

|  | Aggregate<br>Fair Value | Unrealized<br>Losses |
|--|-------------------------|----------------------|
| Government agency security due in less than one year | \$ 1,002,190            | \$ (413)             |

*Concentrations of Credit Risk*

Financial instruments that potentially subject the Company to credit risk primarily consist of cash and cash equivalents and available-for-sale marketable securities. The Company maintains deposits in federally insured financial institutions in excess of federally insured limits.

Management believes that the Company is not exposed to significant credit risk due to the financial position of the depository institutions in which those deposits are held.

*Fair Value of Financial Instruments*



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The carrying amounts of the Company's financial instruments, which include cash and cash equivalents, marketable securities, accounts payable, warrants and loans payable, approximate their fair values at December 31, 2008 and 2009.

### *Preferred Stock Warrant Liability*

Warrants to purchase the Company's convertible preferred stock are classified as liabilities and are recorded at their estimated fair value. At each reporting period, any change in fair value of the freestanding warrants is recorded as other income (expense).

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**Table of Contents****AVEO Pharmaceuticals, Inc.****Notes to Consolidated Financial Statements (Continued)****December 31, 2009****2. Significant Accounting Policies (Continued)***Property and Equipment*

Property and equipment are stated at cost and are depreciated using the straight-line method over the estimated useful lives of the respective assets. Maintenance and repair costs are charged to expense as incurred.

*Long-lived Assets*

The Company periodically assesses the impairment of long-lived assets in accordance with ASC Topic 360, *Property, Plant, and Equipment*. The Company reviews long-lived assets, including property and equipment, for impairment whenever changes in business circumstances indicate that the carrying amount of the asset may not be fully recoverable. The Company has not recognized any impairment losses through December 31, 2009.

*Comprehensive Income*

Comprehensive income is defined as the change in equity of a business enterprise during a period from transactions and other events and circumstances from nonowner sources. Accumulated other comprehensive income consists entirely of unrealized gains/losses on available-for-sale securities.

*Stock-Based Compensation*

Effective January 1, 2006, the Company adopted the provisions of ASC Topic 718, *Compensation-Stock Compensation*, using the prospective-transition method. Under the prospective-transition method, nonvested awards outstanding at the date of adoption continue to be accounted for in the same manner as they had been accounted for prior to adoption. All awards granted, modified or settled after the date of adoption are recognized in the Company's statements of operations on a straight-line basis over their requisite service periods based on their grant fair values as calculated using the measurement and recognition provisions of ASC 718. During the years ended December 31, 2007, 2008 and 2009 the Company recorded the following stock-based compensation expense as a result of the adoption of ASC Topic 718:

|   | <b>Years Ended<br/>December 31,</b> |                     |                     |
|---|-------------------------------------|---------------------|---------------------|
|   | <b>2007</b>                         | <b>2008</b>         | <b>2009</b>         |
| Research and development                      | \$ 424,326                          | \$ 810,425          | \$ 1,245,003        |
| General and administrative                    | 363,991                             | 1,495,190           | 1,141,979           |
| <b>Total stock-based compensation expense</b> | <b>\$ 788,317</b>                   | <b>\$ 2,305,615</b> | <b>\$ 2,386,982</b> |

Allocations to research and development and general and administrative expense are based upon the department to which the associated employee reported. No related tax benefits of the stock-based compensation expense have been recognized. Share-based payments issued to nonemployees are recorded at their fair values, and are periodically revalued as the equity instruments vest and are recognized as expense over the related service period.

*Income Taxes*

The Company provides for income taxes using the liability method. Under this method, deferred tax assets and liabilities are determined based on differences between financial reporting and tax bases of assets and liabilities, and are measured using the enacted tax rates and laws that will be in effect when the differences are expected to reverse.

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**Table of Contents**

**AVEO Pharmaceuticals, Inc.**

**Notes to Consolidated Financial Statements (Continued)**

**December 31, 2009**

**2. Significant Accounting Policies (Continued)**

On January 1, 2009 the Company adopted FASB Interpretation No. 48, *Accounting for Uncertainty In Income Taxes* (codified within ASC Topic 740, *Income Taxes*). See Note 10 for details.

*Segment and Geographic Information*

Operating segments are defined as components of an enterprise engaging in business activities for which discrete financial information is available and regularly reviewed by the chief operating decision maker in deciding how to allocate resources and in assessing performance. The Company views its operations and manages its business in one operating segment and the Company operates in only one geographic segment.

*Use of Estimates*

The preparation of financial statements in conformity with accounting principles generally accepted in the United States requires the Company's management to make estimates and assumptions that affect the amounts reported in the financial statements and accompanying notes. Actual results could differ from those estimates.

*Recently Adopted Accounting Standards*

Effective January 1, 2009, the Company 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. The adoption of this accounting standard did not have a significant 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. The Company adopted this guidance effective June 15, 2009. The adoption did not impact the Company's 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. The Company's adoption of this standard had no material impact on its financial position or results of operations.

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 principles. Pursuant to the provisions of ASC 105, the Company has updated references to Generally Accepted Accounting Principles (GAAP) in the Company's financial statements issued for the year ended December 31, 2009. The adoption of ASC 105 did not impact the Company's financial position or results of operations.

*Recently Issued Accounting Standards*

In August 2009, the FASB issued Accounting Standards Update No. 2009-05, *Measuring Liabilities at Fair Value* (ASU 2009-05). ASU 2009-05 amends Accounting Standards Codification Topic 820, *Fair Value*



**Table of Contents**

**AVEO Pharmaceuticals, Inc.**

**Notes to Consolidated Financial Statements (Continued)**

**December 31, 2009**

**2. Significant Accounting Policies (Continued)**

*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 Company's 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. The Company is required to adopt Update No. 2009-13 as of January 1, 2011 and is in the process of determining the impact that the adoption of Update No. 2009-13 will have on its future results of operations or financial position.

**3. Net Loss Per Common Share**

Basic net loss per share is calculated by dividing the net loss attributable to common stockholders by the weighted-average number of common shares outstanding during the period, without consideration for common stock equivalents. Diluted net loss per share is computed by dividing the net loss attributable to common stockholders by the weighted-average number of common share equivalents outstanding for the period determined using the treasury-stock method. For purposes of this calculation, convertible preferred stock, stock options and warrants are considered to be common stock equivalents and are only included in the calculation of diluted net loss per share when their effect is dilutive.

**Table of Contents****AVEO Pharmaceuticals, Inc.****Notes to Consolidated Financial Statements (Continued)****December 31, 2009****3. Net Loss Per Common Share (Continued)**

As disclosed previously, pro forma net loss per share assumes the conversion of all convertible preferred stock at the beginning of the period (or at the original date of issuance, if later) as follows:

|  | 2007            | Years Ended<br>December 31,<br>2008 | 2009            |
|--|-----------------|-------------------------------------|-----------------|
| <b>Historical net loss per share</b>   |                 |                                     |                 |
| Numerator:   |                 |                                     |                 |
| Net loss   | \$ (24,981,820) | \$ (32,473,124)                     | \$ (44,093,388) |
| Denominator:   |                 |                                     |                 |
| Weighted average common shares outstanding   | 1,396,323       | 1,540,575                           | 1,607,329       |
| Basic and diluted net loss per share   | \$ (17.89)      | \$ (21.08)                          | \$ (27.43)      |
| <b>Pro forma net loss per common share (unaudited)</b>   |                 |                                     |                 |
| Numerator:   |                 |                                     |                 |
| Net loss used to compute pro forma net loss per share  |                 |                                     | \$ (44,093,388) |
| Denominator:   |                 |                                     |                 |
| Basic and diluted weighted-average common shares, as used above  |                 |                                     | 1,607,329       |
| Add: Pro forma adjustments to reflect assumed weighted-average effect of conversion of convertible preferred stock |                 |                                     | 18,160,753      |
| Weighted-average shares used in computing pro forma  |                 |                                     |                 |
| basic and diluted net loss per common share  |                 |                                     | 19,768,082      |
| Pro forma basic and diluted net loss per common share  |                 |                                     | \$ (2.23)       |

**4. Property and Equipment**

Property and equipment consists of the following:

|                                 | Estimated<br>Useful Life | December 31,<br>2008 | December 31,<br>2009 |
|---------------------------------|--------------------------|----------------------|----------------------|
| Laboratory equipment            | 5 years                  | \$ 6,382,069         | \$ 7,159,729         |
| Computer equipment and software | 3 years                  | 1,254,083            | 1,390,339            |
| Office furniture                | 5 years                  | 96,610               | 188,596              |

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|  |  |              |              |
|--|--|--------------|--------------|
| Leasehold improvements                         | Shorter of asset's useful life<br>or remaining term of lease | 3,498,177    | 3,768,013    |
| Construction in process                        |  | 6,317        | 464,500      |
|  |  | 11,237,256   | 12,971,177   |
| Less accumulated depreciation and amortization |  | (7,484,816)  | (8,773,702)  |
| Property and equipment, net                    |  | \$ 3,752,440 | \$ 4,197,475 |

Depreciation expense for the years ended December 31, 2007, 2008 and 2009 was \$1,334,239, \$1,320,754 and \$1,288,886 respectively.



**Table of Contents****AVEO Pharmaceuticals, Inc.****Notes to Consolidated Financial Statements (Continued)****December 31, 2009****5. Accrued Expenses**

Accrued expenses consisted of the following:

|                       | <b>December 31,<br/>2008</b> | <b>December 31,<br/>2009</b> |
|-----------------------|------------------------------|------------------------------|
| Salaries and benefits | \$ 1,854,711                 | \$ 2,141,484                 |
| Clinical expenses     | 1,140,433                    | 4,612,255                    |
| Other                 | 413,380                      | 635,394                      |
|                       | <b>\$ 3,408,524</b>          | <b>\$ 7,389,133</b>          |

**6. Loans Payable**

The Company previously entered into a \$7.5 million financing agreement with a financial institution for an equipment capital expenditure line (the Equipment Line) and a refinancing line of existing equipment debt (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). Borrowings under the Refinancing Line were repaid over 36 months at a rate of 7.86% with the final maturity in January 2007. There is no remaining borrowing ability under the Refinancing Line. The Equipment Line is secured by an interest in the specific financed assets. There is a requirement to maintain minimum unrestricted cash equal to the greater of \$12 million or nine months cash burn. Monthly cash burn is calculated using an average of adjusted net loss for the most recent six months less current portion of long-term debt divided by twelve. In the event of violation of the minimum cash requirement, the Company must provide a letter of credit or security deposit equal to 70% of the outstanding balance of the equipment financing agreement. The Company was in compliance with this covenant as of December 31, 2009. The principal outstanding at December 31, 2009 and 2008 is \$101,867 and \$1,466,725, respectively. At December 31, 2009 there was no remaining ability to borrow under the Equipment Line.

On March 29, 2006, the Company entered into a \$15 million financing agreement with a financial institution for general corporate purposes. On May 15, 2008, the Company repaid the remaining principal of \$10.1 million due on this loan and entered into a new \$21 million financing agreement. Under ASC 470-50, *Modifications and Extinguishments (Debt)*, the repayment was considered an extinguishment of debt; as such, the remaining loan discount and prepaid loan fees of approximately \$249,000 were recorded as loss on loan extinguishment. The full amount of the new loan was drawn down in 2008.

In May 2009, the Company triggered a provision allowing a six month extension to the original twelve month interest only period. The interest only period extended through November 2009. The remaining principal and associated interest is due and payable in equal monthly installments based upon a 30-month amortization schedule beginning December 2009. The loan also calls for a deferred charge of 5.95% to be paid upon maturity. The deferred charge of \$1,249,500 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. The Company has also 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 the borrower's assets, except for intellectual property and the capital equipment securing the Equipment and Refinancing Lines. The financing agreement defines events of default, including a material adverse effect clause. The material adverse effect clause defines an event of default in the event of a material adverse effect of the Company's business operations, properties, assets or condition, the ability of the Company to repay the loan, or the Company's interest in or the lender's security interest in the collateral. As of December 31, 2009, there have been no events of default under the loan. The principal outstanding under these loans at December 31, 2009 and



**Table of Contents****AVEO Pharmaceuticals, Inc.****Notes to Consolidated Financial Statements (Continued)****December 31, 2009****6. Loans Payable (Continued)**

2008 is \$20,378,854 and \$21,000,000, respectively. The Company incurred approximately \$205,000 in loan issuance costs paid directly to the financing institution, which have been offset against the loan proceeds as a loan discount.

In connection with the 2008 financing agreement, a warrant was issued to the financing institution for the purchase of \$472,500 of the Company's Series D convertible preferred stock (Series D Preferred Stock), or the next round of preferred stock if the exercise price paid by investors in that round was less than \$2.50 per share. Upon the close of the Series E convertible preferred stock (Series E Preferred Stock) financing in March 2009, the warrant became exercisable for Series D Preferred Stock at the price paid by investors of \$2.50 per share. During 2008, upon issuance of the warrants, the Company recorded the relative fair value of the warrants of approximately \$313,700 as a long-term liability in accordance with ASC 480, *Distinguishing Liabilities from Equity*, and as a discount to the related loan outstanding and will amortize the value of the discount to interest expense over the term of the loan using the effective interest method. The resulting effective interest rate including the fair value of the warrant, the loan issuance costs and the deferred charge approximates 13.6%. The relative fair value of the warrant was calculated using the Black-Scholes option-pricing model with the following assumptions: volatility 68.16%, expected term equal to the contractual life of the warrant (seven years), risk-free interest rate 3.4% and no dividend yield. The fair value of all preferred stock warrants outstanding, including the Series D warrants issued in 2008, was remeasured as of December 31, 2009 and 2008 with the net change in fair value recorded within other income (expense). The warrants will be revalued at each reporting period until they are exercised or otherwise expire. Immediately prior to the closing of the Company's initial public offering, the preferred stock warrant liability will be reclassified into additional paid-in capital as a result of the conversion of warrants to purchase convertible preferred stock into warrants to purchase common stock. The Company recorded \$675,500 and \$464,700 of noncash interest expense for the years ended December 31, 2009 and 2008, respectively, from amortization of the loan discounts.

Under the original loan, which was extinguished in May 2008, the Company determined that a beneficial conversion feature existed with respect to a conversion option given to the financing institution. Such beneficial conversion feature of approximately \$208,000 was calculated as the intrinsic value of the difference between the conversion option of \$3.5 million and such conversion option less its relative share of total discounts on the debt. Since the option was contingent upon the occurrence of a future event, the conversion feature was not recognized until the contingency occurred or was resolved, and accordingly, the \$208,000 was recognized in March 2007 upon the closing of the Series D Preferred Stock financing (see Note 11). The financing institution did not exercise this option to convert and, accordingly, such option has terminated.

Future minimum payments under the loans payable outstanding as of December 31, 2009 are as follows:

| <b>Years Ending December 31:</b>      |               |
|---------------------------------------|---------------|
| 2010                                  | \$ 9,605,224  |
| 2011                                  | 9,507,993     |
| 2012                                  | 3,993,114     |
|                                       | 23,106,331    |
| Less amount representing interest     | (2,625,611)   |
| Less discount                         | (735,961)     |
| Less current portion                  | (7,466,973)   |
| Loans payable, net of current portion | \$ 12,277,786 |



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**Table of Contents****AVEO Pharmaceuticals, Inc.****Notes to Consolidated Financial Statements (Continued)****December 31, 2009****7. Collaboration and License Agreements***(a) Out-License Agreements**Merck & Co., Inc. (Merck)*

In November 2003, the Company entered into a license and research collaboration agreement with Merck to discover and validate oncology targets. Under the agreement, Merck paid the Company an up-front payment of \$7.0 million, which was amortized over the period of substantial involvement of 3.5 years, and made research funding payments of approximately \$6.0 million over the course of the three-year research program.

In April 2005, the Company and Merck expanded the collaboration, and as part of that expansion, the Company received cash payments for an aggregate of \$4.0 million, paid in two equal annual installments in each of May 2005 and April 2006. These payments were initially deferred and were amortized to revenue over the remaining period of the Company's substantial involvement, which was through April 2007. In addition, Merck purchased 1,666,667 shares of Series C convertible preferred stock (Series C Preferred Stock) at a per share price of \$3.00, resulting in gross proceeds to the Company of approximately \$5.0 million. In addition, if all development and regulatory milestones are reached with respect to six molecular targets, potential additional milestone payments could total, in the aggregate, \$249.0 million. The Company is 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, the Company entered into a second license and research collaboration agreement with Merck which provides for the use of the Company's Human Response Platform. Over the course of the collaborative research program, which has concluded, the Company received approximately \$4.5 million in research funding. In addition, Merck purchased 666,667 shares of Series C Preferred Stock, at a per share price of \$3.00, resulting in gross proceeds to the Company of approximately \$2.0 million. If all development and regulatory milestones under the agreement are achieved, potential milestone payments could total, in the aggregate, \$4.9 million.

Revenue earned under all Merck agreements was \$3,243,600 for the year ended December 31, 2007, for a total of \$21.8 million earned under these agreements. No revenue was earned after 2007.

