Verastem, Inc.
Form 424B4
January 27, 2012

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Registration No. 333-177677
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PROSPECTUS January 26, 2012

5,500,000 shares

Common Stock

This is the initial public offering of our common stock. No public market currently exists for our common stock. We are offering all of the shares of common stock offered by this prospectus.

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

Investing in our common stock involves a high degree of risk. Before buying any shares, you should carefully read the discussion of material risks of investing in our common stock in "Risk factors" beginning on page 11.

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.

	Per share	Total
Public offering price	$ 10.00	$ 55,000,000
Underwriting discounts and commissions	$ 0.70	$ 3,850,000
Proceeds to Verastem, before expenses	$ 9.30	$ 51,150,000

Certain of our existing stockholders and their affiliated entities have indicated an interest in purchasing an aggregate of up to approximately $14.8 million in shares of our common stock in this offering at the initial public offering price. However, because indications of interest are not binding agreements or commitments to purchase, these stockholders may determine to purchase fewer shares than they indicate an interest in purchasing or not to purchase any shares in this offering. In addition, the underwriters could determine to sell fewer shares to these stockholders than the stockholders indicate an interest in purchasing or not to sell any shares to these stockholders.

The underwriters may also purchase up to an additional 825,000 shares of our common stock at the public offering price, less the underwriting discounts and commissions payable by us, to cover over-allotments, if any, within 30 days from the date of this prospectus. If the underwriters exercise this option in full, the total underwriting discounts and commissions will be $4,427,500 and our total proceeds, after underwriting discounts and commissions but before expenses, will be $58,822,500.

The underwriters are offering the common stock as set forth under "Underwriting." Delivery of the shares will be made on or about February 1, 2012.

UBS Investment Bank **Leerink Swann**

Lazard Capital Markets

Oppenheimer & Co.

Rodman & Renshaw, LLC

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We have not authorized anyone to provide any information other than that contained in this prospectus or in any free writing prospectus prepared by or on behalf of us or to which we have referred you. We take no responsibility for, and can provide no assurance as to the reliability of, any other information that others may give you. We are offering to sell, and seeking offers to buy, shares of our common stock only in jurisdictions where such offers and sales are permitted. The information in this prospectus or any free writing prospectus is accurate only as of its date, regardless of its time of delivery or of any sale of shares of our common stock. Our business, financial condition, results of operations and prospects may have changed since that date.

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Prospectus summary

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

OUR BUSINESS

We are a biopharmaceutical company focused on discovering and developing proprietary small molecule drugs targeting cancer stem cells along with proprietary companion diagnostics. A cancer stem cell is a particularly aggressive type of tumor cell, resistant to conventional cancer therapy, that we believe is an underlying cause of tumor recurrence and metastasis. We also believe that the presence of cancer stem cells in tumors may be a key reason for the ultimate failure of many existing chemotherapeutics and other cancer therapies to achieve a durable clinical response. Building on discoveries by our scientific co-founders, Robert Weinberg, Ph.D., Eric Lander, Ph.D., and Piyush Gupta, Ph.D., published in the peer reviewed scientific journal *Cell*, we use our proprietary technology to create a stable population of cancer stem cells to screen for and identify small molecule compounds that target cancer stem cells. We believe that our technology and approach provide an opportunity to develop a next generation of oncology therapeutics addressing the large unmet medical need of patients with many types of cancers.

THE PROBLEM

Cancer is one of the world's most serious health problems and the second most common cause of death in the United States after heart disease. Current treatments for cancer include surgery, radiation therapy, chemotherapy, hormone therapy and targeted therapy. According to estimates by the National Institutes of Health, in the United States in 2010, the direct medical costs of cancer of all types exceeded $100 billion. IMS Health estimates that in the United States in 2010, approximately $22 billion was spent on drugs to treat cancer, representing the largest class of drug spending in the United States. Despite years of intensive research and clinical use, current treatments often fail to cure cancer. Cancer patients who relapse often develop metastatic disease. Metastatic disease is the cause of more than 90% of cancer deaths.

We believe that cancer stem cells, or CSCs, which are also sometimes referred to as tumor-initiating cancer cells, are responsible for the initiation, metastasis and recurrence of many cancers and may be a key reason for the ultimate failure of many current therapies to achieve a durable clinical response. CSCs have the ability to:

- move freely and proliferate without attachment to other cells or surfaces;
- initiate a tumor;
- self-renew;
- produce other cancer cell types; and
- resist many current cancer treatments.

CSCs have been identified in many types of cancer, including breast, pancreatic, colon, brain, lung and leukemia. As illustrated in the figure below, while current treatments may succeed at initially decreasing tumor burden, they may leave behind a population of CSCs that can regenerate tumors.

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OUR SOLUTION

Our solution is to discover and develop a next generation of oncology therapeutics targeting CSCs along with companion diagnostics. We believe that by developing therapeutics that target CSCs we can address the problem of cancer recurrence and metastasis so as to deliver a durable clinical response.

Our scientific co-founders at the Whitehead Institute for Biomedical Research, an affiliate of the Massachusetts Institute of Technology, or MIT, and the Broad Institute, an affiliate of MIT and Harvard University, made discoveries that link the epithelial-to-mesenchymal transition, or EMT, to the emergence of CSCs. This transition involves the transformation of one type of cancer cell into a more aggressive and drug resistant type of cancer cell. Our solution utilizes proprietary technology based on these discoveries along with rapid and automated assays, referred to as high-throughput screening, to identify drugs targeting CSCs and develop companion diagnostics. To achieve a durable clinical response, we believe that it may be necessary to kill both CSCs and other types of cancer cells in a tumor, as illustrated in the figure below, either with a combination of current cancer treatments and CSC-targeted drugs or a single therapeutic found to target both cancer cell populations.

Our proprietary technology

A persistent problem in the discovery of drugs targeting CSCs is the difficulty of isolating large numbers of CSCs. Without such large numbers, the discovery of drugs targeting CSCs using high-throughput screening is extremely difficult. Moreover, when CSCs are isolated, they typically do not remain stable in culture. Instead, over a short period of time, CSCs convert into other types of cancer cells. To address this problem, our scientific co-founders developed proprietary technology based on the EMT process to create a stable population of CSCs that are suitable for use in high-throughput screening of small molecule compounds. We license this proprietary technology from the Whitehead Institute.

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To identify compounds that are selective for CSCs, we grow cancer non-stem cells in the laboratory and then induce the EMT process to create a stable population of CSCs. As illustrated in the figure below, we then screen compounds to assess their ability to kill the CSCs. Because these CSCs are stable in culture, the screening process can be conducted using high-throughput technology on a large number and wide variety of small molecule compound libraries. These compound libraries include new chemical entities, approved drugs and compounds that are in preclinical and clinical development. We then profile the compounds that are identified as targeting CSCs using additional assays to identify suitable clinical candidates.

OUR PRODUCT CANDIDATES AND COMPANION DIAGNOSTICS

Using our proprietary technology, we have identified a pipeline of small molecule compounds with the potential to target CSCs. Our most advanced product candidates are VS-507, VS-4718 and VS-5095. We are currently evaluating VS-507, VS-4718 and VS-5095 in preclinical studies as potential therapies for breast and other cancers. We believe that these compounds may be especially beneficial as therapeutics in aggressive cancers with a high percentage of CSCs, such as triple negative breast cancer, or TNBC. TNBC is a type of breast cancer in which a high percentage of CSCs has been identified and that has a poorer prognosis and lower overall survival rate than other types of breast cancer. We also are currently evaluating additional proprietary product candidates in preclinical studies for their use in breast and other cancers.

Our scientific co-founders identified VS-507 as a drug candidate for killing breast cancer stem cells and published their research in *Cell* in 2009. This study included an analysis of the effect of VS-507 on TNBC cell lines. We believe that the targeted action of VS-507 on CSCs is effected through the inhibition of a network of proteins, known as the Wnt/beta-catenin cell signaling pathway, which Dr. Weinberg described in 2011 in *Cell* as critical for the development and maintenance of CSCs. Additional third-party published research has reported that VS-507's activity may be mediated through the blockade of the Wnt/beta-catenin cell signaling pathway. In mouse models of breast cancer, VS-507 treatment decreased biophysical or biochemical markers, referred to as biomarkers, of CSCs. In contrast, treatment in the same model with a standard chemotherapeutic agent, paclitaxel, increased biomarkers of CSCs. Assuming successful completion of preclinical studies, we expect to file an investigational new drug application, or IND, with the U.S. Food and Drug Administration, or FDA, in late 2012 to initiate a Phase 1 clinical trial of VS-507.

We identified the CSC-targeted activity of VS-4718 and VS-5095 using our proprietary technology. In preclinical testing, these compounds were found to be potent and selective inhibitors of Focal Adhesion Kinase, or FAK, a protein which is involved in cell adhesion and motility. FAK expression is greater in many tumor types compared to normal tissue, particularly in cancers that have a high invasive and metastatic capability. In preclinical mouse models, both VS-4718 and VS-5095 demonstrated good oral bioavailability and pharmacokinetic and pharmacodynamic properties and reduced both primary tumor growth and metastatic burden. We expect to file an IND with the FDA in early 2013 to initiate a Phase 1 clinical trial of one of VS-4718 or VS-5095.

An important element of our business strategy is the development and use of proprietary, companion diagnostics in connection with the development of our therapeutic drug candidates. CSCs are often characterized by a distinctive set of biomarkers, which we believe may be a key to identifying patients

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with tumors that are likely to respond to therapies targeting CSCs. We plan to use diagnostics, based on these biomarkers, as part of a personalized medicine approach to identify patients with aggressive tumors that have a high percentage of CSCs. We also believe that these diagnostics may be used to monitor patients' progress on therapy and aid physicians' ongoing treatment decisions. In addition, we expect that our use of proprietary diagnostics may accelerate the clinical development process for our drug candidates by enabling smaller, targeted trials and providing early, objective signals of drug activity.

OUR STRATEGY

Our goal is to build a leading biopharmaceutical company focused on the discovery, development and, ultimately, commercialization of novel drugs and companion diagnostics targeting CSCs. Key elements of our strategy to achieve this goal are:

- continue to screen and identify small molecules that target CSCs;
- in-license rights to additional compounds to expand our pipeline of candidates that target CSCs;
- rapidly advance our drug candidates into clinical development;
- develop diagnostics for therapeutic products targeting CSCs;
- collaborate selectively to augment and accelerate development and commercialization; and
- maintain scientific leadership in the CSC field.

OUR MANAGEMENT TEAM AND SCIENTIFIC CO-FOUNDERS AND ADVISORS

Our management team includes our President and Chief Executive Officer, Chairman and co-founder Christoph Westphal, M.D., Ph.D., our Chief Operating Officer, Robert Forrester, and our Vice President, Head of Research, Jonathan Pachter, Ph.D.

- Dr. Westphal has been involved in founding a number of biotechnology companies as chief executive officer, including Sirtris Pharmaceuticals, Inc., which was acquired by GlaxoSmithKline plc in 2008, as well as Alnylam Pharmaceuticals, Inc. and Momenta Pharmaceuticals, Inc. Dr. Westphal also co-founded Alnara Pharmaceuticals, Inc., which was acquired by Eli Lilly and Co. in 2010.
- Mr. Forrester has held executive level positions at both private and public life science companies, including Forma Therapeutics, Inc., CombinatoRx, Inc., now Zalicus Inc., and Coley Pharmaceutical Group, Inc., which was acquired by Pfizer Inc. in 2007.
- Dr. Pachter has over 20 years of experience in leading the discovery of small molecule and monoclonal antibody therapeutics for the treatment of cancer, most recently as the Senior Director of Cancer Biology at OSI Pharmaceuticals Inc., which was acquired by Astellas Pharma Inc. in 2010.