*Merck (Formerly Schering-Plough Corporation)*

In March 2007, the Company entered into an agreement with Schering-Plough, through its subsidiary Schering Corporation, acting through its Schering-Plough Research Institute division, under which it granted Schering-Plough (now Merck) exclusive, worldwide rights to develop and commercialize all of the Company's monoclonal antibody antagonists of hepatocyte growth factor (HGF), including AV-299. The Company also granted Merck an exclusive, worldwide license to related biomarkers for diagnostic use. Under the agreement, the Company received an up-front payment of \$7.5 million in May 2007, which is being amortized over the Company's period of substantial involvement, or through completion of the first phase 2 proof-of-concept trial for AV-299, which is expected to be in the first half of 2012. In addition, Schering-Plough purchased 4,000,000 shares of Series D Preferred Stock, at a per share price of \$2.50, resulting in gross proceeds to the Company of \$10.0 million. The amount paid for the Series D Preferred Stock represented fair value as it was the same as the amounts paid by unrelated investors in March and April 2007. Merck will also fund research of up to \$3.0 million per year for the first three years of the agreement and reimburse development expenses through completion of the first phase 2 proof-of-concept trial for AV-299, unless extended by mutual written agreement of the parties. 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, the Company is eligible to receive royalties on Merck's net sales of AV-299.



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**Table of Contents****AVEO Pharmaceuticals, Inc.****Notes to Consolidated Financial Statements (Continued)****December 31, 2009****7. Collaboration and License Agreements (Continued)**

Under the agreement, the Company received cash payments related to upfront license fees, milestone payments, research and development funding, and equity of \$10,576,000, \$9,522,000, and \$25,833,000 and recorded revenue of \$10,853,000, \$13,349,000 and \$6,624,000 for the years ended December 31, 2009, 2008 and 2007, respectively.

*OSI Pharmaceuticals (OSI)*

In September 2007, the Company entered into a collaboration and license agreement with OSI Pharmaceuticals, Inc., (OSI), which provides for the use of the Company's proprietary *in vivo* models by the Company's scientists at its facilities, use of the Company's 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. Under the agreement, OSI paid the Company an up-front payment of \$7.5 million, which was recorded in deferred revenue and is being amortized over the Company's period of substantial involvement which is now determined to be through July 2011. OSI also paid the Company \$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 research payments of \$625,000 per quarter through July 2009. In addition, OSI purchased 1,833,334 shares of Series C Preferred Stock, at a per share price of \$3.00, resulting in gross proceeds to the Company of \$5.5 million. The Company determined that the price paid of \$3.00 per share by OSI included a premium of \$0.50 over the price per share of the Company's Series D Preferred Stock sold in April 2007; accordingly, the Company 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, the Company and OSI expanded the strategic partnership and the Company granted OSI a non-exclusive license to use the Company's proprietary bioinformatics platform, and non-exclusive perpetual licenses to use bioinformatics data and a Company proprietary gene index related to a specific target pathway. Further, as part of the expanded strategic partnership, the Company granted OSI an option, exercisable upon payment of an option fee, to receive non-exclusive perpetual rights to certain elements of the Company's Human Response Platform and to use the Company's bioinformatics platform, and the Company granted OSI the right to obtain certain of its tumor models and tumor archives. In consideration for such additional rights, under the amended agreement, OSI paid the Company an up-front payment of \$5.0 million, which was recorded in deferred revenue and will be amortized over the Company's 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 Preferred Stock, at a per share price of \$4.00, resulting in gross proceeds to the Company of \$15.0 million. The Company determined that the price of \$4.00 per share paid by OSI included a premium of \$1.04 per share over the fair value of the Series E Preferred Stock of \$2.96 as calculated by the Company in its retrospective stock valuation. The valuation used the Market Approach to estimate the Company's enterprise value and the Probability Weighted Expected Return Method (PWERM) to allocate the enterprise value to each class of the Company's equity securities; accordingly, the Company will recognize the premium of \$3,900,000 as additional license revenue on a straight-line basis over the period of substantial involvement.

Under the amended agreement, if all applicable milestones are achieved, payments for the successful achievement of discovery, development and commercialization milestones could total, in the aggregate, over \$94.0 million for each target and its associated products. In addition, the Company is eligible to receive up to \$27.0 million in milestones for certain deliverables and research milestones. OSI has the option to receive non-exclusive perpetual rights to certain elements of the Company's Human Response Platform and to use the Company's bioinformatics platform and to certain of its tumor models and tumor archives for an option fee. If

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**Table of Contents****AVEO Pharmaceuticals, Inc.****Notes to Consolidated Financial Statements (Continued)****December 31, 2009****7. Collaboration and License Agreements (Continued)**

OSI elects to exercise this option and the Company transfers the relevant technology to OSI, OSI will be required to pay the Company license expansion fees of \$25 million. If OSI does not elect to exercise this option, OSI must pay a lesser amount in order to retain its rights to the bioinformatics platform and any new targets. Upon commercialization of products under the agreement, the Company is eligible to receive tiered royalty payments on sales of products by OSI, its affiliates and sublicensees. All milestones earned to date are for selection of targets, delivery of models or delivery of cell lines. These milestones are not considered to be at risk and substantive, therefore, the milestone payments are being deferred and when earned, will be recognized on a straight line basis over the remaining estimated period of substantial involvement.

Under these agreements, the Company received cash payments related to upfront license fees, milestone payments, research and development funding, and equity of \$26,546,000, \$1,989,000 and \$15,500,000 and recorded revenue of \$9,787,000, \$6,145,000 and \$1,083,000 for the years ended December 31, 2009, 2008 and 2007, respectively.

*Biogen Idec International GmbH (Biogen Idec)*

In March 2009, the Company entered into an exclusive option and license agreement with Biogen Idec International GmbH, a subsidiary of Biogen Idec Inc., collectively referred to herein as *Biogen Idec*, regarding the development and commercialization of the Company's 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 terms of the agreement, Biogen Idec paid the Company an upfront cash payment of \$5.0 million in March 2009, which will be amortized over the Company's period of substantial involvement once determined. In addition, Biogen Idec purchased 7,500,000 shares of Series E Preferred Stock at a per share price of \$4.00, resulting in gross proceeds to the Company of \$30.0 million. The Company determined that the price of \$4.00 paid by Biogen Idec included a premium of \$1.09 per share over the fair value of the Series E Preferred Stock of \$2.91 as calculated by the Company in its retrospective stock valuation. The valuation used the Market Approach to estimate the Company's enterprise value and the Probability Weighted Expected Return Method (PWERM) to allocate the enterprise value to each class of the Company's equity securities; accordingly, the Company will recognize the premium of \$8,175,000 as revenue on a straight-line basis over the period of substantial involvement. In June 2009, the Company received a \$5.0 million milestone payment for achievement of the first pre-clinical discovery milestone under the agreement. The Company could also receive (i) additional 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. Since the \$5.0 million milestone payment received in June is a near term milestone and not considered to be substantive and at risk, the revenue will be amortized as additional license revenue over the Company's period of substantial involvement. Once a development candidate has been selected in the first quarter of 2010, the Company will begin amortizing all license revenue under the agreement over the projected twenty year patent life of the candidate.

If Biogen Idec exercises its exclusive option under the agreement, Biogen Idec will pay the Company royalties on Biogen Idec's sales of ErbB3 antibody products in its territory, and the Company will pay Biogen Idec royalties on the Company's sale of ErbB3 antibody products in the United States, Canada and Mexico. Under the agreement, the Company received cash payments related to upfront license fees, milestone payments, and equity of \$40,000,000 for the year ended December 31, 2009. The Company has not yet recorded any revenue under the agreement as the period of substantial involvement had not yet been determined as of December 31, 2009.



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**AVEO Pharmaceuticals, Inc.**

**Notes to Consolidated Financial Statements (Continued)**

**December 31, 2009**

**7. Collaboration and License Agreements (Continued)**

*(b) In-license Agreements*

*Mitsubishi Pharma Corporation (Mitsubishi)*

In December 2005, the Company entered into an exclusive license agreement to develop and commercialize Mitsubishi's novel multiple kinase inhibitor, AV-412, in all territories outside of Asia. The agreement called for the Company to make an initial payment of \$2.5 million, which was accrued for as of December 31, 2005, and research and development expense and sales and development milestone payments of up to \$37.5 million for cancer indications. The Company paid the \$2.5 million to Mitsubishi in January 2006. The first milestone payment of \$1.0 million was paid in 2006 and was charged to research and development expense. The Company terminated the agreement effective January 26, 2010. Costs to wind down the project are expected to be minimal.

*Kirin Brewery Co. Ltd. (Kirin)*

In December 2006, the Company entered into an exclusive license agreement with Kirin Brewery Co. Ltd. (now Kyowa Hakko Kirin) to research, develop, manufacture and commercialize tivozanib (f/k/a KRN951), pharmaceutical compositions thereof and associated biomarkers in all territories in the world except for Asia. Upon entering into the license agreement, the Company made a one-time cash payment in the amount of \$5.0 million, which the Company accrued in December 2006 as research and development expense and paid in January 2007. The Company will be required to make a \$10.0 million milestone payment to Kyowa Hakko Kirin in connection with the Company's phase 3 clinical trial of tivozanib, which the Company expects to pay in the first quarter of 2010. In addition, the Company may be required to make up to an aggregate of \$50.0 million in additional milestone payments upon the achievement of specified regulatory milestones. The Company is also required to pay tiered royalty payments on net sales it makes of tivozanib in its territory. The royalty rates under the agreement range from the low to mid teens as a percentage of the Company's net sales of tivozanib.

The Company also has the right to grant sublicenses under the license agreement, subject to certain restrictions. In the event the Company sublicenses the rights licensed to it as part of the agreement, the Company is required to pay Kyowa Hakko Kirin a specified percentage of any amounts the Company receives from any third party sublicenses, other than amounts it receives in respect of research and development funding or equity investments, subject to certain limitations.

*Other License Agreements*

The Company has entered into various cancelable license agreements for patented technology and other technology related to research projects, including technology to humanize AV-299 and other antibody product candidates. Certain of these arrangements related to the humanization and discovery of the Company's antibody products required the Company to pay an aggregate of \$1.5 million and \$500,000, for the years ended December 31, 2008 and 2007, respectively, in up-front licensing fees and milestones payments. There were no up-front licensing fees and milestone payments in 2009. The Company is also obligated to pay annual maintenance payments of \$475,000, which are recognized as research and development expense over the maintenance period. Under one of these agreements, if the parties agree to the use of the licensed technology in development of a product, the Company will be required to make a \$1.0 million license payment per product. These agreements also 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.

Certain other research agreements require the Company to remit royalties in amounts ranging from 0.5% to 1.5% based on net sales of products utilizing the licensed technology. Total license expense incurred under these



**Table of Contents****AVEO Pharmaceuticals, Inc.****Notes to Consolidated Financial Statements (Continued)****December 31, 2009****7. Collaboration and License Agreements (Continued)**

other license agreements amounted to \$0.44 million, \$0.46 million and \$0.79 million, for the years ended December 31, 2009, 2008 and 2007, respectively. The Company has not paid any royalties to date.

**8. Related-Party Transactions**

During 2004, the Company entered into a sublease agreement with Millennium Pharmaceuticals (Millennium) (Note 9), which had a board member who was also a member of the Company's Board. For the years ended December 31, 2009, 2008 and 2007 the Company made payments of \$3.32 million, \$3.29 million and \$3.33 million, respectively, to Millennium for rent, operating expenses and utilities. At December 31, 2009 and 2008, the Company had outstanding payables to Millennium of \$80,400 and \$148,300, respectively.

**9. Commitments and Contingencies***Operating Leases*

The Company leases office and lab space and equipment under various operating lease agreements. Rent expense under the operating leases amounted to \$2.18 million, \$2.03 million and \$1.97 million for the years ended December 31, 2009, 2008 and 2007, respectively.

In July 2004, the Company entered into a sublease agreement with Millennium, to sublease 55,200 square feet of office and lab space. The sublease will expire on February 28, 2014. In conjunction with the signing of this lease, the Company entered into a standby letter of credit in the amount of \$552,000 to expire on July 12, 2005, subject to automatic extensions for periods of one year as a security deposit on said lease. The letter of credit has been collateralized by a money market account held by the bank which issued the letter of credit and has been automatically extended through July 12, 2010. The Company has classified this money market account within restricted cash on its balance sheets at December 31, 2009 and 2008. The Company received six free months of rent under this arrangement and has straight-lined the total rent payments over the lease term resulting in deferred rent of approximately \$969,000 and \$1.1 million at December 31, 2009 and 2008, respectively.

In September 2008, the Company entered into a sublease agreement with Alkermes, Inc., to sublease 7,407 square feet of office space. The sublease will expire on April 30, 2012. In conjunction with the lease, the Company entered into a standby letter of credit in the amount of \$55,392 to expire on May 30, 2010 subject to automatic extensions for periods of one year as a security deposit on said lease. The letter of credit has been collateralized by a money market account held by the bank which issued the letter of credit. The Company has classified this money market account within restricted cash on its balance sheet at December 31, 2009 and 2008, respectively. The Company received six free weeks of rent under this arrangement and has straight-lined the total rent payments over the lease term resulting in deferred rent of approximately \$26,800 and \$26,000 at December 31, 2009 and 2008, respectively.

Future annual minimum lease payments under all noncancelable operating leases at December 31, 2009 are as follows:

**Years Ending December 31:**

|      |              |
|------|--------------|
| 2010 | \$ 2,365,000 |
| 2011 | 2,453,000    |

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|      |              |
|------|--------------|
| 2012 | 2,289,000    |
| 2013 | 2,208,000    |
| 2014 | 368,000      |
|      | \$ 9,683,000 |

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**Table of Contents****AVEO Pharmaceuticals, Inc.****Notes to Consolidated Financial Statements (Continued)****December 31, 2009****9. Commitments and Contingencies (Continued)***Employment Agreements*

Certain key executives are covered by severance and change in control agreements. Under these agreements, if the executive is terminated without cause or if the executive terminates his employment for good reason, such executive will be entitled to receive severance equal to his base salary, benefits and prorated bonuses for a period of time equal to either 12 months or 18 months, depending on the terms of such executive's individual agreement. In addition, in December 2007, the Company approved a key employee change in control severance benefits plan, which was amended in November 2009, and which provides for severance and other benefits under certain qualifying termination events upon a change in control for a period of time ranging from 6 months to 18 months, depending upon the level of the key employee.

**10. Income Taxes**

The Company accounts for income taxes under the provisions of ASC Topic 740, *Income Taxes*. The Company recorded a tax benefit for the year ended December 31, 2009 in the amount of \$100,056 representing a current benefit for federal income taxes related to certain refundable credits. The Company did not record a federal or state tax provision for the years ended December 31, 2007 and 2008.

A reconciliation of the expected income tax benefit computed using the federal statutory income tax rate to the Company's effective income tax rate is as follows for the years ended December 31, 2007, 2008 and 2009:

|   | December 31,<br>2007 | December 31,<br>2008 | December 31,<br>2009 |
|---|----------------------|----------------------|----------------------|
| Income tax computed at federal statutory tax rate | 34.0%                | 34.0%                | 34.0%                |
| State taxes, net of federal benefit               | 6.3%                 | 6.3%                 | 6.3%                 |
| Research and development credits                  | 5.2%                 | 4.1%                 | 2.5%                 |
| Permanent differences                             | (0.8)%               | (1.5)%               | (1.0)%               |
| Other   | %                    | (3.9)%               | %                    |
| Change in valuation allowance                     | (44.7)%              | (39.0)%              | (41.6)%              |
| <b>Total</b>                                      | <b>0.0%</b>          | <b>0.0%</b>          | <b>0.2%</b>          |

The Company has incurred net operating losses from inception. At December 31, 2009, the Company had domestic federal and state net operating loss carryforwards of approximately \$130,915,000 and \$102,231,000, respectively, available to reduce future taxable income, which expire at various dates. The federal net operating loss carryforwards expire beginning in 2022 through 2029 and the state loss carryforwards expire beginning in 2010 through 2014. The Company also had federal and state research and development tax credit carryforwards of approximately \$3,462,000 and \$2,072,000, respectively, available to reduce future tax liabilities and which expire at various dates. The federal credits expire beginning in 2022 through 2029 and the state credits begin to expire in 2010. The net operating loss and research and development carryforwards are subject to review and possible adjustment by the Internal Revenue Service and may be limited in the event of certain changes in the ownership interest of significant stockholders.