Our management team is supported by our scientific advisory board comprised of leading academic and industry scientists. Our scientific advisory board consists of:

Scientific advisory board

Robert Weinberg, Ph.D. *Scientific co-founder*	Founding Member of the Whitehead Institute for Biomedical

	Research, Professor of Biology at the Massachusetts Institute of Technology and recipient of the 1997 National Medal of Science
Eric Lander, Ph.D. *Scientific co-founder*	Founding Director of the Broad Institute, Professor of Biology at the Massachusetts Institute of Technology and Professor of Systems Biology at Harvard Medical School

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Scientific advisory board

Piyush Gupta, Ph.D. *Scientific co-founder*	Member of the Whitehead Institute for Biomedical Research and Assistant Professor of Biology at the Massachusetts Institute of Technology
Julian Adams, Ph.D.	President of Research and Development of Infinity Pharmaceuticals, Inc., former Senior Vice President of Drug Discovery and Development of Millennium Pharmaceuticals, Inc. and co-inventor and co-developer of Velcade
José Baselga, M.D., Ph.D.	Chief of Hematology and Oncology at Massachusetts General Hospital, Associate Director of the Massachusetts General Hospital Cancer Center and Professor of Medicine at Harvard Medical School
George Daley, M.D., Ph.D.	Professor of Hematology and Oncology and Director of the Stem Cell Transplantation Program at Children's Hospital and Professor of Biological Chemistry and Molecular Pharmacology at Harvard Medical School
Peter Elliott, Ph.D.	Former Senior Vice President and Head of Research and Development of Sirtris Pharmaceuticals, Inc., former Vice President of Pharmacology and Drug Development of Millennium Pharmaceuticals, Inc. and co-developer of Velcade
Daniel Haber, M.D., Ph.D.	Director of the Massachusetts General Hospital Cancer Center and Professor of Medicine at Harvard Medical School
Joseph (Yossi) Schlessinger, Ph.D.	Chairman and Professor in the Department of Pharmacology at Yale School of Medicine
Phillip A. Sharp, Ph.D.	Institute Professor at the David H. Koch Institute for Integrative Cancer Research at the Massachusetts Institute of Technology and recipient of the 1993 Nobel Prize in Medicine and Physiology
Roger Tung, Ph.D.	President and Chief Executive Officer of Concert Pharmaceuticals, Inc., former Vice President of Drug Discovery of Vertex Pharmaceuticals, Inc. and co-inventor of Lexiva and Agenerase
Christopher Walsh, Ph.D.	Hamilton Kuhn Professor in the Department of Biological Chemistry and Molecular Pharmacology at Harvard Medical School
Eric Winer, M.D.	Director of the Breast Oncology Center at the Dana Farber Cancer Institute and Professor of Medicine at Harvard Medical School

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 immediately following this prospectus summary. These risks include the following:

> We have incurred significant losses since our inception and will need substantial additional funding. To date, we have not generated any revenues. We expect to incur losses for the

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foreseeable future and may never achieve profitability. Our net loss was $7.7 million for the nine months ended September 30, 2011 and $784,000 for the period from August 4, 2010 (inception) to December 31, 2010. As of September 30, 2011, we had a deficit accumulated during the development stage of $8.5 million.

> We have a short operating history. All of our product candidates are still in preclinical development, and we have not received marketing approval from the FDA or any other regulatory authority for any product candidate.

> Our approach to the discovery and development of product candidates that target CSCs is unproven. Our focus on using our proprietary EMT technology to screen for and identify product candidates targeting CSCs may not result in the discovery and development of commercially viable drugs to treat cancer. Research on CSCs is an emerging field and, consequently, there is ongoing debate regarding the existence of CSCs, whether the appropriate nomenclature to refer to these cells is cancer stem cells, tumor-initiating cells or another term and the importance of these cells as an underlying cause of tumor recurrence and metastasis. We do not believe that any drugs that target CSCs have been successfully developed to date for the treatment of cancer.

> We may be unable to acquire or in-license from third parties any compounds or product candidates that we identify using our proprietary EMT technology or otherwise.

> Clinical trials of our product candidates may not be successful. If we are unable to obtain required marketing approvals for, commercialize, obtain and maintain patent protection for or gain sufficient market acceptance by physicians, patients and healthcare payors of our product candidates, or experience significant delays in doing so, our business will be materially harmed and our ability to generate revenue will be materially impaired.

> If we are unable to successfully develop companion diagnostics for our therapeutic product candidates, or experience significant delays in doing so, we may not realize the full commercial potential of our therapeutics.

> We may depend on collaborations with third parties for the development and commercialization of our product candidates. If those collaborations are not successful, we may not be able to capitalize on the market potential of these product candidates.

OUR CORPORATE INFORMATION

We were incorporated under the laws of the State of Delaware in August 2010. Our principal executive offices are located at 215 First Street, Suite 440, Cambridge, Massachusetts 02142 and our telephone number is (617) 252-9300. Our website address is www.verastem.com. The information contained on, or that can be accessed through, our website is not a part of this prospectus. We have included our website address in this prospectus solely as an inactive textual reference.

In this prospectus, unless otherwise stated or the context otherwise requires, references to "Verastem," "we," "us," "our" and similar references refer to Verastem, Inc. The Verastem name and logo are our trademarks. The other trademarks, trade names and service marks appearing in this prospectus are the property of their respective owners.

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The offering

Common stock offered by us	5,500,000 shares
Common stock to be outstanding after this offering	20,234,116 shares
Over-allotment option	The underwriters have an option for a period of 30 days to purchase up to 825,000 additional shares of our common stock to cover over-allotments.
Use of proceeds	We intend to use the net proceeds from this offering for preclinical and clinical development of our lead product candidates, discovery, research and preclinical studies of our other product candidates, additional compounds and companion diagnostics and other general corporate purposes.
Risk factors	You should read the "Risk factors" section starting on page 11 of this prospectus for a discussion of factors to consider carefully before deciding to invest in shares of our common stock.
NASDAQ Global Market symbol	VSTM

The number of shares of our common stock to be outstanding after this offering is based on 2,993,322 actual shares of our common stock outstanding as of December 31, 2011, including 1,434,734 shares of unvested restricted stock subject to repurchase by us, and 11,740,794 additional shares of our common stock issuable upon the automatic conversion of all outstanding shares of our preferred stock upon the closing of this offering.

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

- 405,141 shares of our common stock issuable upon the exercise of stock options outstanding as of December 31, 2011 at a weighted-average exercise price of $0.75 per share;
- 30,101 additional shares of our common stock available for future issuance as of December 31, 2011 under our 2010 equity incentive plan;
- 600,000 shares of our common stock issuable pursuant to restricted stock units granted, effective upon the closing of this offering, under our 2012 incentive plan;
- 2,828,571 additional shares of our common stock that will be available for future issuance, as of the closing of this offering, under our 2012 incentive plan; and
- 142,857 shares of our common stock issuable upon exercise of a warrant, with an exercise price equal to the average closing price of our common stock during the five days preceding the date of issuance, that we have agreed to issue to Poniard Pharmaceuticals, Inc. upon achievement of a milestone pursuant to a license agreement.

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Unless otherwise indicated, all information in this prospectus assumes:

- no exercise of the outstanding options or the warrant described above and no issuance of shares under the restricted stock units described above;
- no exercise by the underwriters of their option to purchase up to 825,000 additional shares of our common stock to cover over-allotments;
- the automatic conversion of all outstanding shares of our preferred stock into an aggregate of 11,740,794 shares of our common stock upon the closing of this offering; and
- the restatement of our amended and restated certificate of incorporation and the amendment and restatement of our bylaws upon the closing of this offering.

In addition, unless otherwise indicated, all information in this prospectus gives effect to the one-for-3.5 reverse stock split of our common stock that was effected on January 10, 2012.

Certain of our existing stockholders, including our principal stockholders Advanced Technology Ventures VIII, L.P., Bessemer Venture Partners, CHP III, L.P., Longwood Fund, LP, and MPM Bioventures V, LP, and their affiliated entities, have indicated an interest in purchasing an aggregate of up to approximately $14.8 million in shares of our common stock in this offering at the initial public offering price. Based on the initial public offering price of $10.00 per share, these stockholders would purchase an aggregate of up to approximately 1,478,500 of the 5,500,000 shares in this offering based on these indications of interest. However, because indications of interest are not binding agreements or commitments to purchase, these stockholders may determine to purchase fewer shares than they indicate an interest in purchasing or not to purchase any shares in this offering. In addition, the underwriters could determine to sell fewer shares to these stockholders than the stockholders indicate an interest in purchasing or not to sell any shares to these stockholders.

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Summary financial information

You should read the following summary financial data together with our financial statements and the related notes appearing at the end of this prospectus and the "Selected financial data" and "Management's discussion and analysis of financial condition and results of operations" sections of this prospectus. We have derived the statements of operations data for the period from August 4, 2010 (inception) to December 31, 2010 from our audited financial statements included in this prospectus. We have derived the statements of operations data for the nine months ended September 30, 2011 and the period from August 4, 2010 (inception) to September 30, 2011 and the balance sheet data as of September 30, 2011 from our unaudited financial statements included in this prospectus. The unaudited financial data include, in the opinion of our management, all adjustments, consisting only of normal recurring adjustments, that are necessary for a fair presentation of our financial position and results of operations for these periods. 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 to be expected for a full fiscal year.

Statement of operations data:	**Period from August 4, 2010 (inception) to December 31, 2010**	**Nine months ended September 30, 2011**	**Period from August 4, 2010 (inception) to September 30, 2011**
	(in thousands, except per share data)		
Operating expenses:			
Research and development	$ 400	$ 5,483	$ 5,883
General and administrative	384	2,195	2,579
Total operating expenses	784	7,678	8,462
Operating loss	(784)	(7,678)	(8,462)
Net loss	$ (784)	$ (7,678)	$ (8,462)
Accretion of preferred stock	(2)	(18)	(20)
Net loss applicable to common stockholders	$ (786)	$ (7,696)	$ (8,482)
Net loss per share applicable to common stockholders basic and diluted	$ (0.91)	$ (6.27)	$ (7.70)
Weighted-average number of common shares used in net loss per share applicable to common stockholders basic and diluted	850	1,226	1,097
Pro forma net loss per share applicable to common stockholders basic and diluted	$ (0.60)	$ (1.33)	
Weighted-average number of common shares used in pro forma net loss per share applicable to common stockholders basic and diluted	1,325	5,850	

Pro forma basic and diluted net loss per common share is calculated assuming the automatic conversion of all outstanding shares of our preferred stock, excluding shares of our series C preferred stock that we issued and sold in November 2011.

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The pro forma balance sheet data set forth below gives effect to:

- our issuance and sale in November 2011 of an aggregate of 9,067,825 shares of our series C preferred stock at a price per share of $2.25 for an aggregate purchase price of $20.4 million; and
- the automatic conversion of all outstanding shares of our preferred stock, including shares of our series C preferred stock that we issued and sold in November 2011, into an aggregate of 11,740,794 shares of our common stock upon the closing of this offering.

The pro forma as adjusted balance sheet data set forth below give further effect to our issuance and sale of 5,500,000 shares of our common stock in this offering at the initial public offering price of $10.00 per share, after deducting underwriting discounts and commissions and estimated offering expenses payable by us.

	As of September 30, 2011		
Balance sheet data:	**Actual**	**Pro forma**	**Pro forma as adjusted**
		(in thousands)	
Cash and cash equivalents	$ 41,421	$ 61,824	$ 110,874
Working capital	39,419	59,822	108,872
Total assets	42,364	62,767	111,817
Redeemable convertible preferred stock	47,878		
Deficit accumulated during the development stage	(8,462)	(8,462)	(8,462)
Total stockholders' (deficit) equity	(7,639)	60,642	109,692

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Risk factors

Investing in our common stock involves a high degree of risk. Before investing in our common stock, you should consider carefully the risks described below, together with the other information contained in this prospectus, including our financial statements and the related notes appearing at the end of this prospectus. If any of the following risks occur, our business, financial condition, results of operations and future growth prospects could be materially and adversely affected. In these circumstances, the market price of our common stock could decline, and you may lose all or part of your investment.