**Table of Contents****AVEO Pharmaceuticals, Inc.****Notes to Consolidated Financial Statements (Continued)****December 31, 2009****10. Income Taxes (Continued)**

The Company's net deferred tax assets as of December 31 are as follows:

|                                  | <b>2008</b>   | <b>2009</b>   |
|----------------------------------|---------------|---------------|
| NOL carryforwards                | \$ 43,051,000 | \$ 50,921,000 |
| Research and development credits | 4,868,000     | 4,829,000     |
| Deferred revenue                 | 5,292,000     | 14,136,000    |
| Other temporary differences      | 2,300,000     | 2,368,000     |
| Valuation allowance              | (55,511,000)  | (72,254,000)  |
|                                  | \$            | \$            |

A full valuation allowance has been recorded in the accompanying consolidated financial statements to offset these deferred tax assets because the future realizability of such assets is uncertain. This determination is based primarily on historical losses without considering the impact of any potential upturn in the Company's business. Accordingly, future favorable adjustments to the valuation allowance may be required, if and when circumstances change. The valuation allowance increased by \$16,743,000 during 2009, primarily due to an increase in net operating loss carryforwards related to the Company's net loss.

In June 2006, FASB issued Interpretation No. 48, *Accounting for Uncertainty in Income Taxes, an interpretation of FAS 109* (codified within ASC Topic 749, *Income Taxes*), which provides a comprehensive model for the financial statement recognition, measurement, presentation and disclosure of uncertain tax positions taken or expected to be taken in income tax returns. Unrecognized tax benefits represent tax positions for which reserves have been established. The Company adopted this new accounting guidance on January 1, 2009. The implementation did not have a material impact on the Company's consolidated financial statements, results of operations or cash flows. At the adoption date of January 1, 2009, the Company had \$1.2 million of unrecognized tax benefits. A full valuation allowance has been provided against the Company's deferred tax assets, so that the effect of the unrecognized tax benefits is to reduce the gross amount of the deferred tax asset and the corresponding valuation allowance. Therefore, there is no effect of adopting this guidance. Since the Company has incurred net operating losses since inception, it has never been subject to a revenue agent review. As a result, all periods since inception remain subject to examination by U.S. federal and Massachusetts jurisdictions.

The Company may from time to time be assessed interest or penalties by major tax jurisdictions. The Company recognizes interest and penalties related to uncertain tax positions in income tax expense. No interest and penalties have been recognized by the Company to date.

The Company anticipates that the amount of unrecognized tax benefits recorded will not change in the next twelve months.

The following is a reconciliation of the Company's gross uncertain tax positions at December 31, 2009:

**Year ended  
December 31,  
2009**

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|  |              |
|--|--------------|
| Amount established upon adoption         | \$ 1,200,000 |
| Additions for current year tax positions |              |
| Additions for prior year tax positions   |              |
| Reductions of prior year tax positions   |              |
| Balance as of end of year                | \$ 1,200,000 |

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**Table of Contents****AVEO Pharmaceuticals, Inc.****Notes to Consolidated Financial Statements (Continued)****December 31, 2009****11. Convertible Preferred Stock**

The Company's Convertible Preferred Stock consisted of the following:

|   | December 31,<br>2008 | December 31,<br>2009 |
|---|----------------------|----------------------|
| Series A convertible preferred stock, \$.001 par value: 12,448,000 shares authorized; 12,400,000 and 12,428,198 shares issued and outstanding at December 31, 2008 and 2009, respectively (at liquidation value) (no shares authorized, issued or outstanding pro forma)  | \$ 15,500,000        | \$ 15,560,000        |
| Series B convertible preferred stock, \$.001 par value: 27,215,385 shares authorized; 26,906,354 shares issued and outstanding at December 31, 2008 and 2009, respectively (at liquidation value) (no shares authorized, issued or outstanding pro forma)   | 43,722,826           | 43,722,826           |
| Series C convertible preferred stock, \$.001 par value: 4,166,668 shares authorized, issued and outstanding at December 31, 2008 and 2009, respectively (at liquidation value) (no shares authorized, issued or outstanding pro forma).   | 11,583,336           | 11,583,336           |
| Series D convertible preferred stock, \$.001 par value: 24,439,800 and 21,794,310 shares authorized at December 31, 2008 and 2009, respectively; 21,165,510 shares issued and outstanding at December 31, 2008 and 2009, respectively (at liquidation value) (no shares authorized, issued or outstanding pro forma). | 52,913,775           | 52,913,775           |
| Series E convertible preferred stock, \$.001 par value: 15,000,000 shares authorized; 11,250,000 shares issued and outstanding at December 31, 2009 (at liquidation value) (no shares authorized, issued or outstanding pro forma).   |                      | 32,925,000           |
|   | \$ 123,719,937       | \$ 156,704,937       |

Between March and April 2007, the Company issued 21,165,510 shares of Series D Preferred Stock at a price per share of \$2.50, resulting in gross proceeds to the Company of \$52.9 million. The Series D Preferred Stock carries the same terms and conditions as Series A convertible preferred stock (Senior A Preferred Stock) and Series B convertible preferred stock (Series B Preferred Stock). In conjunction with this financing transaction, the Company increased its stock option pool by 3,750,000 shares.

In October 2007, the Company issued 1,833,334 shares of Series C Preferred Stock to OSI (see Note 7) at a per-share price of \$3.00, resulting in gross proceeds to the Company of \$5.5 million. The Series C Preferred Stock carries the same terms and conditions as Series A, B and D Preferred Stock except that Series C Preferred Stock has an antidilution price of \$2.50 per share.

In March 2009, the Company issued 7,500,000 shares of Series E Preferred Stock to Biogen Idec (see Note 7) at a price per share of \$4.00, resulting in gross proceeds to the Company of \$30 million. Additionally, in July 2009, the Company issued 3,750,000 shares of Series E Preferred Stock to OSI (see Note 7) at \$4.00 per share, resulting in gross proceeds to the Company of \$15.0 million. The Series E Preferred Stock carries the same terms and conditions as the Series A, B, and D Preferred Stock.

The holders of the Series A, Series B, Series C, Series D and Series E Preferred Stock (the Preferred Stock) have the following rights:

*Dividends*

The holders of the Preferred Stock are entitled to receive dividends when, and as declared by, the Board.



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**AVEO Pharmaceuticals, Inc.**

**Notes to Consolidated Financial Statements (Continued)**

**December 31, 2009**

**11. Convertible Preferred Stock (Continued)**

*Voting*

The holders of the Preferred Stock are entitled to the number of votes equal to the number of shares of common stock into which each preferred share is convertible at the time of such vote.

*Liquidation*

In the event of voluntary or involuntary liquidation, dissolution, or winding-up of the Company, the holders of Preferred Stock are entitled to receive, on a pari passu basis, in preference to the holders of common stock: (i) in the case of Series A Preferred Stock, an amount equal to the greater of (a) \$1.25 per share, adjusted for certain dilutive events, plus any accrued and unpaid dividends or (b) an amount per share as would have been payable had each share been converted to common stock immediately prior to a liquidation event; (ii) in the case of Series B Preferred Stock, an amount equal to the greater of (a) \$1.625 per share, adjusted for certain dilutive events, plus any accrued and unpaid dividends or (b) an amount per share as would have been payable had each share been converted to common stock immediately prior to a liquidation event; (iii) in the case of Series C Preferred Stock, an amount equal to the greater of (a) \$3.00 per share, adjusted for certain dilutive events, plus any accrued and unpaid dividends or (b) an amount per share as would have been payable had each share been converted to common stock immediately prior to a liquidation event; (iv) in the case of Series D Preferred Stock, an amount equal to the greater of (a) \$2.50 per share, adjusted for certain dilutive events, plus any accrued and unpaid dividends or (b) an amount per share as would have been payable had each share been converted to common stock immediately prior to a liquidation event; (v) in the case of Series E Preferred Stock, an amount equal to the greater of (a) \$4.00 per share, adjusted for certain dilutive events, plus any accrued and unpaid dividends or (b) an amount per share as would have been payable had each share been converted to common stock immediately prior to a liquidation event. Any remaining assets shall be allocated ratably to the holders of the common stock. As the convertible preferred stock may become redeemable upon an event that is outside of the control of the Company, the value of the convertible preferred stock has been classified outside of permanent equity.

*Conversion*

Pursuant to a Certificate of Amendment to the Company's Certificate of Incorporation filed on February 18, 2010, every four shares of Preferred Stock are now convertible at the option of the holder into one share of common stock, adjustable for certain dilutive events, such as stock splits or stock dividends. The Preferred Stock will convert upon the closing of an initial public offering of the Company's common stock in which the per-share price is at least \$19.52, adjusted for certain dilutive events, and which results in net proceeds to the Company of at least \$25 million or upon the consent of the holders of at least 67% of the Preferred Stock outstanding. On February 11, 2010, the Company received the requisite consent of holders of Preferred Stock to convert the Preferred Stock into the Company's common stock upon the closing of an initial public offering prior to June 30, 2010.

The Company has evaluated each of its series of convertible preferred stock and determined that they should be considered an equity host and not a debt host. This evaluation is necessary to determine if any embedded features require bifurcation and therefore, accounted for separately as a derivative liability. The Company's analysis followed the whole instrument approach which compares an individual feature against the entire preferred stock instrument which includes that feature. The Company's analysis was based on a consideration of the economic characteristics and risks and more specifically evaluated all the stated and implied substantive terms and features including (i) whether the preferred stock included redemption features, (ii) how and when any redemption features could be exercised, (iii) whether the preferred stockholders were entitled to dividends, (iv) the voting rights of the preferred stock and (v) the existence and nature of any conversion rights. As a result of the Company's determination that the preferred stock is an equity host, the embedded conversion option is not considered a derivative liability.



**Table of Contents****AVEO Pharmaceuticals, Inc.****Notes to Consolidated Financial Statements (Continued)****December 31, 2009****12. Warrants and Common Stock**

As of December 31, 2009, the Company had the following warrants outstanding:

|                          | Number of<br>Shares | Exercise<br>Price | Expiration<br>Date |
|--------------------------|---------------------|-------------------|--------------------|
| Series B Preferred Stock | 100,000             | \$ 1.625          | 2013               |
| Series D Preferred Stock | 628,800             | \$ 2.500          | 2013-2018          |
|                          | 728,800             |                   |                    |

As of December 31, 2009, the Company had 25,500,000 authorized shares of common stock, \$0.001 par value, of which 1,640,714 shares were issued and outstanding. The Company has reserved the following shares of common stock at December 31, 2009:

|   |            |
|---|------------|
| Conversion of Series A Preferred Stock              | 3,107,046  |
| Conversion of Series B Preferred Stock and warrants | 6,751,579  |
| Conversion of Series C Preferred Stock              | 1,041,666  |
| Conversion of Series D Preferred Stock and warrants | 5,448,564  |
| Conversion of Series E Preferred Stock              | 2,812,500  |
| Common stock options                                | 3,275,906  |
|   | 22,437,261 |

**13. Preferred Stock Warrant Liability**

Warrants for shares of redeemable instruments are required to be accounted for as liabilities. Increases or decreases in fair value are recorded as other income or expense in the statements of operations. As a result, the Company's outstanding preferred stock warrants are revalued at the end of each reporting period using the Black-Scholes option pricing valuation model. Changes in fair value, based on the fair value of the Company's convertible preferred stock and other valuation assumptions, are reflected in the Company's statements of operations as other income or expense. Unless previously exercised, upon the closing of an initial public offering of the Company's common stock that results in the conversion of all outstanding shares of convertible preferred stock to common stock, the preferred stock warrants will convert into warrants to purchase shares of common stock, based on the then applicable conversion ratio for the related series of preferred stock. As of December 31, 2008 and 2009, each share of Series A, B and D Preferred Stock is convertible into one share of common stock. All preferred stock warrants were immediately exercisable upon their issuance.

The following table sets forth the fair values of preferred stock warrants as of December 31, 2008 and 2009:

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| Series   | Shares as of |            | Fair Value as of |              |
|----------|--------------|------------|------------------|--------------|
|          | 12/31/2008   | 12/31/2009 | 12/31/2008       | 12/31/2009   |
| Series A | 48,000       |            | \$ 72,480        | \$           |
| Series B | 100,000      | 100,000    | 148,000          | 207,000      |
| Series D | 628,800      | 628,800    | 990,522          | 1,251,528    |
| Total    | 776,800      | 728,800    | \$ 1,211,002     | \$ 1,458,528 |

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**Table of Contents****AVEO Pharmaceuticals, Inc.****Notes to Consolidated Financial Statements (Continued)****December 31, 2009****13. Preferred Stock Warrant Liability (Continued)**

The fair value of the preferred stock warrants was determined using the Black-Scholes valuation model with the following weighted-average assumptions:

|                         | <b>Years Ended December 31,</b> |             |
|-------------------------|---------------------------------|-------------|
|                         | <b>2008</b>                     | <b>2009</b> |
| Risk-free interest rate | 1.3%-2.42%                      | 2.20%-3.85% |
| Dividend yield          |                                 |             |
| Expected term (years)   | 4-10                            | 4-9         |
| Volatility              | 68.7%                           | 70.35%      |

**14. Stock-Based Compensation**

The Company maintains the 2002 Stock Incentive Plan (the Plan) for employees, consultants, advisors, and directors. The Plan provides for the grant of incentive and nonqualified stock options and restricted stock grants. The Plan also provides for the issuance of shares of common stock as determined by the Board. The Company has reserved 4,269,062 shares of common stock under the Plan, and at December 31, 2009, the Company has 395,876 shares available for future issuance under the Plan. Shares issued upon exercise of options are generally issued from new shares of the Company. The Plan provides that the exercise price of incentive stock options cannot be less than 100% of the fair market value of the common stock on the date of the award for participants who own less than 10% of the total combined voting power of stock of the Company and not less than 110% for participants who own more than 10% of the Company's voting power. Options and restricted stock granted under the Plan vest over periods as determined by the Board, which generally are equal to four years. Options generally expire ten years from the date of grant.

As discussed in Note 2, the Company adopted ASC 718, *Compensation-Stock Compensation*, effective January 1, 2006. The fair value of each stock option granted subsequent to the date of adoption is estimated on the date of grant using the Black-Scholes option-pricing model using the assumptions noted in the following table:

|                         | <b>Years Ended December 31,</b> |             |               |
|-------------------------|---------------------------------|-------------|---------------|
|                         | <b>2007</b>                     | <b>2008</b> | <b>2009</b>   |
| Risk-free interest rate | 3.49%-5.03%                     | 1.55%-3.34% | 1.98%-3.04%   |
| Dividend yield          |                                 |             |               |
| Expected term (years)   | 5.58                            | 5.61        | 5.50-6.25     |
| Volatility              | 68.16%                          | 68.70%      | 70.35%-72.04% |

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

Since the Company is privately held, it does not have relevant historical data to support its expected term and volatility. As such, the Company has used an average of several peer companies' volatilities to determine a reasonable estimate of its volatility. For purposes of identifying similar entities, the Company considered characteristics such as industry, length of trading history, similar vesting terms and in-the-money option status.

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For periods prior to 2009, the Company used an average of several peer companies with the characteristics described above to calculate its expected term given its limited history. For 2009, due to lack of available quarterly data, the Company 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

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**Table of Contents****AVEO Pharmaceuticals, Inc.****Notes to Consolidated Financial Statements (Continued)****December 31, 2009****14. Stock-Based Compensation (Continued)**

be the average of the vesting term and the contractual term of the option. Additionally, under the provisions of ASC 718, the Company is required to include an estimate of the value of the awards that will be forfeited in calculating compensation costs, which the Company estimates based upon actual historical forfeitures. The forfeiture estimates are recognized over the requisite service period of the awards on a straight-line basis. Based upon these assumptions, the weighted-average grant date fair value of stock options granted during the years ended December 31, 2009, 2008, and 2007 was \$6.48, \$4.00 and \$3.36 per share, respectively.

The Company has historically granted stock options at exercise prices not less than the fair market value of its common stock as determined by its board of directors, with input from management. The Company's board of directors has historically determined the estimated fair value of its 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 the Company sold shares of convertible preferred stock, the superior rights and preferences of securities senior to its common stock at the time of each grant, the results of operations, financial position, status of its research and development efforts, its stage of development and business strategy and the likelihood of achieving a liquidity event such as an initial public offering or sale of the Company.

The following table presents recent grant dates and related exercise prices of stock options granted to employees:

| <b>Date</b>       | <b>Number of<br/>Options<br/>Granted</b> | <b>Exercise Price</b> | <b>Reassessed Fair<br/>Value of<br/>Common<br/>Stock<br/>Per Share at<br/>Date of<br/>Grant</b> | <b>Intrinsic Value<br/>at Date of Grant</b> |
|-------------------|--|-----------------------|---|---|
| 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   |
| <b>Total</b>      | <b>991,857</b>                           |                       |   |   |

The exercise price for stock options granted above was set by the Company's board of directors based upon its valuation models. The Company's 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* (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 its 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:

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an initial public offering (IPO);

sale of the Company at an equity value greater than the combined liquidation preference of the preferred shares; and

sale of the Company at an equity value equal to or less than the combined liquidation preference of the preferred shares.

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**AVEO Pharmaceuticals, Inc.**

**Notes to Consolidated Financial Statements (Continued)**

**December 31, 2009**

**14. Stock-Based Compensation (Continued)**

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

In the IPO scenario of the Company's retrospective and contemporaneous valuations on November 28, 2008 and January 15, 2009 the Company applied the guideline transactions method under the market approach as provided in the Practice Aid and for subsequent valuations, the Company applied the guideline public company method under the market approach as provided in the Practice Aid due to the limited number of biotechnology company IPOs in 2008 and 2009. The Company's 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 the Company's retrospective and contemporaneous valuations, the Company applied the guideline transactions method under the market approach as provided in the Practice Aid. The Company's selection of guideline transactions took into account the timing of the transactions and the characteristics of the acquired companies. The Company 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 the Company's retrospective and contemporaneous valuations, it assumed sale or liquidation of the Company at an equity value equal to the liquidation preference of the Company's preferred shares.

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 the Company's application of CAPM, on each of the valuation dates disclosed, the Company 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 the Company's 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 the Company's pre-commercial stage of development prior to the IPO and also includes the Company's:

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

short operating history and history of operating losses since inception;



**Table of Contents****AVEO Pharmaceuticals, Inc.****Notes to Consolidated Financial Statements (Continued)****December 31, 2009****14. Stock-Based Compensation (Continued)**

need for substantial additional financing to achieve its goals; and

dependence on a limited number of collaboration partners.

In the Company's retrospective valuations for the period November 2008 to September 2009 and the Company's contemporaneous valuations for December 2009 and January 2010, it estimated the following probabilities and future sale and IPO dates:

| <b>Appraisal Date</b>  | <b>11/28/08</b> | <b>1/15/09</b> | <b>3/20/09</b> | <b>6/1/09</b> | <b>9/25/09</b> | <b>12/17/09</b> | <b>2/2/10</b> |
|--|-----------------|----------------|----------------|---------------|----------------|-----------------|---------------|
| 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           |
| <b>Probabilities</b>   |                 |                |                |               |                |                 |               |
| 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       |
| 1 <sup>st</sup> IPO date   | 12/31/09        | 12/31/09       | 3/31/10        | 3/31/10       | 3/31/10        | 3/31/10         | 3/31/10       |
| 2 <sup>nd</sup> 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 the Company's common stock at each valuation date is equal to the sum of the probability weighted present values for each scenario.

The Company has 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 the Company's common stock increased throughout 2009 thereby reducing the difference between the fair value of the Company's common stock and the estimated initial public offering price range. The increases were caused by business and scientific milestones, financing transactions and the proximity to a potential initial public offering. The retrospective fair value of the Company's common stock underlying 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 the following:

initiation of a phase 1 clinical trial for AV-299, for which the first patient dosed triggered a \$3 million milestone payment from Merck; and

because of the unfavorable conditions in the public markets, the Company deemed the probability of an IPO to be low or 20 percent.

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**AVEO Pharmaceuticals, Inc.**

**Notes to Consolidated Financial Statements (Continued)**

**December 31, 2009**

**14. Stock-Based Compensation (Continued)**

The retrospective fair value of the Company's common stock underlying options for 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:

the Company received a term sheet for the Biogen agreement for ErBb3 that included a proposed \$30 million investment in new Series E Preferred Stock which would be priced at a premium to its other classes of preferred stock;

the expected proceeds from the Biogen agreement would improve the Company's position for funding future cash needs;

due to the Company's progress, including continued progress of its phase 2 clinical trial showing a favorable safety profile in patients with advanced RCC, the Company deemed that the probability of an IPO increased to 25% and the probability of a sale below liquidation preference decreased to 5%; and

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

The retrospective fair value of the Company's common stock underlying options for 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, which included a \$30 million investment in Series E Preferred Stock at \$4.00 per share and a \$5 million upfront payment;

the Company initiated a phase 1b/2a clinical trial of tivozanib as monotherapy for the treatment of non-small cell lung cancer; and

due to the Company's progress including continued progress of its phase 2 clinical trial showing a favorable safety profile in patients with advanced RCC, the Company deemed that the probability of an IPO increased to 35%, although the assumed timing was adjusted to March 31, 2010 due to its assessment of current market conditions.

The retrospective fair value of the Company's common stock underlying options for 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:

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in May 2009, the Company announced additional data from the Company's 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 the Company's progress in its lead program and data noted above, the Company deemed that the probability of an IPO increased to 40%; and

the timeline for sale above liquidation preference was extended to September 30, 2011, which is closer to the date the Company anticipates that data will become available from its phase 3 clinical trial of tivozanib.

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**AVEO Pharmaceuticals, Inc.**

**Notes to Consolidated Financial Statements (Continued)**

**December 31, 2009**

**14. Stock-Based Compensation (Continued)**

The retrospective fair value of the Company's common stock underlying options for 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 million investment in Series E Preferred Stock at \$4.00 per share and a \$5 million upfront payment;

the Company's plans to commence the phase 3 clinical trial of tivozanib; and

due to the Company's progress and plans for commencement of a phase 3 clinical trial, the Company 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 the Company's common stock underlying options for 18,887 shares granted on December 17, 2009 was determined to be \$11.32 per share. The increase in value from the September 2009 valuation was primarily due to the following:

initiation of the phase 3 clinical trial of tivozanib; and

due to the Company's progress and the initiation of the phase 3 clinical trial of tivozanib, the Company 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 the Company's common stock underlying options for 398,182 shares granted on February 2, 2010 was determined to be \$12.24 per share. The increase in value from the December 2009 valuation was primarily due to a reduction in the period of time before the expected completion of an IPO.

Valuation models require the input of highly subjective assumptions. Because the Company's 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 the Company's common stock. The foregoing valuation methodologies are not the only valuation methodologies available and will not be used to value the Company's common stock once this offering is complete. The Company cannot make assurances of any particular valuation of its 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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As of December 31, 2009, the total unrecognized compensation expense, net of related forfeiture estimates, was \$4,438,256 which the Company expects to recognize over a weighted-average period of approximately 2.3 years. The intrinsic value of options exercised during the years 2007, 2008 and 2009 was \$305,700, \$147,700, and \$326,500, respectively.

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**Table of Contents****AVEO Pharmaceuticals, Inc.****Notes to Consolidated Financial Statements (Continued)****December 31, 2009****14. Stock-Based Compensation (Continued)**

The following table summarizes the activity of the Company's stock option plan for the year ended December 31, 2009:

|   | Number of<br>Options | Weighted-<br>Average<br>Exercise<br>Price | Weighted-<br>Average<br>Remaining<br>Contractual<br>Life<br>(in years) | Aggregate<br>Intrinsic<br>Value |
|---|----------------------|---|--|---------------------------------|
| Outstanding at December 31, 2008                | 2,862,133            | \$ 3.68                                   |  |                                 |
| Granted   | 591,175              | \$ 8.92                                   |  |                                 |
| Exercised                                       | (54,247)             | \$ 2.92                                   |  |                                 |
| Forfeited                                       | (123,155)            | \$ 5.96                                   |  |                                 |
| Outstanding at December 31, 2009                | 3,275,906            | \$ 4.56                                   | 6.47   | \$ 22,140,205                   |
| Exercisable at December 31, 2009                | 2,240,282            | \$ 3.28                                   | 5.49   | \$ 17,971,682                   |
| Vested or expected to vest at December 31, 2009 | 3,193,371            | \$ 4.48                                   | 6.40   | \$ 21,896,645                   |

*Stock Option Grants to Nonemployees*

During 2007 and 2008 the Company granted 2,500 and 50,625 shares of nonqualified common stock options, respectively, to nonemployee consultants, with an average exercise price of \$5.60 and \$6.84 and per share, respectively. There were no stock options granted to nonemployee consultants during 2009. The Company valued these grants using the Black-Scholes option-pricing model and recognizes expense related to these awards using the graded-vesting method. For 2007, 2008 and 2009 option grants, the Company has assumed risk-free rates of return of 2.25% to 4.70% expected option lives equal to the contractual term, no dividends and stock price volatility of 68.16%, 68.70% and 70.35%, respectively, in calculating the options' fair values. The unvested shares held by consultants have been and will be revalued using the Company's estimate of fair value at each reporting period through the remaining vesting period. The reassessment may result in additional charges to expense in the future. Compensation expense of approximately \$33,500, \$123,300, and \$266,600 was recorded during the years ended December 31, 2007, 2008 and 2009, respectively, relating to nonemployee stock option awards.

*Restricted Stock*

The Company has sold or issued shares of restricted stock to nonemployee founders, consultants and certain executives from time to time between 2002 and 2005. Generally, the terms of the restricted stock agreements provide that the Company has the right to purchase from the individuals, at the original purchase price, some or all of the unvested shares upon certain conditions such as discontinuance of employment or consulting services. The Company determines the value of such awards as the difference between the exercise price and the fair value of the underlying stock on the date of grant. This value, if any, is recognized on a straight-line basis as compensation expense over the period in which the restrictions lapse. The vesting of the awards is determined by the board of directors and all awards generally vest over a period of four years. The Company periodically reassesses the value of each nonemployee award through the remaining vesting period, which may result in additional charges to expense in the future. Compensation expense, relating to restricted stock, of \$9,100 and \$9,100 was recorded in the years

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ended December 31, 2007 and 2008, respectively. There was no compensation expense, relating to restricted stock for the year ended December 31, 2009.

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**Table of Contents****AVEO Pharmaceuticals, Inc.****Notes to Consolidated Financial Statements (Continued)****December 31, 2009****14. Stock-Based Compensation (Continued)**

Changes in the Company's restricted stock for the years ended December 31, 2008 and 2009 were as follows:

|   | <b>Restricted<br/>Shares</b> | <b>Weighted-<br/>Average<br/>Grant Date<br/>Fair Value</b> |
|---|------------------------------|--|
| Nonvested restricted stock at December 31, 2007 | 1,432                        | \$ 1.32  |
| Granted   |                              |  |
| Forfeited                                       |                              |  |
| Vested  | (1,432)                      | 1.32   |
| Nonvested restricted stock at December 31, 2008 |                              |  |

Nonvested restricted stock at December 31, 2009

The total fair value of shares that vested during the years ended December 31, 2007 and 2008 was \$9,900 and \$9,900, respectively.

**15. Employee Benefit Plan**

In 2002, the Company established the AVEO Pharmaceuticals, Inc. 401(k) Plan (the Plan) for its employees, which is designed to be qualified under Section 401(k) of the Internal Revenue Code. Eligible employees are permitted to contribute to the Plan within statutory and Plan limits. For the year ended December 31, 2006, the Company began making matching contributions of 50% of the first 5% of employee contributions. The Company made matching contributions of \$190,600, \$253,700, and \$301,300 for the years ended December 31, 2007, 2008, and 2009, respectively.

**16. Subsequent Events**

*Resolutions adopted by the Board of Directors and Stockholders*

The following resolutions were adopted by the Board of Directors on February 2, 2010 and approved by our stockholders on February 11, 2010:

Approval of an amendment of Certificate of Incorporation which increased authorized Common Stock by 1,875,000 shares related to the increase in shares reserved under the 2002 Stock Plan with a corresponding increase in the number of shares not subject to anti-dilution protection under the Preferred Stock terms.

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Adoption of the 2010 Employee Stock Purchase Plan, subject to the closing of a public offering, pursuant to which the Company may sell up to an aggregate of 250,000 shares of Common Stock.

Adoption of the 2010 Stock Plan, subject to the closing of a public offering, pursuant to which the Company may grant incentive stock options, nonqualified stock options, stock appreciation rights, restricted stock, restricted stock units and other stock-based awards for the purchase of that number of shares of Common Stock equal to the sum of any shares reserved for issuance under the 2002 Stock Plan that remain available for grant under the 2002 Stock Plan immediately prior to the closing of a public offering and any shares of Common Stock subject to awards under the 2002 Stock Plan which expire,

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**AVEO Pharmaceuticals, Inc.**

**Notes to Consolidated Financial Statements (Continued)**

**December 31, 2009**

**16. Subsequent Events (Continued)**

terminate or are otherwise surrendered, canceled, forfeited or repurchased by the Company without having been fully exercised or resulting in any Common Stock being issued, not to exceed in the aggregate 2.5 million shares.

Approval of the Restated Certificate of Incorporation to be effective upon the closing of the initial public offering, which authorizes 100,000,000 shares of common stock and 5,000,000 shares of preferred stock.

On February 18, 2010, the Company effected a 1-for-4 reverse split of all outstanding shares of common stock. All common share and per share data presented in the accompanying consolidated financial statements and the notes thereto have been retroactively restated to reflect this event.

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**Table of Contents****AVEO PHARMACEUTICALS, INC.****Condensed Consolidated Balance Sheets****(in thousands, except per share amounts)***(unaudited)*

|   | September 30,<br>2010 | December 31,<br>2009 |
|---|-----------------------|----------------------|
| <b>Assets</b>   |                       |                      |
| Current assets:   |                       |                      |
| Cash and cash equivalents   | \$ 40,046             | \$ 45,290            |
| Marketable securities   | 46,976                | 6,011                |
| Accounts receivable   | 220                   | 487                  |
| Prepaid expenses and other current assets   | 3,598                 | 1,306                |
| <b>Total current assets</b>   | <b>90,840</b>         | <b>53,094</b>        |
| Property and equipment, net   | 4,488                 | 4,197                |
| Other assets  | 577                   | 1,946                |
| Restricted cash   | 607                   | 607                  |
| <b>Total assets</b>   | <b>\$ 96,512</b>      | <b>\$ 59,844</b>     |
| <b>Liabilities and stockholders equity (deficit)</b>  |                       |                      |
| Current liabilities:  |                       |                      |
| Accounts payable  | \$ 8,797              | \$ 7,491             |
| Accrued expenses  | 9,111                 | 7,389                |
| Loans payable, net of discount  | 3,398                 | 7,467                |
| Deferred revenue  | 11,945                | 11,782               |
| Deferred rent   | 264                   | 176                  |
| <b>Total current liabilities</b>  | <b>33,515</b>         | <b>34,305</b>        |
| Loans payable, net of current portion and discount  | 19,742                | 12,278               |
| Deferred revenue, net of current portion  | 16,736                | 23,320               |
| Deferred rent, net of current portion   | 621                   | 819                  |
| Other liabilities   | 2,487                 | 1,249                |
| Warrants to purchase convertible preferred stock  |                       | 1,459                |
| Convertible preferred stock, \$.001 par value: 0 and 80,624 shares authorized at September 30, 2010 and December 31, 2009, respectively; 0 and 75,917 shares issued and outstanding at September 30, 2010 and December 31, 2009, respectively |                       | 156,705              |
| Stockholders equity (deficit):  |                       |                      |
| Preferred Stock, \$.001 par value: 5,000 and 0 shares authorized at September 30, 2010 and December 31, 2009, respectively; no shares issued and outstanding at September 30, 2010 and December 31, 2009, respectively                        |                       |                      |
| Common stock, \$.001 par value: 100,000 and 25,500 shares authorized at September 30, 2010 and December 31, 2009, respectively; 30,935 and 1,641 shares issued and outstanding at September 30, 2010 and December 31, 2009, respectively      | 31                    | 2                    |
| Additional paid-in capital  | 249,580               | 7,432                |
| Accumulated deficit   | (226,200)             | (177,725)            |
| <b>Total stockholders equity (deficit)</b>  | <b>23,411</b>         | <b>(170,291)</b>     |



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|  |           |           |
|--|-----------|-----------|
| Total liabilities and stockholders' equity (deficit) | \$ 96,512 | \$ 59,844 |
|--|-----------|-----------|

The accompanying notes are an integral part of these unaudited, condensed consolidated financial statements.

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**Table of Contents****AVEO PHARMACEUTICALS, INC.****Condensed Consolidated Statements of Operations****(in thousands, except per share amounts)***(unaudited)*

|   | <b>Three Months</b>                 |             | <b>Nine Months</b>                  |             |
|---|-------------------------------------|-------------|-------------------------------------|-------------|
|   | <b>Ended September 30,<br/>2010</b> | <b>2009</b> | <b>Ended September 30,<br/>2010</b> | <b>2009</b> |
| Collaboration revenue   | \$ 6,222                            | \$ 5,917    | \$ 32,725                           | \$ 14,683   |
| Operating expenses:   |                                     |             |                                     |             |
| Research and development  | 20,252                              | 16,526      | 68,867                              | 38,326      |
| General and administrative  | 3,611                               | 2,509       | 10,199                              | 7,504       |
|   | 23,863                              | 19,035      | 79,066                              | 45,830      |
| Loss from operations  | (17,641)                            | (13,118)    | (46,341)                            | (31,147)    |
| Other income and expense:   |                                     |             |                                     |             |
| Other income (expense), net   | 10                                  | (56)        | 140                                 | (273)       |
| Interest expense  | (1,029)                             | (678)       | (2,361)                             | (2,141)     |
| Interest income   | 52                                  | 54          | 87                                  | 121         |
| Other income (expense), net   | (967)                               | (680)       | (2,134)                             | (2,293)     |
| Net loss before taxes   | (18,608)                            | (13,798)    | (48,475)                            | (33,440)    |
| Tax benefit   |                                     |             |                                     | 63          |
| Net loss  | (18,608)                            | (13,798)    | (48,475)                            | (33,377)    |
| Net loss per share basic and diluted  | \$ (0.60)                           | \$ (8.56)   | \$ (2.13)                           | \$ (20.87)  |
| Weighted-average number of common shares used in net loss per share basic and diluted | 30,889                              | 1,611       | 22,773                              | 1,599       |

The accompanying notes are an integral part of these unaudited, condensed consolidated financial statements.