RISKS RELATED TO OUR FINANCIAL POSITION AND NEED FOR ADDITIONAL CAPITAL

We have incurred significant losses since our inception. We expect to incur losses for the foreseeable future and may never achieve or maintain profitability.

Since inception, we have incurred significant operating losses. Our net loss was $7.7 million for the nine months ended September 30, 2011 and $784,000 for the period from August 4, 2010 (inception) to December 31, 2010. As of September 30, 2011, we had a deficit accumulated during the development stage of $8.5 million. To date, we have not generated any revenues and have financed our operations through private placements of our preferred stock. We have devoted substantially all of our efforts to research and development. We have not initiated clinical development of any product candidates and expect that it will be many years, if ever, before we have a product candidate ready for commercialization. We expect to continue to incur significant expenses and increasing operating losses for the foreseeable future. The net losses we incur may fluctuate significantly from quarter to quarter. We anticipate that our expenses will increase substantially if and as we:

- continue our research and preclinical development of our product candidates;
- seek to identify additional product candidates that target cancer stem cells, or CSCs;
- acquire or in-license other products and technologies;
- initiate clinical trials for our product candidates;
- seek marketing approvals for our product candidates that successfully complete clinical trials;
- ultimately establish a sales, marketing and distribution infrastructure to commercialize any products for which we may obtain marketing approval;
- maintain, expand and protect our intellectual property portfolio;
- hire additional clinical, quality control and scientific personnel; and
- add operational, financial and management information systems and personnel, including personnel to support our product development and planned future commercialization efforts.

To become and remain profitable, we must develop and eventually commercialize a product or products with significant market potential. This will require us to be successful in a range of challenging activities, including completing preclinical testing and clinical trials of our product candidates, obtaining marketing approval for these product candidates and manufacturing, marketing and selling those products for which we may obtain marketing approval. We may never succeed in these activities and, even if we do, may never generate revenues that are significant or large enough to achieve profitability. We are currently only in the preclinical testing stages for our most advanced product candidates and have not yet completed formulation development of any of our lead product candidates, VS-507, VS-4718 and VS-5095. If we do achieve profitability, we may not be able to sustain or increase profitability on a quarterly or annual basis. Our failure to become and remain

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profitable would decrease the value of the company and could impair our ability to raise capital, maintain our research and development efforts, expand our business or continue our operations. A decline in the value of our company could also cause you to lose all or part of your investment.

Our short operating history may make it difficult for you to evaluate the success of our business to date and to assess our future viability.

We are an early stage company. We commenced active operations in the second half of 2010. Our operations to date have been limited to organizing and staffing our company, business planning, raising capital, acquiring and developing our technology, identifying potential product candidates and undertaking preclinical studies of our most advanced product candidates. All of our product candidates are still in preclinical development. We have not yet demonstrated our ability to initiate or successfully complete any clinical trials, including large-scale, pivotal clinical trials, obtain marketing approvals, manufacture a commercial scale product, or arrange for a third party to do so on our behalf, or conduct sales and marketing activities necessary for successful product commercialization. It takes about ten to 15 years to develop one new medicine from the time it is discovered to when it is available for treating patients. Consequently, any predictions you make about our future success or viability may not be as accurate as they could be if we had a longer operating history.

In addition, as a new business, we may encounter unforeseen expenses, difficulties, complications, delays and other known and unknown factors. We will need to transition from a company with a research focus to a company capable of supporting commercial activities. We may not be successful in such a transition.

We will need substantial additional funding. If we are unable to raise capital when needed, we would be forced to delay, reduce or eliminate our product development programs or commercialization efforts.

We expect our expenses to increase in connection with our ongoing activities, particularly as we continue the research and development and later initiate clinical trials of, and seek marketing approval for, our product candidates. In addition, if we obtain marketing approval for any of our product candidates, we expect to incur significant commercialization expenses related to product sales, marketing, manufacturing and distribution. Furthermore, upon the closing of this offering, we expect to incur additional costs associated with operating as a public company. Accordingly, we will need to obtain substantial additional funding in connection with our continuing operations. If we are unable to raise capital when needed or on attractive terms, we would be forced to delay, reduce or eliminate our research and development programs or any future commercialization efforts.

We expect that the net proceeds from this offering, together with our existing cash and cash equivalents, will enable us to fund our operating expenses and capital expenditure requirements for at least the next 48 months. Our future capital requirements will depend on many factors, including:

- the scope, progress, results and costs of compound discovery, preclinical development, laboratory testing and clinical trials for our product candidates;
- the extent to which we acquire or in-license other products and technologies;
- the costs, timing and outcome of regulatory review of our product candidates;
- the costs of future commercialization activities, including product sales, marketing, manufacturing and distribution, for any of our product candidates for which we receive marketing approval;

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- revenue, if any, received from commercial sales of our product candidates, should any of our product candidates receive marketing approval;

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

- our ability to establish collaborations on favorable terms, if at all.

Identifying potential product candidates and conducting preclinical testing and clinical trials is a time-consuming, expensive and uncertain process that takes years to complete, and we may never generate the necessary data or results required to obtain marketing approval and achieve product sales. In addition, our product candidates, if approved, may not achieve commercial success. Our commercial revenues, if any, will be derived from sales of products that we do not expect to be commercially available for many years, if at all. Accordingly, we will need to continue to rely on additional financing to achieve our business objectives. Adequate additional financing may not be available to us on acceptable terms, or at all.

Raising additional capital may cause dilution to our stockholders, including purchasers of common stock in this offering, restrict our operations or require us to relinquish rights to our technologies or product candidates.

Until such time, if ever, as we can generate substantial product revenues, we expect to finance our cash needs through a combination of equity offerings, debt financings, collaborations, strategic alliances and licensing arrangements. We do not have any committed external source of funds. To the extent that we raise additional capital through the sale of equity or convertible debt securities, your ownership interest will be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect your rights as a common stockholder. Debt financing, if available, may involve agreements that include covenants limiting or restricting our ability to take specific actions, such as incurring additional debt, making capital expenditures or declaring dividends.