**Table of Contents****AVEO PHARMACEUTICALS, INC.****Condensed Consolidated Statements of Cash Flows****(in thousands)****(unaudited)**

|  | <b>Nine Months<br/>Ended September 30,</b> |             |
|--|--|-------------|
|  | <b>2010</b>                                | <b>2009</b> |
| <b>Operating activities</b>  |  |             |
| Net loss   | \$ (48,475)                                | \$ (33,377) |
| Adjustments to reconcile net loss to net cash used in operating activities:  |  |             |
| Depreciation and amortization  | 980  | 973         |
| Stock-based compensation   | 2,920                                      | 1,702       |
| Non-cash interest expense  | 584  | 537         |
| Loss on loan extinguishment  | 582  |             |
| Loss on disposal of property and equipment                                   | 1  |             |
| Remeasurement of warrants to purchase convertible preferred stock            | (713)                                      | 273         |
| Amortization of premium on investments                                       | 113  | 288         |
| Changes in operating assets and liabilities:                                 |  |             |
| Accounts receivable  | 267  | 1,540       |
| Prepaid expenses and other current assets                                    | (2,323)                                    | (652)       |
| Other noncurrent assets  | 1,369                                      | 61          |
| Accounts payable   | 1,306                                      | 254         |
| Accrued expenses   | 1,722                                      | 4,271       |
| Deferred rent  | (110)                                      | (105)       |
| Deferred revenue   | (6,421)                                    | 23,891      |
| Net cash used in operating activities  | (48,198)                                   | (344)       |
| <b>Investing activities</b>  |  |             |
| Purchases of property and equipment  | (1,271)                                    | (1,209)     |
| Purchases of marketable securities   | (95,370)                                   | (35,927)    |
| Proceeds from maturities and sales of marketable securities                  | 54,292                                     | 25,148      |
| Net cash used in investing activities  | (42,349)                                   | (11,988)    |
| <b>Financing activities</b>  |  |             |
| Proceeds from issuance of common stock, net of issuance costs                | 80,301                                     |             |
| Proceeds from issuance of convertible preferred stock, net of issuance costs |  | 32,862      |
| Proceeds from exercise of stock options                                      | 725  | 65          |
| Net proceeds from refinance of loans payable                                 | 7,555                                      |             |
| Principal payments on loans payable  | (3,278)                                    | (1,225)     |
| Net cash provided by financing activities                                    | 85,303                                     | 31,702      |
| Net increase (decrease) in cash and cash equivalents                         | (5,244)                                    | 19,370      |
| Cash and cash equivalents at beginning of period                             | 45,290                                     | 20,814      |
| Cash and cash equivalents at end of period                                   | \$ 40,046                                  | \$ 40,184   |

**Supplemental cash flow and noncash investing and financing**

|   |          |          |
|---|----------|----------|
| Issuance of warrants in conjunction with loan | \$ 780   | \$       |
| Cash paid for interest                        | \$ 1,701 | \$ 1,619 |
| Cash paid for income taxes                    | \$       | \$       |

The accompanying notes are an integral part of these unaudited, condensed consolidated financial statements.

**Table of Contents****AVEO Pharmaceuticals, Inc.****Notes to Condensed Consolidated Financial Statements****(Unaudited)****(1) Organization**

AVEO Pharmaceuticals, Inc. (the Company) is a biopharmaceutical company focused on discovering, developing and commercializing novel cancer therapeutics. The Company's product candidates are directed against important mechanisms, or targets, known or believed to be involved in cancer. Tivozanib, the Company's lead product candidate currently in phase 3 clinical development, is a highly potent and selective oral inhibitor of the vascular endothelial growth factor, or VEGF, receptors 1, 2 and 3. The Company also has a pipeline of monoclonal antibodies, including AV-299, a product candidate that is currently in phase 2 clinical development, derived from its Human Response Platform, a novel method of building preclinical models of human cancer. As used throughout these unaudited, condensed consolidated financial statements, the terms AVEO, we, us, and our refer to the business of AVEO Pharmaceuticals, Inc. and its subsidiaries.

**(2) Basis of Presentation**

These condensed consolidated financial statements include the accounts of the Company and its wholly-owned subsidiary. We have eliminated all significant intercompany accounts and transactions in consolidation.

The accompanying condensed consolidated financial statements have been prepared in accordance with generally accepted accounting principles for interim financial information and with the instructions to Form 10-Q and Article 10 of Regulation S-X. Accordingly, they do not include all of the information and footnotes required by generally accepted accounting principles for complete financial statements. In the opinion of management, all adjustments, consisting of normal recurring accruals and revisions of estimates, considered necessary for a fair presentation of the accompanying condensed consolidated financial statements have been included. Interim results for the three and nine months ended September 30, 2010 are not necessarily indicative of the results that may be expected for the fiscal year ending December 31, 2010 or any other future period.

The information presented in the condensed consolidated financial statements and related footnotes at September 30, 2010, and for the three and nine months ended September 30, 2010 and 2009, is unaudited and the condensed consolidated balance sheet amounts and related footnotes at December 31, 2009 have been derived from our audited financial statements. For further information, refer to the consolidated financial statements and accompanying footnotes included in the final prospectus relating to our initial public offering filed with the Securities and Exchange Commission (SEC) on March 12, 2010.

**(3) Significant Accounting Policies*****Basic and Diluted Loss per Common Share***

Basic net loss per common share is computed by dividing net loss by the weighted-average number of common shares outstanding during the reporting period. Preferred shares are not included in the calculation of net loss per share until their conversion to common shares. Diluted net loss per common share is computed by dividing net loss by the weighted-average number of common shares and dilutive common share equivalents then outstanding. Potential common stock equivalent shares consist of the incremental common shares issuable upon the exercise of stock options and warrants. Since the Company had a net loss for all periods presented, the effect of all potentially dilutive securities is anti-dilutive. Accordingly, basic and diluted net loss per common share is the same.

The following table sets forth for the periods presented the potential common shares (prior to consideration of the treasury stock method) excluded from the calculation of net loss per common share because their inclusion would have been anti-dilutive:

| <b>Three Months<br/>Ended September 30,</b> | <b>Nine months<br/>Ended September 30,</b> |
|---|--|
|---|--|

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|                                       | 2010<br>(in thousands) | 2009<br>(in thousands) | 2010<br>(in thousands) | 2009<br>(in thousands) |
|---------------------------------------|------------------------|------------------------|------------------------|------------------------|
| Weighted average options outstanding  | 3,516                  | 3,151                  | 3,468                  | 3,067                  |
| Weighted average warrants outstanding | 339                    | 194                    | 252                    | 194                    |
|                                       | 3,855                  | 3,345                  | 3,720                  | 3,261                  |

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**Table of Contents****Stock-Based Compensation**

The fair value of all awards is recognized in the Company's statements of operations on a straight-line basis over their requisite service periods based on their grant date fair values as calculated using the measurement and recognition provisions of Financial Accounting Standards Board (FASB) Accounting Standards Codification (ASC) Topic 718, *Stock Compensation*. During the three and nine months ended September 30, 2010 and 2009, respectively, the Company recorded the following stock-based compensation expense:

|                            | Three Months Ended<br>September 30, |        | Nine Months Ended<br>September 30, |          |
|----------------------------|-------------------------------------|--------|------------------------------------|----------|
|                            | 2010                                | 2009   | 2010                               | 2009     |
|                            | (in thousands)                      |        | (in thousands)                     |          |
| Research and development   | \$ 503                              | \$ 278 | \$ 1,283                           | \$ 910   |
| General and administrative | 502                                 | 364    | 1,637                              | 792      |
|                            | \$ 1,005                            | \$ 642 | \$ 2,920                           | \$ 1,702 |

Allocations to research and development expenses and general and administrative expenses are based upon the department to which the associated employee reported. No related tax benefits of the stock-based compensation expense have been recognized. Share-based payments issued to non-employees are recorded at their fair values, and are periodically revalued as the equity instruments vest and are recognized as expense over the related service period.

**Revenue Recognition**

The Company's revenue is generated primarily through collaborative research and development and licensing agreements. The terms of these agreements typically include payment to the Company of one or more of the following: nonrefundable, up-front license fees; premiums on the sale of equity; milestone payments; and royalties on product sales. In addition, the Company generates revenue through agreements that generally provide for fees for research and development services rendered. These service agreements also contemplate royalty payments to the Company on future sales of its collaborators' products. To date, the Company has earned several milestone payments but has not earned royalty revenue as a result of product sales.

For arrangements that include multiple deliverables, the Company identifies separate units of accounting if certain criteria are met. Accordingly, revenues from licensing and collaboration agreements are recognized based on the performance requirements of the agreement.

Nonrefundable up-front license fees, where the Company has ongoing involvement or performance obligations, are recorded as deferred revenue in the balance sheet and amortized on a straight-line basis into collaboration revenue in the statements of operations over the term of the performance obligations.

Payments or reimbursements resulting from the Company's research and development efforts are recognized as the services are performed and are presented on a gross basis in the statements of operations in accordance with ASC 605-45, *Revenue Recognition - Principal Agent Considerations*, 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.

At the inception of each agreement that includes milestone payments, the Company evaluates whether each milestone is substantive and at risk to both parties on the basis of the contingent nature of the milestone, specifically reviewing factors such as the scientific and other risks that must be overcome to achieve the milestone, as well as the level of effort and investment required. Revenues from milestones, if they are nonrefundable and deemed substantive, are recognized upon successful accomplishment of the milestones. Milestones that are not considered substantive are accounted for as license payments and recognized on a straight-line basis over the remaining period of performance.

Amounts received prior to satisfying the above revenue recognition criteria are recorded as deferred revenue in the accompanying balance sheets.

*Principles of Consolidation*

The Company's consolidated financial statements include the Company's accounts and the accounts of the Company's wholly-owned subsidiary, AVEO Pharma Limited. All intercompany transactions have been eliminated.

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**Table of Contents*****Research and Development Expenses***

Research and development expenses are charged to expense as incurred. Research and development expenses consist of costs incurred in performing research and development activities, including personnel-related costs, stock-based compensation, facilities, research-related overhead, clinical trial costs, contracted services, license fees, and other external costs.

Nonrefundable advance payments for goods and services that will be used in future research and development activities are expensed when the activity has been performed or when the goods have been received rather than when the payment is made in accordance with the provisions of ASC 730-20-25-13.

***Cash and Cash Equivalents***

The Company considers highly liquid investments with a maturity of three months or less when purchased to be cash equivalents. Cash equivalents at September 30, 2010 and December 31, 2009 consist of money market funds and commercial paper.

***Fair Value Measurements***

The Company uses ASC Topic 820, *Fair Value Measurements and Disclosures* (formerly FASB Statement No. 157, *Fair Value Measurements*), to provide guidance for using fair value to measure assets and liabilities. ASC 820 applies whenever other standards require (or permit) assets or liabilities to be measured at fair value but does not expand the use of fair value in any new circumstances. ASC 820 also requires expanded disclosure of the effect on earnings for items measured using unobservable data, establishes a fair value hierarchy that prioritizes the information used to develop those assumptions and requires separate disclosure by level within the fair value hierarchy.

The Company records cash equivalents, marketable securities and warrants to purchase preferred stock at fair value. ASC 820 establishes a fair value hierarchy for those instruments measured at fair value that distinguishes between fair value measurements based on market data (observable inputs) and those based on the Company's own assumptions (unobservable inputs). The hierarchy consists of three levels:

Level 1 Quoted market prices in active markets for identical assets or liabilities. Assets utilizing Level 1 inputs include U.S. government securities.

Level 2 Inputs other than Level 1 inputs that are either directly or indirectly observable, such as quoted market prices, interest rates and yield curves. Assets utilizing Level 2 inputs include U.S. government agency securities, including direct issuance bonds, and corporate bonds.

Level 3 Unobservable inputs developed using estimates and assumptions developed by the Company, which reflect those that a market participant would use. The Company currently has no assets or liabilities valued with Level 3 inputs.

The following tables summarize the cash equivalents and marketable securities measured at fair value on a recurring basis in the accompanying consolidated balance sheets as of September 30, 2010 and December 31, 2009.

|                       | <b>Fair Value Measurements of Cash Equivalents and Marketable Securities as of September 30, 2010</b> |                |                |              |
|-----------------------|---|----------------|----------------|--------------|
|                       | <b>Level 1</b>  | <b>Level 2</b> | <b>Level 3</b> | <b>Total</b> |
|                       | <b>(in thousands)</b>   |                |                |              |
| Cash equivalents      | \$ 33,949   | \$ 2,816       | \$             | \$ 36,765    |
| Marketable securities |   | 46,976         |                | 46,976       |

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|  |                       |                |                |              |
|--|-----------------------|----------------|----------------|--------------|
|  | \$ 33,949             | \$ 49,792      | \$             | \$ 83,741    |
| <b>Fair Value Measurements of Cash Equivalents and Marketable Securities as of December 31, 2009</b> |                       |                |                |              |
|  | <b>Level 1</b>        | <b>Level 2</b> | <b>Level 3</b> | <b>Total</b> |
|  | <b>(in thousands)</b> |                |                |              |
| Cash equivalents   | \$ 38,404             | \$             | \$             | \$ 38,404    |
| Marketable securities  | 6,011                 |                |                | 6,011        |
|  | \$ 44,415             | \$             | \$             | \$ 44,415    |

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The Company's Level 2 securities in 2010 include commercial paper issuances and U.S. government agency securities and are valued using third-party pricing sources. These sources generally use interest rates and yield curves observable at commonly quoted intervals of similar assets as observable inputs for pricing.

Marketable securities at September 30, 2010 and December 31, 2009 primarily consist of U.S. Treasuries, U.S. government agency securities and corporate debt maintained by an investment manager. Credit risk is reduced as a result of the Company's policy to limit the amount invested in any one issue. Marketable securities consist primarily of investments which have original maturities at the date of purchase in excess of three months, but not longer than 24 months. The Company classifies these investments as available-for-sale. Unrealized gains and losses are included in other comprehensive loss as a component of stockholders' deficit until realized. The cost of securities sold is based on the specific identification method. There were no realized gains or losses recognized on the sale or maturity of securities during the three and nine months ended September 30, 2010 and 2009.

The fair value on the warrants to purchase preferred stock is valued based on Level 3 inputs at December 31, 2009. In connection with the initial public offering consummated by the Company in March 2010, such warrants to purchase preferred stock were converted into warrants to purchase common stock.

Available-for-sale securities at September 30, 2010 and December 31, 2009 consist of the following:

|                              | Amortized<br>Cost | Unrealized<br>Gains | Unrealized<br>Losses | Fair Value |
|------------------------------|-------------------|---------------------|----------------------|------------|
|                              | (in thousands)    |                     |                      |            |
| <b>September 30, 2010:</b>   |                   |                     |                      |            |
| Corporate debt securities    | \$ 32,368         | \$ 10               | \$ (13)              | \$ 32,365  |
| Government agency securities | 14,608            | 3                   |                      | 14,611     |
|                              | \$ 46,976         | \$ 13               | \$ (13)              | \$ 46,976  |
| <b>December 31, 2009:</b>    |                   |                     |                      |            |
| U.S. treasuries              | \$ 2,003          | \$                  | \$                   | \$ 2,003   |
| Government agency securities | 4,008             |                     |                      | 4,008      |
|                              | \$ 6,011          | \$                  | \$                   | \$ 6,011   |

The aggregate fair value of securities in an unrealized loss position for less than 12 months at September 30, 2010 was \$12.2 million, representing four securities. There were no securities that were in an unrealized loss position for greater than 12 months at September 30, 2010. The unrealized loss was caused by a temporary change in the market for those securities. There was no change in the credit risk of the securities. To determine whether an other-than-temporary impairment exists, the Company performs an analysis to assess whether it intends to sell or whether it would more likely than not be required to sell the security before the expected recovery of the amortized cost basis. Where the Company intends to sell a security, or may be required to do so, the security's decline in fair value is deemed to be other-than-temporary and the full amount of the unrealized loss is recorded in the statement of operations as an other-than-temporary impairment charge. When this is not the case, the Company performs additional analysis on all securities with unrealized losses to evaluate losses associated with the creditworthiness of the security. Credit losses are identified where the Company does not expect to receive cash flows, based on using a single best estimate, sufficient to recover the amortized cost basis of a security and these are recognized in other income (expense), net.

All marketable securities at September 30, 2010 and December 31, 2009 had maturities of one year or less.

**Concentrations of Credit Risk**

Financial instruments that potentially subject the Company to credit risk primarily consist of cash and cash equivalents and available-for-sale marketable securities. The Company maintains deposits in federally insured financial institutions in excess of federally insured limits.

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Management believes that the Company is not exposed to significant credit risk due to the financial position of the depository institutions in which those deposits are held.

### *Fair Value of Financial Instruments*

The carrying amounts of the Company's financial instruments, which include cash and cash equivalents, marketable securities, accounts payable, warrants and loans payable, approximate their fair values at September 30, 2010 and December 31, 2009.

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**Table of Contents*****Property and Equipment***

Property and equipment are stated at cost and are depreciated using the straight-line method over the estimated useful lives of the respective assets. Maintenance and repair costs are charged to expense as incurred.

***Long-lived Assets***

The Company periodically assesses the impairment of long-lived assets in accordance with ASC Topic 360, *Property, Plant, and Equipment*. The Company reviews long-lived assets, including property and equipment, for impairment whenever changes in business circumstances indicate that the carrying amount of the asset may not be fully recoverable. The Company has not recognized any impairment losses through September 30, 2010.

***Comprehensive Income (Loss)***

Comprehensive income (loss) is defined as the change in equity of a business enterprise during a period from transactions and other events and circumstances from non-owner sources. Accumulated other comprehensive loss as of September 30, 2010 and 2009 consists entirely of unrealized gains/losses on available-for-sale securities.

|  | <b>Nine months Ended<br/>September 30,</b> |                    |
|--|--|--------------------|
|  | <b>2010</b>                                | <b>2009</b>        |
|  | <b>(in thousands)</b>                      |                    |
| Net loss                                 | \$ (48,475)                                | \$ (33,377)        |
| Unrealized gain on marketable securities |  | 11                 |
| <b>Comprehensive loss</b>                | <b>\$ (48,475)</b>                         | <b>\$ (33,366)</b> |

***Income Taxes***

The Company provides for income taxes using the liability method. Under this method, deferred tax assets and liabilities are determined based on differences between financial reporting and tax bases of assets and liabilities, and are measured using the enacted tax rates and laws that will be in effect when the differences are expected to reverse.

On January 1, 2009, the Company adopted FASB Interpretation No. 48, *Accounting for Uncertainty In Income Taxes* (codified within ASC Topic 740, *Income Taxes*), which provides a comprehensive model for the financial statement recognition, measurement, presentation and disclosure of uncertain tax positions taken or expected to be taken in income tax returns. Unrecognized tax benefits represent tax positions for which reserves have been established.

***Segment and Geographic Information***

Operating segments are defined as components of an enterprise engaging in business activities for which discrete financial information is available and regularly reviewed by the chief operating decision maker in deciding how to allocate resources and in assessing performance. The Company views its operations and manages its business in one operating segment and the Company operates in only one geographic segment.

***Use of Estimates***

The preparation of financial statements in conformity with accounting principles generally accepted in the United States requires the Company's management to make estimates and assumptions that affect the amounts reported in the financial statements and accompanying notes. Actual results could differ from those estimates.

***New Accounting Pronouncements***

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In October 2009, the FASB issued Accounting Standards Update ( ASU ) 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. The Company is required to adopt Update No. 2009-13 as of January 1, 2011 and is in the process of determining the impact that the adoption of Update No. 2009-13 will have on its future results of operations or financial position.

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In February 2010, the FASB issued amended guidance on subsequent events. Under this amended guidance, SEC filers are no longer required to disclose the date through which subsequent events have been evaluated in originally issued and revised financial statements. This guidance was effective immediately and the Company adopted these new requirements upon issuance of this guidance.

In April 2010, the FASB issued ASU No. 2010-17, *Revenue Recognition – Milestone Method* (ASU 2010-17). ASU 2010-17 provides guidance in applying the milestone method of revenue recognition to research or development arrangements. This guidance concludes that the milestone method is a valid application of the proportional performance model when applied to research or development arrangements. Accordingly, an entity can make an accounting policy election to recognize a payment that is contingent upon the achievement of a substantive milestone in its entirety in the period in which the milestone is achieved. The guidance is effective for fiscal years, and interim periods within those years, beginning on or after June 15, 2010. The adoption of this accounting standard is not expected to impact the Company's financial position or results of operations.

***Subsequent Events***

The Company evaluated all events or transactions that occurred after September 30, 2010 up through the date the Company issued these financial statements in connection with the filing of the Company's September 30, 2010 Form 10-Q. The Company also evaluated all events or transactions that occurred after September 30, 2010 up through the date the Company reissued these financial statements in this registration statement.

**(4) Collaborations and License Agreements**
***Merck (Formerly Schering-Plough Corporation)***

In March 2007, the Company entered into an agreement with Schering-Plough Corporation (Schering Plough), through its subsidiary Schering Corporation, acting through its Schering-Plough Research Institute division, under which it granted Schering-Plough (now Merck & Co., Inc. (Merck)) exclusive, worldwide rights to develop and commercialize all of the Company's monoclonal antibody antagonists of hepatocyte growth factor (HGF), including AV-299. The Company also granted Merck an exclusive, worldwide license to related biomarkers for diagnostic use. On September 28, 2010, the Company received written notice from Merck of termination of the collaboration agreement effective as of December 27, 2010, at which point the Company will be responsible for funding all future development, manufacturing and commercialization costs for the AV-299 program. The Company will no longer receive any future milestone payments from Merck. Under the agreement, the Company received an up-front payment of \$7.5 million in May 2007, which is being amortized over the Company's period of substantial involvement, initially estimated to be through completion of the first phase 2 proof-of-concept trial for AV-299 (which was expected to be the first half of 2012), but has been adjusted to reflect the termination of the agreement effective on December 27, 2010. The period of substantial involvement will now expire on December 27, 2010. As of September 30, 2010, there was \$2.2 million of deferred revenue that will be recognized over this period. In addition, Schering-Plough purchased 4,000,000 shares of Series D Convertible Preferred Stock (Series D Preferred Stock), at a per share price of \$2.50, resulting in gross proceeds to the Company of \$10.0 million. In connection with the initial public offering consummated by the Company in March 2010 and the related 1:4 reverse stock split of the common stock, each four shares of outstanding Series D Preferred Stock were converted into one share of common stock. The amount paid for the Series D Preferred Stock represented fair value as it was the same as the amounts paid by unrelated investors in March and April 2007. Merck funded research of \$3.0 million per year for the first three years of the agreement. In June 2010, the Company earned and received an \$8.5 million milestone payment in connection with the enrollment of patients in the phase 2 clinical trial being conducted by the Company. Since the \$8.5 million milestone payment earned in June 2010 was considered substantive and at risk, it has been included in revenue for the nine months ended September 30, 2010.

***OSI Pharmaceuticals (OSI)***

In September 2007, the Company entered into a collaboration and license agreement with OSI Pharmaceuticals, Inc., a wholly-owned subsidiary of Astellas US Holding Inc., a holding company owned by Astellas Pharma Inc. (OSI), which provides for the use of the Company's proprietary *in vivo* models by the Company's scientists at its facilities, use of the Company's 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. Under the agreement, OSI paid the Company an up-front payment of \$7.5 million, which was recorded in deferred revenue and is being amortized over the Company's period of substantial involvement which is now determined to be through July 2011. OSI also paid the Company \$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 research payments of \$625,000 per quarter through July 2009. In addition, OSI purchased

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1,833,334 shares of Series C Preferred Stock, at a per share price of \$3.00, resulting in gross proceeds to the Company of \$5.5 million. The Company determined that the price paid of \$3.00 per share

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by OSI included a premium of \$0.50 over the price per share of the Company's Series D Preferred Stock sold in April 2007; accordingly, the Company will recognize the premium of \$917,000 as additional license revenue on a straight-line basis over the period of substantial involvement. In connection with the initial public offering consummated by the Company in March 2010 and the related 1:4 reverse stock split of the common stock, each four shares of outstanding Series C Preferred Stock were converted into one share of common stock.

In July 2009, the Company and OSI expanded the strategic partnership and the Company granted OSI a non-exclusive license to use the Company's proprietary bioinformatics platform, and non-exclusive perpetual licenses to use bioinformatics data and a Company proprietary gene index related to a specific target pathway. Further, as part of the expanded strategic partnership, the Company granted OSI an option, exercisable upon payment of an option fee, to receive non-exclusive perpetual rights to certain elements of the Company's Human Response Platform and to use the Company's bioinformatics platform, and the Company granted OSI the right to obtain certain of its tumor models and tumor archives. In consideration for such additional rights, under the amended agreement, OSI paid the Company an up-front payment of \$5.0 million, which was recorded in deferred revenue and will be amortized over the Company's 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 (Series E Preferred Stock), at a per share price of \$4.00, resulting in gross proceeds to the Company of \$15.0 million. In connection with the initial public offering consummated by the Company in March 2010 and the related 1:4 reverse stock split of the common stock, each four shares of outstanding Series E Preferred Stock were converted into one share of common stock. The Company determined that the price of \$4.00 per share paid by OSI included a premium of \$1.04 per share over the fair value of the Series E Preferred Stock of \$2.96 as calculated by the Company in its retrospective stock valuation. The valuation used the Market Approach to estimate the Company's enterprise value and the Probability Weighted Expected Return Method (PWERM) to allocate the enterprise value to each class of the Company's equity securities; accordingly, the Company will recognize the premium of \$3,900,000 as additional license revenue on a straight-line basis over the period of substantial involvement.

Under the amended agreement, if all applicable milestones are achieved, payments for the successful achievement of discovery, development and commercialization milestones could total, in the aggregate, over \$94.0 million for each target and its associated products. In addition, the Company is eligible to receive up to \$27.0 million in milestones for certain deliverables and research milestones. OSI has the option to receive non-exclusive perpetual rights to certain elements of the Company's Human Response Platform and to use the Company's bioinformatics platform and to certain of its tumor models and tumor archives for an option fee. If OSI elects to exercise this option and the Company transfers the relevant technology to OSI, OSI will be required to pay the Company license expansion fees of \$25.0 million. If OSI does not elect to exercise this option, OSI must pay a lesser amount in order to retain its rights to the bioinformatics platform and any new targets. Upon commercialization of products under the agreement, the Company is eligible to receive tiered royalty payments on sales of products by OSI, its affiliates and sublicensees. All milestone payments earned to date are for selection of targets, delivery of models or delivery of cell lines. These milestones are not considered to be at risk and substantive, therefore, the milestone payments are being deferred and, when earned, will be recognized on a straight line basis over the remaining estimated period of substantial involvement.

***Biogen Idec International GmbH (Biogen Idec)***

In March 2009, the Company entered into an exclusive option and license agreement with Biogen Idec International GmbH, a subsidiary of Biogen Idec Inc., collectively referred to herein as "Biogen Idec", regarding the development and commercialization of the Company's 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 terms of the agreement, Biogen Idec paid the Company an upfront cash payment of \$5.0 million in March 2009, which will be amortized over the Company's period of substantial involvement, defined as the twenty-year patent life of the development candidate. In addition, Biogen Idec purchased 7,500,000 shares of Series E Preferred Stock at a per share price of \$4.00, resulting in gross proceeds to the Company of \$30.0 million. In connection with the initial public offering consummated by the Company in March 2010 and the related 1:4 reverse stock split of the common stock, each four shares of outstanding Series E Preferred Stock were converted into one share of common stock. The Company determined that the price of \$4.00 paid by Biogen Idec included a premium of \$1.09 per share over the fair value of the Series E Preferred Stock of \$2.91 as calculated by the Company in its retrospective stock valuation. The valuation used the Market Approach to estimate the Company's enterprise value and the PWERM to allocate the enterprise value to each class of the Company's equity securities; accordingly, the Company will recognize the premium of \$8,175,000 as revenue on a straight-line basis over the period of substantial involvement. The Company received a \$5.0 million milestone payment for achievement of the first pre-clinical discovery milestone under the agreement in June 2009 which was not considered at risk and was therefore deferred and is being recognized over the period of substantial involvement. The Company earned the second \$5.0 million milestone payment upon selection of a development candidate in March 2010. This milestone was considered substantive and at risk and has been included in revenue for the quarter ended March 31, 2010. The Company could also receive (i) an additional pre-clinical discovery and development milestone payment of \$5.0 million, 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.



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If Biogen Idec exercises its exclusive option under the agreement, Biogen Idec will pay the Company royalties on Biogen Idec's sales of ErbB3 antibody products in its territory, and the Company will pay Biogen Idec royalties on the Company's sale of ErbB3 antibody products in the United States, Canada and Mexico.

***Kirin Brewery Co. Ltd. (Kirin)***

In December 2006, the Company entered into an exclusive license agreement with Kirin Brewery Co. Ltd. (now Kyowa Hakko Kirin) to research, develop, manufacture and commercialize tivozanib (f/k/a KRN951), pharmaceutical compositions thereof and associated biomarkers in all territories in the world except for Asia. Upon entering into the license agreement, the Company made a one-time cash payment in the amount of \$5.0 million. In March 2010, the Company made a \$10.0 million milestone payment to Kyowa Hakko Kirin in connection with the initial dosing of patients in the Company's phase 3 clinical trial of tivozanib. In addition, the Company may be required to make up to an aggregate of \$50.0 million in additional milestone payments upon the achievement of specified regulatory milestones. The Company is also required to pay tiered royalty payments on net sales it makes of tivozanib in its territory. The royalty rates under the agreement range from the low to mid teens as a percentage of the Company's net sales of tivozanib.

The Company also has the right to grant sublicenses under the license agreement, subject to certain restrictions. In the event the Company sublicenses the rights licensed to it as part of the agreement, the Company is required to pay Kyowa Hakko Kirin a specified percentage of any amounts the Company receives from any third party sublicenses, other than amounts it receives in respect of research and development funding or equity investments, subject to certain limitations.

**(5) Loans Payable**

On May 15, 2008, the Company entered into a \$21.0 million financing agreement with Hercules Technology Growth Capital Inc., or Hercules Technology Growth, and Comerica Bank, referred to as the prior loan agreement. The full amount of the loan was drawn down in 2008. On May 28, 2010, the Company entered into a new loan and security agreement with Hercules Technology II, L.P. and Hercules Technology III, L.P., affiliates of Hercules Technology Growth, referred to as the new loan agreement, pursuant to which the Company received a loan in the aggregate principal amount of \$25.0 million and repaid the remaining outstanding principal and interest under the prior loan agreement of \$17.4 million. Under ASC 470-50, *Modifications and Extinguishments (Debt)*, the repayment was considered an extinguishment of debt; as such, the remaining loan discount and prepaid loan fees of approximately \$582,000 related to the prior loan agreement were recorded as loss on loan extinguishment. The Company is required to repay the aggregate principal balance of the loan that is outstanding under the new loan agreement in 30 equal monthly installments of principal starting on April 1, 2011, provided, however, that such date will be extended under certain circumstances specified in the new loan agreement. Per annum interest is payable at the greater of 11.9% and an amount equal to 11.9% plus the prime rate of interest minus 4.75%, provided however, that the per annum interest shall not exceed 15.0%. The Company must make interest payments on the loan each month following the date of borrowing under the new loan agreement. The entire principal balance and all accrued but unpaid interest will be due and payable on September 1, 2013, provided, however, such amounts will be due and payable on a later date under certain circumstances specified in the new loan agreement. The loan is secured by a lien on all of the Company's personal property as of, or acquired after, the date of the new loan agreement, except for intellectual property.

The new loan agreement requires a deferred charge of \$1.25 million to be paid in May 2012 related to the termination of the prior loan agreement. The new loan also includes an additional deferred charge of \$1.24 million due upon the maturity of the new loan which has been recorded as a loan discount and is being amortized to interest expense over the term of the new loan agreement using the effective interest rate method. The Company 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. The Company incurred approximately \$193,000 in loan issuance costs related to the new loan agreement paid directly to the lenders, which have been offset against the loan proceeds as a loan discount. As part of the new loan agreement, the Company issued warrants to the lenders on June 2, 2010 to purchase up to 156,641 shares of the Company's common stock at an exercise price equal to \$7.98 per share. These warrants expire seven years from issuance. The Company recorded the relative fair value of the warrants of approximately \$780,000 as equity and as a discount to the related loan outstanding and will amortize the value of the discount to interest expense over the term of the loan using the effective interest method. The relative fair value of the warrant was calculated using the Black-Scholes option-pricing model with the following assumptions: volatility of 64.12%, an expected term equal to the contractual life of the warrant (seven years), a risk-free interest rate of 2.81% and no dividend yield. The resulting effective interest rate including the fair value of the warrant, the loan issuance costs and the deferred charge approximates 16.1%.



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The new loan agreement defines events of default, including the occurrence of an event that results in a material adverse effect upon the Company's business operations, properties, assets or condition (financial or otherwise), its ability to perform its obligations under and in accordance with the terms of the new loan agreement, or upon the ability of the lenders to enforce any of their rights or remedies with respect to such obligations, or upon the collateral under the new loan agreement or upon the liens of the lenders on such collateral or upon the priority of such liens. Hercules also received an option, subject to the Company's written consent, not to be unreasonably withheld, to purchase, either with cash or through conversion of outstanding principal under the loan, up to \$2.0 million of equity of the Company sold in any sale by the Company to third parties of equity securities resulting in at least \$10.0 million in net cash proceeds to the Company, subject to certain exceptions. The Company has evaluated the embedded conversion option, and has concluded that it does not need to be bifurcated and separately accounted for. No amount will be recognized for the conversion feature until such time as the conversion feature is exercised and it can be determined whether a beneficial conversion feature exists. As of September 30, 2010, there have been no events of default under the loan. As of September 30, 2010, the principal balance outstanding was \$25.0 million.