If we raise additional funds through collaborations, strategic alliances or licensing arrangements with third parties, we may have to relinquish valuable rights to our technologies, future revenue streams, research programs or product candidates or to grant licenses on terms that may not be favorable to us. If we are unable to raise additional funds through equity or debt financings when needed, we may be required to delay, limit, reduce or terminate our product development or future commercialization efforts or grant rights to develop and market product candidates that we would otherwise prefer to develop and market ourselves.

RISKS RELATED TO THE DISCOVERY, DEVELOPMENT AND COMMERCIALIZATION OF OUR PRODUCT CANDIDATES

Our approach to the discovery and development of product candidates that target CSCs is unproven, and we do not know whether we will be able to develop any products of commercial value.

Our scientific approach focuses on using proprietary technology to create a stable population of CSCs in the laboratory that we then use to screen for and identify product candidates targeting these CSCs. Research on CSCs is an emerging field and, consequently, there is ongoing debate regarding the existence of CSCs, whether the appropriate nomenclature to refer to these cells is cancer stem cells, tumor-initiating cells or another term and the importance of these cells as an underlying cause of tumor recurrence and metastasis.

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Risk factors

Although there is general consensus that some cancer cells have tumor-initiating capacity, there also is some debate in the scientific community regarding the defining characteristics of these cells, which we call CSCs, and the origin of these cells. Some believe that normal adult stem cells mutate and transform into CSCs. Others believe that all cancer cells have tumor-initiating capabilities, these capabilities cannot be attributed to a factor intrinsic to a particular cell and, therefore, a definitive CSC cannot be isolated or targeted. We believe that the discovery by our scientific co-founders of the link between the epithelial-to-mesenchymal transition, or EMT, and the emergence of cancer stem cells is one way a cancer cell can transition to a CSC, but this view is not universally accepted.

Even if our beliefs regarding the existence, characteristics and function of CSCs are correct, any drugs that we develop may not effectively target CSCs. We do not believe that any drugs that target CSCs have been successfully developed to date for the treatment of cancer. If we are able to develop a drug that targets CSCs in preclinical studies, we may nonetheless not succeed in demonstrating safety and efficacy of the drug in human clinical trials. Our focus on using our proprietary technology to screen for and identify product candidates targeting CSCs may not result in the discovery and development of commercially viable drugs to treat cancer.

We may not be successful in our efforts to identify or discover additional potential product candidates.

A key element of our strategy is to identify and test additional compounds that target CSCs in a variety of different types of cancer. A significant portion of the research that we are conducting involves new compounds, new uses of existing compounds and new and unproven drug discovery methods, including our proprietary technology. The drug discovery that we are conducting using our EMT technology may not be successful in identifying compounds that are useful in treating cancer. Our research programs may initially show promise in identifying potential product candidates, yet fail to yield product candidates for clinical development for a number of reasons, including:

- the research methodology used may not be successful in identifying potential product candidates; or
- potential product candidates may, on further study, be shown to have harmful side effects or other characteristics that indicate that they are unlikely to be products that will receive marketing approval and achieve market acceptance.

In particular, because our EMT technology induces the EMT process to create a stable population of CSCs, it is possible that these stable CSCs may not react in precisely the same manner as naturally occurring CSCs when treated with a particular product candidate. As a result, a product candidate that shows initial promise in targeting our stable population of CSCs may not have the same effect on tumors with naturally occurring CSCs.

Research programs to identify new product candidates require substantial technical, financial and human resources. We may choose to focus our efforts and resources on a potential product candidate that ultimately proves to be unsuccessful.

If we are unable to identify suitable compounds for preclinical and clinical development, we will not be able to obtain product revenues in future periods, which likely would result in significant harm to our financial position and adversely impact our stock price.

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Risk factors

We may not be successful in obtaining necessary rights to compounds and product candidates for our development pipeline through acquisitions and in-licenses.

Because we are screening a range of compounds, including compounds with proprietary rights held by third parties, for their activity against CSCs, the growth of our business will depend in significant part on our ability to acquire or in-license rights to these compounds. However, we may be unable to acquire or in-license any compounds or product candidates from third parties that we identify using our proprietary EMT technology or otherwise. The licensing and acquisition of proprietary compounds is a competitive area, and a number of more established companies are also pursuing strategies to license or acquire compounds and product candidates that we may consider attractive. These established companies may have a competitive advantage over us due to their size, cash resources and greater clinical development and commercialization capabilities.

For example, although the Broad Institute has granted us a right of first negotiation for specified compounds and other intellectual property owned by the Broad Institute, we may be unable to negotiate a license within the specified time frame. If we are unable to do so, the Broad Institute may offer the intellectual property to other parties. In addition, the Whitehead Institute and affiliated parties have retained the right to use the EMT technology that we license from it for research, teaching and educational purposes and could seek to license to third parties any intellectual property rights that it discovers using the EMT technology while pursuing these purposes. Pursuant to our drug discovery platform license agreement with the Whitehead Institute, we will have an opportunity, subject to the Whitehead Institute's obligations under any third-party research funding agreements, to negotiate a license to any such intellectual property under the drug discovery platform license agreement that is developed or conceived on or prior to a specified date in Robert Weinberg's laboratory at the Whitehead Institute. Our failure to reach an agreement with either the Broad Institute or the Whitehead Institute for any applicable intellectual property could result in a third party acquiring the related rights.

In addition, companies that perceive us to be a competitor may be unwilling to assign or license rights to us. We also may be unable to license or acquire the relevant compound or product candidate on terms that would allow us to make an appropriate return on our investment.

In addition, we expect competition for acquisition and in-licensing product candidates that are attractive to us may increase in the future, especially if our approach of targeting CSCs gains greater scientific acceptance, which may mean fewer suitable opportunities for us as well as higher acquisition or licensing prices. If we are unable to successfully obtain rights to suitable compounds or product candidates, our business, financial condition and prospects for growth could suffer.

All of our product candidates are still in preclinical development. Preclinical testing and clinical trials of our product candidates may not be successful. If we are unable to commercialize our product candidates or experience significant delays in doing so, our business will be materially harmed.