Future minimum payments under the loans payable outstanding as of September 30, 2010 are as follows:

| <b>Years Ending December 31:</b>                          |                  |
|---|------------------|
| 2010 (3 months remaining)                                 | \$ 752           |
| 2011  | 9,451            |
| 2012  | 12,860           |
| 2013  | 10,030           |
|   | 33,093           |
| Less amount representing interest                         | (5,606)          |
| Less discount   | (1,860)          |
| Less deferred charges                                     | (2,487)          |
| Less current portion                                      | (3,398)          |
| <b>Loans payable, net of current portion and discount</b> | <b>\$ 19,742</b> |

**(6) Stock-based Compensation****Stock Plans**

A summary of the status of the Company's stock incentive plans at September 30, 2010 and changes during the nine months then ended is presented in the table and narrative below:

|  | <b>Options</b>   | <b>Weighted-Average Exercise Price</b> | <b>Weighted-Average Remaining Contractual Term</b> | <b>Aggregate Intrinsic Value</b> |
|--|------------------|--|--|----------------------------------|
| Outstanding at December 31, 2009                 | 3,275,906        | \$ 4.56                                |  |                                  |
| Granted  | 624,740          | 10.63                                  |  |                                  |
| Exercised  | (346,642)        | 2.09                                   |  |                                  |
| Cancelled  | (72,863)         | 6.64                                   |  |                                  |
| <b>Outstanding at September 30, 2010</b>         | <b>3,481,141</b> | <b>\$ 5.85</b>                         | <b>6.75</b>  | <b>\$ 18,838,528</b>             |
| Vested or expected to vest at September 30, 2010 | 3,398,606        | \$ 5.75                                | 6.70   | \$ 18,711,989                    |

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|                                   |           |    |      |      |               |
|-----------------------------------|-----------|----|------|------|---------------|
| Exercisable at September 30, 2010 | 2,357,499 | \$ | 4.26 | 5.83 | \$ 16,262,551 |
|-----------------------------------|-----------|----|------|------|---------------|

The aggregate intrinsic value in the table above represents the value (the difference between the Company's closing common stock price on the last trading day of the nine months ended September 30, 2010 and the exercise price of the options, multiplied by the number of in-the-money options) that would have been received by the option holders had all option holders exercised their options on September 30, 2010. As of September 30, 2010, there was \$5,086,329 of total unrecognized stock-based compensation expense related to stock options granted under the plans. The expense is expected to be recognized over a weighted-average period of 2.0 years.

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Stock-based payments to employees are required to be measured at fair value. The Company uses the Black-Scholes pricing model in order to calculate the estimated fair value of its stock option grants. Since the Company completed its initial public offering in March 2010, it did not have sufficient history as a publicly traded company to evaluate its volatility. As such, the Company has used an average of several peer companies' volatilities to determine a reasonable estimate of its volatility. For purposes of identifying similar entities, the Company considered characteristics such as industry, length of trading history, market capitalization and similar product pipelines. The Company utilized a weighted average method of using its own data for the quarters that it has been public, along with data it obtained from its peer companies. Due to the lack of available quarterly data for these peer companies and insufficient history as a public company, the Company 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.

The Company issued stock options during the three and nine months ended September 30, 2010. During the three and nine months ended September 30, 2010 and 2009, respectively, the assumptions used in the Black-Scholes pricing model for new grants were as follows:

|                          | <b>Three Months Ended September 30,</b> |             |
|--------------------------|---|-------------|
|                          | <b>2010</b>                             | <b>2009</b> |
| Volatility factor        | 66.80%                                  | 72.04%      |
| Risk-free interest rate  | 1.59%                                   | 2.87%       |
| Dividend yield           |   |             |
| Expected term (in years) | 6.25                                    | 6.25        |

|                          | <b>Nine months Ended September 30,</b> |             |
|--------------------------|--|-------------|
|                          | <b>2010</b>                            | <b>2009</b> |
| Volatility factor        | 63.92%-66.80%                          | 72.04%      |
| Risk-free interest rate  | 1.59%-2.92%                            | 1.98%-2.87% |
| Dividend yield           |  |             |
| Expected term (in years) | 5.50-6.25                              | 6.25        |

The following resolutions were adopted by the Board of Directors on February 2, 2010 and approved by the Company's stockholders on February 11, 2010:

Approval of an amendment of Certificate of Incorporation which increased the Company's authorized Common Stock by 1,875,000 shares related to the increase in shares reserved under the 2002 Stock Incentive Plan with a corresponding increase in the number of shares not subject to anti-dilution protection under the Preferred Stock terms.

Adoption of the 2010 Employee Stock Purchase Plan pursuant to which the Company may sell up to an aggregate of 250,000 shares of Common Stock.

Adoption of the 2010 Stock Incentive Plan, pursuant to which the Company may grant incentive stock options, nonqualified stock options, stock appreciation rights, restricted stock, restricted stock units and other stock-based awards for the purchase of that number of shares of Common Stock equal to the sum of any shares reserved for issuance under the 2002 Stock Incentive Plan that remain available for grant under the 2002 Stock Incentive Plan immediately prior to the closing of a public offering and any shares of Common Stock subject to awards under the 2002 Stock Incentive Plan which expire, terminate or are otherwise surrendered, cancelled, forfeited or repurchased by the Company at their original issuance price pursuant to a contractual repurchase right, up to a maximum of 2,500,000 shares.

**(7) Income Taxes**

The Company accounts for income taxes under the provisions of ASC Topic 740, *Income Taxes*. The Company recorded a tax benefit for the three and nine months ended September 30, 2009 in the amount of \$62,997 representing a current benefit for federal income taxes related to certain refundable credits. The Company has not recorded a federal or state income tax provision or benefit for the three and nine months ended

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September 30, 2010.

As a result of the initial public offering of the Company's common stock in March of 2010, the Company underwent a change in ownership for purposes of Internal Revenue Code Section 382. As a result, the Company believes the utilization of federal net operating loss carryforwards and research credit carryforwards as of the date of the initial public offering will be subject to an annual limitation based on the value of the Company immediately before the stock offering. The annual limitation will be increased in the first five years after the change in ownership as a result of the Company's built-in-gains. This limitation is not expected to result in the loss of any of these tax attributes during the carryforward period.

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### **(8) Common Stock**

#### ***Reverse Stock Split***

On February 2, 2010, the Company's Board of Directors, and on February 11, 2010, the Company's stockholders, approved a 1-for-4 reverse stock split of the Company's common stock. The reverse stock split was effected on February 18, 2010. All share and per share amounts in the consolidated financial statements have been retroactively adjusted for all periods presented to give effect to the reverse stock split, including reclassifying an amount equal to the reduction in par value to additional paid-in capital.

#### ***Initial Public Offering***

In March 2010, the Company raised \$81.0 million in gross proceeds from the sale of 9,000,000 shares of its common stock in an initial public offering at \$9.00 per share. The net offering proceeds after deducting approximately \$3.1 million in offering related expenses and underwriters discounts were approximately \$72.2 million. In March 2010, the underwriters of the initial public offering exercised their option to purchase, and in April 2010, the Company closed the sale to such underwriters of, an additional 968,539 shares of common stock at \$9.00 per share resulting in additional net proceeds to the Company of approximately \$8.1 million. All outstanding shares of the Company's convertible preferred stock were converted into 18,979,155 shares of common stock upon the completion of the initial public offering.

In connection with the initial public offering, the Company reclassified its liability related to preferred stock warrants into additional paid-in capital as a result of the conversion of warrants to purchase convertible preferred stock into warrants to purchase common stock.

### **(9) Subsequent Events**

#### ***Private Placement***

On October 28, 2010, the Company entered into a definitive agreement with respect to the private placement of 4.5 million shares of its unregistered common stock at \$13.50 per share to a group of institutional and accredited investors. The Company completed the private placement on November 3, 2010, resulting in approximately \$56.6 million in net proceeds to the Company. The Company has agreed to file a registration statement with the Securities and Exchange Commission registering the resale of the shares of common stock issued in the private placement.

#### ***Qualifying Therapeutic Discovery Project Grants***

On October 29, 2010, the Company received notification from the Internal Revenue Service that it has been awarded three separate grants in the aggregate amount of \$733,438 pursuant to the qualifying therapeutic discovery grant program established by the Internal Revenue Service and the Secretary of Health and Human Services under the Patient Protection and Affordable Care Act of 2010. The grants have been made with respect to certain of the Company's qualifying research and development programs.

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**Table of Contents****PART II****INFORMATION NOT REQUIRED IN PROSPECTUS****ITEM 13. Other Expenses of Issuance and Distribution.**

The following table sets forth the fees and expenses to be incurred in connection with the registration of the securities being registered hereby, all of which will be borne by us. Except for the SEC registration fee, all amounts are estimates.

|   | <b>Amount</b>     |
|---|-------------------|
| Securities and Exchange Commission Registration Fee | \$ 5,083          |
| Accountants Fees and Expenses                       | \$ 50,000         |
| Legal Fees and Expenses                             | \$ 400,000        |
| Miscellaneous                                       | \$ 69,917         |
| <b>Total Expenses</b>                               | <b>\$ 525,000</b> |

**ITEM 14. Indemnification of Directors and Officers.**

Section 102 of the Delaware General Corporation Law permits a corporation to eliminate the personal liability of its directors to the corporation or its stockholders for monetary damages for a breach of fiduciary duty as a director, except where the director breached his or her duty of loyalty, failed to act in good faith, engaged in intentional misconduct or knowingly violated a law, authorized the payment of a dividend or approved a stock repurchase in violation of Delaware corporate law or obtained an improper personal benefit. Our certificate of incorporation provides that no director shall be personally liable to us or our stockholders for monetary damages for any breach of fiduciary duty as a director, notwithstanding any provision of law imposing such liability, except to the extent that the Delaware General Corporation Law prohibits the elimination or limitation of liability of directors for breaches of fiduciary duty.

Section 145 of the Delaware General Corporation Law provides that a corporation has the power to indemnify a director, officer, employee or agent of the corporation and certain other persons serving at the request of the corporation for another corporation, partnership, joint venture, trust or other enterprise in related capacities against expenses (including attorneys fees), judgments, fines and amounts paid in settlements actually and reasonably incurred by the person in connection with an action, suit or proceeding to which he or she is or is threatened to be made a party by reason of such position, if such person acted in good faith and in a manner he or she reasonably believed to be in or not opposed to the best interests of the corporation, and, in any criminal action or proceeding, had no reasonable cause to believe his or her conduct was unlawful, except that, in the case of actions brought by or in the right of the corporation, no indemnification shall be made with respect to any claim, issue or matter as to which such person shall have been adjudged to be liable to the corporation unless and only to the extent that the Court of Chancery or other adjudicating court determines that, despite the adjudication of liability but in view of all of the circumstances of the case, such person is fairly and reasonably entitled to indemnity for such expenses which the Court of Chancery or such other court shall deem proper.

Our certificate of incorporation provides that we will indemnify each person who was or is a party or threatened to be made a party to any threatened, pending or completed action, suit or proceeding whether civil, criminal, administrative or investigative (other than an action by or in the right of us) by reason of the fact that he or she is or was, or has agreed to become, our director or officer, or is or was serving, or has agreed to serve, at our request as a director, officer or trustee of, or in a similar capacity with, another corporation, partnership, joint venture, trust or other enterprise (all such persons being referred to as an Indemnitee), or by reason of any action alleged to have been taken or omitted in such capacity, against all expenses (including attorneys fees), judgments, fines and amounts paid in settlement actually and reasonably incurred by the Indemnitee or on his or her behalf in connection with such action, suit or proceeding and any appeal therefrom, if such Indemnitee acted in good faith and in a manner he or she reasonably believed to be in, or not opposed to, our best interests, and, with respect to any criminal action or proceeding, he or she had no reasonable cause to believe his or her conduct was unlawful.



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Our certificate of incorporation also provides that we will indemnify any Indemnitee who was or is a party to an action or suit by or in the right of us to procure a judgment in our favor by reason of the fact that the Indemnitee is or was, or has agreed to become, our director or officer, or is or was serving, or has agreed to serve, at our request as a director, officer or trustee of, or in a similar capacity with, another corporation, partnership, joint venture, trust or other enterprise, or by reason of any action alleged to have been taken or omitted in such capacity, against all expenses (including attorneys' fees) and, to the extent permitted by law, amounts paid in settlement actually and reasonably incurred in connection with such action, suit or proceeding, and any appeal therefrom, if the Indemnitee acted in good faith and in a manner he or she reasonably believed to be in, or not opposed to, our best interests, except that no indemnification shall be made with respect to any claim, issue or matter as to which such person shall have been adjudged to be liable to us, unless and only to the extent that a court determines that, despite such adjudication but in view of all of the circumstances, he or she is entitled to indemnification for such expenses. Notwithstanding the foregoing, to the extent that any Indemnitee has been successful, on the merits or otherwise, he or she will be indemnified by us against all expenses (including attorneys' fees) actually and reasonably incurred by him or her or on his or her behalf in connection therewith. If we do not assume the defense, expenses must be advanced to an Indemnitee under certain circumstances.

We maintain a general liability insurance policy which covers certain liabilities of our directors and officers arising out of claims based on acts or omissions in their capacities as directors or officers.

Certain of our non-employee directors may, through their relationships with their employers, be insured and/or indemnified against certain liabilities in their capacity as members of our board of directors.

The underwriting agreement we entered into in connection with the initial public offering of our common stock provides that the underwriters will indemnify, under certain conditions, our directors and officers (as well as certain other persons) against certain liabilities arising in connection with such offering.

**ITEM 15. Recent Sales of Unregistered Securities.**

Set forth below is information regarding shares of common stock, preferred stock and warrants issued by us within the past three years that were not registered under the Securities Act. Also included is the consideration, if any, received by us for such shares and warrants and information relating to the section of the Securities Act, or rule of the SEC, under which exemption from registration was claimed.

(a) Issuances of Capital Stock

(1) On March 18, 2009 and July 16, 2009, we sold an aggregate of 11,250,000 shares of our series E convertible preferred stock at a price per share of \$4.00 to accredited investors, for an aggregate purchase price of \$45,000,000.

(2) On March 18, 2008, we sold an aggregate of 125,000 shares of our common stock to an accredited investor affiliated with a director at a price per share of \$0.004, for an aggregate purchase price of \$500.

(3) 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 an accredited investor, for an aggregate purchase price \$5,500,002.

(4) 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.

(5) From January 1, 2007 through March 17, 2010, we issued an aggregate of 221,934 shares of our common stock at prices ranging from \$0.48 to \$12.24 per share to certain of our employees, consultants and directors pursuant to the exercise of stock options under our 2002 stock plan for an aggregate purchase price of \$417,998.

(6) On November 3, 2010, we sold an aggregate of 4,500,000 shares of our common stock at a price per share of \$13.50 in a private placement to accredited investors for an aggregate purchase price of \$60,075,000.



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(b) Warrant Issuances

(1) On May 15, 2008, we issued warrants to accredited investors, in connection with debt financings completed with such accredited investors, to purchase up to an aggregate of 189,000 shares of our series D convertible preferred stock, each at an exercise price of \$2.50 per share.

(2) On June 2, 2010, we issued warrants to accredited investors, in connection with debt financings completed with such accredited investors, to purchase up to an aggregate of 156,641 shares of our common stock, each at an exercise price of \$7.98 per share.

No underwriters were involved in the foregoing issuances of securities. The securities described in paragraphs (a)(1) through (4) and (a)(6) of this Item 15 were issued to accredited investors in reliance upon the exemption from the registration requirements of the Securities Act, as set forth in Section 4(2) under the Securities Act, and, in certain cases, in reliance on Regulation D promulgated thereunder, relative to transactions by an issuer not involving any public offering, to the extent an exemption from such registration was required. The securities described in paragraph (a)(5) of this Item 15 were issued pursuant to written compensatory plans or arrangements with our employees, directors and consultants in reliance on the exemption provided by Rule 701 promulgated under Section 3(b) of the Securities Act, or pursuant to Section 4(2) under the Securities Act, relative to transactions by an issuer not involving any public offering, to the extent an exemption from such registration was required. The securities described in paragraphs (b)(1) and (2) of this Item 15 were issued to accredited investors in reliance upon the exemption from the registration requirements of the Securities Act, as set forth in Section 4(2) under the Securities Act, relative to transactions by an issuer not involving any public offering, to the extent an exemption from such registration was required.