We have invested a significant portion of our efforts and financial resources in the identification and preclinical development of drugs that target CSCs. Our ability to generate product revenues, which we do not expect will occur for many years, if ever, will depend heavily on the successful development and eventual commercialization of our product candidates. The success of our product candidates will depend on several factors, including the following:

> successful completion of preclinical studies and clinical trials;

> receipt of marketing approvals from applicable regulatory authorities;

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- establishing commercial manufacturing capabilities or making arrangements with third-party manufacturers;
- obtaining and maintaining patent and trade secret protection and regulatory exclusivity for our product candidates;
- launching commercial sales of the products, if and when approved, whether alone or in collaboration with others;
- acceptance of the products, if and when approved, by patients, the medical community and third-party payors;
- effectively competing with other therapies; and
- a continued acceptable safety profile of the products following approval.

If we do not achieve one or more of these factors in a timely manner or at all, we could experience significant delays or an inability to successfully commercialize our product candidates, which would materially harm our business.

If clinical trials of our product candidates fail to demonstrate safety and efficacy to the satisfaction of regulatory authorities or do not otherwise produce positive results, we may incur additional costs or experience delays in completing, or ultimately be unable to complete, the development and commercialization of our product candidates.

Before obtaining marketing approval from regulatory authorities for the sale of our product candidates, we must complete preclinical development and then conduct extensive clinical trials to demonstrate the safety and efficacy of our product candidates in humans. Clinical testing is expensive, difficult to design and implement, can take many years to complete and is uncertain as to outcome. A failure of one or more clinical trials can occur at any stage of testing. The outcome of preclinical testing and early clinical trials may not be predictive of the success of later clinical trials, and interim results of a clinical trial do not necessarily predict final results. Moreover, preclinical and clinical data are often susceptible to varying interpretations and analyses, and many companies that have believed their product candidates performed satisfactorily in preclinical studies and clinical trials have nonetheless failed to obtain marketing approval of their products. For example, standard measures of clinical activity with respect to solid tumors, such as Response Criteria in Solid Tumors, or RECIST, measurement guidelines, which are based on gross changes in the size of tumor lesions, may not be sufficient to detect the targeting of CSCs by our product candidates.

We may experience numerous unforeseen events during, or as a result of, clinical trials that could delay or prevent our ability to receive marketing approval or commercialize our product candidates, including:

- regulators or institutional review boards may not authorize us or our investigators to commence a clinical trial or conduct a clinical trial at a prospective trial site;
- we may have delays in reaching or fail to reach agreement on acceptable clinical trial contracts or clinical trial protocols with prospective trial sites;
- clinical trials of our product candidates may produce negative or inconclusive results, and we may decide, or regulators may require us, to conduct additional clinical trials or abandon product development programs;
- the number of patients required for clinical trials of our product candidates may be larger than we anticipate, enrollment in these clinical trials may be slower than we anticipate or participants may drop out of these clinical trials at a higher rate than we anticipate;

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- our third-party contractors may fail to comply with regulatory requirements or meet their contractual obligations to us in a timely manner, or at all;
- we might have to suspend or terminate clinical trials of our product candidates for various reasons, including a finding that the participants are being exposed to unacceptable health risks;
- regulators or institutional review boards may require that we or our investigators suspend or terminate clinical research for various reasons, including noncompliance with regulatory requirements or a finding that the participants are being exposed to unacceptable health risks;
- the cost of clinical trials of our product candidates may be greater than we anticipate;
- the supply or quality of our product candidates or other materials necessary to conduct clinical trials of our product candidates may be insufficient or inadequate; and
- our product candidates may have undesirable side effects or other unexpected characteristics, causing us or our investigators, regulators or institutional review boards to suspend or terminate the trials.

If we are required to conduct additional clinical trials or other testing of our product candidates beyond those that we currently contemplate, if we are unable to successfully complete clinical trials of our product candidates or other testing, if the results of these trials or tests are not positive or are only modestly positive or if there are safety concerns, we may:

- be delayed in obtaining marketing approval for our product candidates;
- not obtain marketing approval at all;
- obtain approval for indications or patient populations that are not as broad as intended or desired;
- obtain approval with labeling that includes significant use or distribution restrictions or safety warnings, including boxed warnings;
- be subject to additional post-marketing testing requirements; or
- have the product removed from the market after obtaining marketing approval.

Our product development costs will also increase if we experience delays in testing or marketing approvals. We do not know whether any clinical trials will begin as planned, will need to be restructured or will be completed on schedule, or at all. Significant clinical trial delays also could shorten any periods during which we may have the exclusive right to commercialize our product candidates or allow our competitors to bring products to market before we do and impair our ability to successfully commercialize our product candidates and may harm our business and results of operations.

If we experience delays or difficulties in the enrollment of patients in clinical trials, our receipt of necessary regulatory approvals could be delayed or prevented.

We may not be able to initiate or continue clinical trials for our product candidates if we are unable to locate and enroll a sufficient number of eligible patients to participate in these trials as required by the U.S. Food and Drug Administration, or FDA, or similar regulatory authorities outside the United States. In addition, many of our competitors have ongoing clinical trials for product candidates that treat the same indications as our product candidates, and patients who would otherwise be eligible for our clinical trials may instead enroll in clinical trials of our competitors' product candidates.

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Risk factors

Patient enrollment is affected by other factors including:

- severity of the disease under investigation;
- eligibility criteria for the study in question;
- perceived risks and benefits of the product candidate under study;
- efforts to facilitate timely enrollment in clinical trials;
- patient referral practices of physicians;
- the ability to monitor patients adequately during and after treatment; and
- proximity and availability of clinical trial sites for prospective patients.

Our inability to enroll a sufficient number of patients for our clinical trials would result in significant delays or may require us to abandon one or more clinical trials altogether. Enrollment delays in our clinical trials may result in increased development costs for our product candidates, which would cause the value of our company to decline and limit our ability to obtain additional financing.

If serious adverse or inappropriate side effects are identified during the development of our product candidates, we may need to abandon or limit our development of some of our product candidates.