All of the purchasers of shares of our convertible preferred stock described above, the purchaser of shares of our common stock affiliated with a director described above, the purchasers of shares of our common stock in connection with the private placement described above and the parties to which warrants were issued described above represented to us in connection with their respective acquisitions described above that they were accredited investors and that they were acquiring the applicable securities for investment and not distribution and to the effect that they could bear the risks of the investment. Such parties received written disclosures that the applicable securities had not been registered under the Securities Act and that any resale must be made pursuant to a registration or an available exemption from such registration.

All of the foregoing securities are deemed restricted securities for purposes of the Securities Act. The certificates representing the issued shares of capital stock and the warrants described in this Item 15 included appropriate legends setting forth that the applicable securities have not been registered and the applicable restrictions on transfer.

**ITEM 16. Exhibits and Financial Statement Schedules.**

The exhibits to the registration statement are listed in the Exhibit Index attached hereto and incorporated by reference herein.

**ITEM 17. Undertakings.**

(a) The undersigned registrant hereby undertakes:

1. To file, during any period in which offers or sales are being made, a post-effective amendment to this registration statement:

- i. To include any prospectus required by section 10(a)(3) of the Securities Act of 1933;

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- ii. To reflect in the prospectus any facts or events arising after the effective date of the registration statement (or the most recent post-effective amendment thereof) which, individually or in the aggregate, represent a fundamental change in the information set forth in the registration statement. Notwithstanding the foregoing, any increase or decrease in volume of securities offered (if the total dollar value of securities offered would not exceed that which was registered) and any deviation from the low or high end of the estimated maximum offering range may be reflected in the form of prospectus filed with the Commission pursuant to Rule 424(b) if, in the aggregate, the changes in volume and price represent no more than 20% change in the maximum aggregate offering price set forth in the Calculation of Registration Fee table in the effective registration statement.
  - iii. To include any material information with respect to the plan of distribution not previously disclosed in the registration statement or any material change to such information in the registration statement;
2. That, for the purpose of determining any liability under the Securities Act of 1933, each such post-effective amendment shall be deemed to be a new registration statement relating to the securities offered therein, and the offering of such securities at that time shall be deemed to be the initial bona fide offering thereof.
3. To remove from registration by means of a post-effective amendment any of the securities being registered which remain unsold at the termination of the offering.
4. That, for the purpose of determining liability under the Securities Act of 1933 to any purchaser, each prospectus filed pursuant to Rule 424(b) as part of a registration statement relating to an offering, other than registration statements relying on Rule 430B or other than prospectuses filed in reliance on Rule 430A, shall be deemed to be part of and included in the registration statement as of the date it is first used after effectiveness. Provided, however, that no statement made in a registration statement or prospectus that is part of the registration statement or made in a document incorporated or deemed incorporated by reference into the registration statement or prospectus that is part of the registration statement will, as to a purchaser with a time of contract of sale prior to such first use, supersede or modify any statement that was made in the registration statement or prospectus that was part of the registration statement or made in any such document immediately prior to such date of first use.

Insofar as indemnification for liabilities arising under the Securities Act of 1933 may be permitted to directors, officers and controlling persons of the registrant pursuant to the foregoing provisions, or otherwise, the registrant has been advised that in the opinion of the Securities and Exchange Commission such indemnification is against public policy as expressed in the Act and is, therefore, unenforceable. In the event that a claim for indemnification against such liabilities (other than the payment by the registrant of expenses incurred or paid by a director, officer or controlling person of the registrant in the successful defense of any action, suit or proceeding) is asserted by such director, officer or controlling person in connection with the securities being registered, the registrant will, unless in the opinion of its counsel the matter has been settled by controlling precedent, submit to a court of appropriate jurisdiction the question whether such indemnification by it is against public policy as expressed in the Act and will be governed by the final adjudication of such issue.



**Table of Contents****SIGNATURES**

Pursuant to the requirements of the Securities Act of 1933, the registrant has duly caused this Registration Statement to be signed on its behalf by the undersigned, thereunto duly authorized, in the City of Cambridge, Commonwealth of Massachusetts, on this 10<sup>th</sup> day of November, 2010.

**AVEO PHARMACEUTICALS, INC.**

By: */s/ TUAN HA-NGOC*  
**Tuan Ha-Ngoc**  
**Chief Executive Officer**

**SIGNATURES AND POWER OF ATTORNEY**

WE, THE UNDERSIGNED OFFICERS AND DIRECTORS OF AVEO PHARMACEUTICALS, INC., hereby severally constitute and appoint Tuan Ha-Ngoc and David Johnston, and each of them singly (with full power to each of them to act alone), our true and lawful attorneys-in-fact and agents, with full power of substitution and resubstitution in each of them for him and in his name, place and stead, and in any and all capacities, to sign any and all amendments (including post-effective amendments) to this Registration Statement, and any other registration statement for the same offering pursuant to Rule 462(b) under the Securities Act of 1933, and to file the same, with all exhibits thereto and other documents in connection therewith, with the Securities and Exchange Commission, granting unto said attorneys-in-fact and agents, and each of them, full power and authority to do and perform each and every act and thing requisite or necessary to be done in and about the premises, as full to all intents and purposes as he might or could do in person, hereby ratifying and confirming all that said attorneys-in-fact and agents or any of them, or their or his substitute or substitutes, may lawfully do or cause to be done by virtue hereof.

Pursuant to the requirements of the Securities Act of 1933, this Registration Statement has been signed by the following persons in the capacities held on the dates indicated.

| <b>Signature</b>   | <b>Title</b>  | <b>Date</b>       |
|--|---|-------------------|
| <i>/s/ TUAN HA-NGOC</i><br><b>Tuan Ha-Ngoc</b>             | Chief Executive Officer and Director<br>(Principal Executive Officer)   | November 10, 2010 |
| <i>/s/ DAVID JOHNSTON</i><br><b>David Johnston</b>         | Chief Financial Officer<br>(Principal Financial and Accounting Officer) | November 10, 2010 |
| <i>/s/ KENNETH M. BATE</i><br><b>Kenneth M. Bate</b>       | Director  | November 10, 2010 |
| <i>/s/ DOUGLAS G. COLE</i><br><b>Douglas G. Cole</b>       | Director  | November 10, 2010 |
| <i>/s/ RONALD A. DEPINHO</i><br><b>Ronald A. DePinho</b>   | Director  | November 10, 2010 |
| <i>/s/ ANTHONY B. EVNIN</i><br><b>Anthony B. Evnin</b>     | Director  | November 10, 2010 |
| <i>/s/ NICHOLAS GALAKATOS</i><br><b>Nicholas Galakatos</b> | Director  | November 10, 2010 |

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|   |          |                   |
|---|----------|-------------------|
| /s/ RUSSELL HIRSCH<br><b>Russell Hirsch</b>       | Director | November 10, 2010 |
| /s/ RAJU KUCHERLAPATI<br><b>Raju Kucherlapati</b> | Director | November 10, 2010 |
| /s/ KENNETH E. WEG<br><b>Kenneth E. Weg</b>       | Director | November 10, 2010 |
| /s/ ROBERT C. YOUNG<br><b>Robert C. Young</b>     | Director | November 10, 2010 |

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| Exhibit Number   | Description of Exhibit  | Incorporated by Reference |             |                | Exhibit Number | Filed Herewith |
|--|---|---------------------------|-------------|----------------|----------------|----------------|
|  |   | Form                      | File Number | Date of Filing |                |                |
| <i>Articles of Incorporation and Bylaws</i>                                      |   |                           |             |                |                |                |
| 3.1  | Restated Certificate of Incorporation of the Registrant   | 8-K                       | 001-34655   | 03/18/2010     | 3.1            |                |
| 3.2  | Second Amended and Restated Bylaws of the Registrant  | S-1/A                     | 333-163778  | 02/08/2010     | 3.5            |                |
| <i>Instruments Defining the Rights of Security Holders, Including Indentures</i> |   |                           |             |                |                |                |
| 4.1  | Specimen Stock Certificate evidencing the shares of common stock  | S-1/A                     | 333-163778  | 03/09/2010     | 4.1            |                |
| <i>Opinion re Legality</i>   |   |                           |             |                |                |                |
| 5.1  | Opinion of Wilmer Cutler Pickering Hale and Dorr LLP  |                           |             |                |                | X              |
| <i>Material Contracts Management Contracts and Compensatory Plans</i>            |   |                           |             |                |                |                |
| 10.1   | 2002 Stock Incentive Plan, as amended   | S-1/A                     | 333-163778  | 02/23/2010     | 10.1           |                |
| 10.2   | Form of Incentive Stock Option Agreement under 2002 Stock Incentive Plan  | S-1                       | 333-163778  | 12/16/2009     | 10.2           |                |
| 10.3   | Form of Nonstatutory Stock Option Agreement under 2002 Stock Incentive Plan   | S-1                       | 333-163778  | 12/16/2009     | 10.3           |                |
| 10.4   | Form of Restricted Stock Agreement under 2002 Stock Incentive Plan  | S-1                       | 333-163778  | 12/16/2009     | 10.4           |                |
| 10.5   | 2010 Stock Incentive Plan   | S-1/A                     | 333-163778  | 02/23/2010     | 10.5           |                |
| 10.6   | Form of Incentive Stock Option Agreement under 2010 Stock Incentive Plan  | S-1/A                     | 333-163778  | 02/08/2010     | 10.6           |                |
| 10.7   | Form of Nonqualified Stock Option Agreement under 2010 Stock Incentive Plan   | S-1/A                     | 333-163778  | 02/08/2010     | 10.7           |                |
| 10.8   | Key Employee Change in Control Severance Benefits Plan  | S-1                       | 333-163778  | 12/16/2009     | 10.8           |                |
| 10.9   | Amended and Restated Employment Agreement, dated as of December 19, 2008, by and between the Registrant and Tuan Ha-Ngoc        | S-1                       | 333-163778  | 12/16/2009     | 10.9           |                |
| 10.10  | Severance and Change in Control Agreement, dated as of December 11, 2009, by and between the Registrant and Tuan Ha-Ngoc        | S-1                       | 333-163778  | 12/16/2009     | 10.10          |                |
| 10.11  | Severance and Change in Control Agreement, dated as of December 11, 2009, by and between the Registrant and Elan Z. Ezickson    | S-1                       | 333-163778  | 12/16/2009     | 10.11          |                |
| 10.12  | Severance and Change in Control Agreement, dated as of December 11, 2009, by and between the Registrant and Jenő Gyuris         | S-1                       | 333-163778  | 12/16/2009     | 10.12          |                |
| 10.13  | Severance and Change in Control Agreement, dated as of December 11, 2009, by and between the Registrant and David B. Johnston   | S-1                       | 333-163778  | 12/16/2009     | 10.13          |                |
| 10.14  | Severance and Change in Control Agreement, dated as of December 11, 2009, by and between the Registrant and William Slichenmyer | S-1                       | 333-163778  | 12/16/2009     | 10.14          |                |
| 10.15  | 2010 Employee Stock Purchase Plan, as amended   | S-1/A                     | 333-163778  | 02/23/2010     | 10.17          |                |

**Table of Contents**

| Exhibit Number   | Description of Exhibit  | Incorporated by Reference |             |                          | Filed Herewith |
|--|---|---------------------------|-------------|--------------------------|----------------|
|  |   | Form                      | File Number | Date of Filing           |                |
| 10.16  | Severance Agreement, dated September 13, 2010, by and between the Registrant and Michael Bailey   | 10-Q                      | 001-34655   | 11/05/10                 | 10.1           |
| 10.17  | Consulting Agreement, executed November 4, 2010 and effective as of January 1, 2010, by and between the Registrant and Ronald DePinho   | 10-Q                      | 001-34655   | 11/05/10                 | 10.2           |
| <i>Material Contracts Financing Agreements</i>                         |   |                           |             |                          |                |
| 10.18  | Loan and Security Agreement dated May 28, 2010 by and among the Registrant, Hercules Technology II, L.P. and Hercules Technology III, L.P.  | 8-K                       | 001-34655   | 06/04/10                 | 10.1           |
| <i>Material Contracts Leases</i>                                       |   |                           |             |                          |                |
| 10.19  | Sublease, dated as of July 2004, by and between the Registrant and Millennium Pharmaceuticals, Inc.   | S-1                       | 333-163778  | 12/16/2009               | 10.19          |
| 10.20  | Sublease, dated as of September 2, 2008, by and between the Registrant and Alkermes, Inc.   | S-1                       | 333-163778  | 12/16/2009               | 10.20          |
| <i>Material Contracts License and Strategic Partnership Agreements</i> |   |                           |             |                          |                |
| 10.21  | Exclusive License Agreement, dated as of March 19, 2002, by and between the Registrant and Dana-Farber Cancer Institute, Inc., as amended on January 1, 2003 and July 22, 2003  | S-1                       | 333-163778  | 12/16/2009               | 10.21          |
| 10.22  | License Agreement, dated as of December 21, 2006, by and between the Registrant and Kirin Brewery Co. Ltd.  | S-1                       | 333-163778  | 12/16/2009               | 10.22          |
| 10.23  | First Amended and Restated License and Research Collaboration Agreement, dated as of April 13, 2005, by and between the Registrant and Merck & Co., Inc.  | S-1/A                     | 333-163778  | 03/09/2010               | 10.24          |
| 10.24  | License and Research Collaboration Agreement, dated as of August 30, 2005, by and between the Registrant and Merck & Co., Inc., as amended by Letter Amendment, dated March 5, 2007, as amended by Amendment No. 1, dated August 12, 2007 | S-1                       | 333-163778  | 12/16/2009               | 10.24          |
| 10.25  | Research, Development and License Agreement, dated as of March 23, 2007, by and between the Registrant and Schering Corporation, acting through its Schering-Plough Research Institute division   | S-1                       | 333-163778  | 12/16/2009               | 10.25          |
| 10.26  | Option and License Agreement, dated as of March 18, 2009, by and between the Registrant and Biogen Idec International GmbH  | S-1                       | 333-163778  | 12/16/2009               | 10.26          |
| 10.27  | Amended and Restated Collaboration and License Agreement, dated as of July 16, 2009, by and between the Registrant and OSI Pharmaceuticals, Inc., as amended by the First Amendment, dated as of February 23, 2010                        | S-1/A<br>10-Q             | 001-34655   | 03/09/2010<br>08/06/2010 | 10.28<br>10.1  |
| <i>Material Contracts Miscellaneous</i>                                |   |                           |             |                          |                |
| 10.28  | Securities Purchase Agreement, among the Registrant and the Purchasers thereto, dated October 28, 2010  | 8-K                       | 001-34655   | 11/3/2010                | 10.1           |
| 10.29  | Registration Rights Agreement, between the Registrant and the Holders thereto, dated October 28, 2010   | 8-K                       | 001-34655   | 11/3/2010                | 10.2           |
| 10.30  | Registration Rights Agreement dated June 23, 2010 by and among the Registrant, Hercules Technology II, L.P. and Hercules Technology III, L.P.   | 8-K                       | 001-34655   | 06/29/10                 | 10.1           |

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| Exhibit<br>Number                 | Description of Exhibit  | Incorporated by Reference |             |                   |                   | Filed<br>Herewith |
|-----------------------------------|---|---------------------------|-------------|-------------------|-------------------|-------------------|
|                                   |   | Form                      | File Number | Date of<br>Filing | Exhibit<br>Number |                   |
| 10.31                             | Warrant dated as of June 2, 2010 issued by the Registrant to Hercules Technology II, L.P.   | 8-K                       | 001-34655   | 06/04/10          | 10.2              |                   |
| 10.32                             | Warrant dated as of June 2, 2010 issued by the Registrant to Hercules Technology III, L.P.  | 8-K                       | 001-34655   | 06/04/10          | 10.3              |                   |
| 10.33                             | Fourth Amended and Restated Investor Rights Agreement dated March 18, 2009 by and among the Registrant and the Purchasers named therein | S-1                       | 333-163778  | 12/16/2009        | 10.28             |                   |
| 10.34                             | Warrant Agreement to Purchase Shares of Preferred Stock, issued to Hercules Technology Growth Capital, Inc., March 29, 2006             | S-1                       | 333-163778  | 12/16/2009        | 10.30             |                   |
| 10.35                             | Warrant Agreement to Purchase Shares of Stock, issued to Hercules Technology Growth Capital, Inc., May 15, 2008                         | S-1                       | 333-163778  | 12/16/2009        | 10.31             |                   |
| 10.36                             | Warrant Agreement to Purchase Shares of Stock, issued to Comerica Bank, May 15, 2008 (assigned to Comerica Ventures Incorporated)       | S-1                       | 333-163778  | 12/16/2009        | 10.32             |                   |
| <b><i>Additional Exhibits</i></b> |   |                           |             |                   |                   |                   |
| 21.1                              | Subsidiaries of the Registrant  |                           |             |                   |                   | X                 |
| 23.1                              | Consent of Ernst & Young LLP  |                           |             |                   |                   | X                 |
| 23.2                              | Consent of Wilmer Cutler Pickering Hale and Dorr LLP (included in Exhibit 5.1)  |                           |             |                   |                   | X                 |
| 24.1                              | Power of Attorney (included on signature page)  |                           |             |                   |                   | X                 |

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