All of our product candidates are still in preclinical development and their risk of failure is high. It is impossible to predict when or if any of our product candidates will prove effective or safe in humans or will receive marketing approval. If our product candidates are associated with undesirable side effects or have characteristics that are unexpected, we may need to abandon their development or limit development to certain uses or subpopulations in which the undesirable side effects or other characteristics are less prevalent, less severe or more acceptable from a risk-benefit perspective. Many compounds that initially showed promise in early stage testing for treating cancer have later been found to cause side effects that prevented further development of the compound.

We may expend our limited resources to pursue a particular product candidate or indication and fail to capitalize on product candidates or indications that may be more profitable or for which there is a greater likelihood of success.

Because we have limited financial and managerial resources, we focus on research programs and product candidates that we identify for specific indications. As a result, we may forego or delay pursuit of opportunities with other product candidates or for other indications that later prove to have greater commercial potential. Our resource allocation decisions may cause us to fail to capitalize on viable commercial products or profitable market opportunities. Our spending on current and future research and development programs and product candidates for specific indications may not yield any commercially viable products. If we do not accurately evaluate the commercial potential or target market for a particular product candidate, we may relinquish valuable rights to that product candidate through collaboration, licensing or other royalty arrangements in cases in which it would have been more advantageous for us to retain sole development and commercialization rights to such product candidate.

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Risk factors

If we are unable to successfully develop companion diagnostics for our therapeutic product candidates, or experience significant delays in doing so, we may not realize the full commercial potential of our therapeutics.

We plan to develop companion diagnostics for our therapeutic product candidates. There has been limited success to date industry wide in developing these types of companion diagnostics. To be successful, we would need to address a number of scientific, technical and logistical challenges. We have only recently initiated development of companion diagnostics. We have limited experience in the development of diagnostics and may not be successful in developing appropriate diagnostics to pair with any of our therapeutic product candidates that receive marketing approval. Companion diagnostics are subject to regulation by the FDA and similar regulatory authorities outside the United States as medical devices and require separate regulatory approval prior to commercialization. Given our limited experience in developing diagnostics, we expect to rely in part on third parties for their design and manufacture. If we, or any third parties that we engage to assist us, are unable to successfully develop companion diagnostics for our therapeutic product candidates, or experience delays in doing so:

- the development of our therapeutic product candidates may be adversely affected if we are unable to appropriately select patients for enrollment in our clinical trials;
- our therapeutic product candidates may not receive marketing approval if safe and effective use of a therapeutic product candidate depends on an *in vitro* diagnostic; and
- we may not realize the full commercial potential of any therapeutics that receive marketing approval if, among other reasons, we are unable to appropriately select patients who are likely to benefit from therapy with our drugs.

As a result, our business would be harmed, possibly materially.

Even if any of our product candidates receive marketing approval, they may fail to achieve the degree of market acceptance by physicians, patients, healthcare payors and others in the medical community necessary for commercial success.

If any of our product candidates receive marketing approval, they may nonetheless fail to gain sufficient market acceptance by physicians, patients, healthcare payors and others in the medical community. For example, current cancer treatments like chemotherapy and radiation therapy are well established in the medical community, and doctors may continue to rely on these treatments. If our product candidates do not achieve an adequate level of acceptance, we may not generate significant product revenues and we may not become profitable. The degree of market acceptance of our product candidates, if approved for commercial sale, will depend on a number of factors, including:

- efficacy and potential advantages compared to alternative treatments;
- the ability to offer our products for sale at competitive prices;
- convenience and ease of administration compared to alternative treatments;
- the willingness of the target patient population to try new therapies and of physicians to prescribe these therapies;
- the strength of marketing and distribution support;
- sufficient third-party coverage or reimbursement; and
- the prevalence and severity of any side effects.

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If, in the future, we are unable to establish sales and marketing capabilities or enter into agreements with third parties to sell and market our product candidates, we may not be successful in commercializing our product candidates if and when they are approved.

We do not have a sales or marketing infrastructure and have no experience in the sale, marketing or distribution of pharmaceutical products. To achieve commercial success for any approved product, we must either develop a sales and marketing organization or outsource these functions to third parties. In the future, we may choose to build a focused sales and marketing infrastructure to market or co-promote some of our product candidates if and when they are approved.

There are risks involved with both establishing our own sales and marketing capabilities and entering into arrangements with third parties to perform these services. For example, recruiting and training a sales force is expensive and time consuming and could delay any product launch. If the commercial launch of a product candidate for which we recruit a sales force and establish marketing capabilities is delayed or does not occur for any reason, we would have prematurely or unnecessarily incurred these commercialization expenses. This may be costly, and our investment would be lost if we cannot retain or reposition our sales and marketing personnel.

Factors that may inhibit our efforts to commercialize our products on our own include:

- our inability to recruit and retain adequate numbers of effective sales and marketing personnel;
- the inability of sales personnel to obtain access to physicians or persuade adequate numbers of physicians to prescribe any future products;
- the lack of complementary products to be offered by sales personnel, which may put us at a competitive disadvantage relative to companies with more extensive product lines; and
- unforeseen costs and expenses associated with creating an independent sales and marketing organization.

If we enter into arrangements with third parties to perform sales, marketing and distribution services, our product revenues or the profitability of these product revenues to us are likely to be lower than if we were to market and sell any products that we develop ourselves. In addition, we may not be successful in entering into arrangements with third parties to sell and market our product candidates or may be unable to do so on terms that are favorable to us. We likely will have little control over such third parties, and any of them may fail to devote the necessary resources and attention to sell and market our products effectively. If we do not establish sales and marketing capabilities successfully, either on our own or in collaboration with third parties, we will not be successful in commercializing our product candidates.

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

The development and commercialization of new drug products is highly competitive. We face competition with respect to our current product candidates, and will face competition with respect to any product candidates that we may seek to develop or commercialize in the future, from major pharmaceutical companies, specialty pharmaceutical companies and biotechnology companies worldwide. There are a number of large pharmaceutical and biotechnology companies that currently market and sell products or are pursuing the development of products for the treatment of the disease indications for which we are developing our product candidates. Some of these competitive products and therapies are based on scientific approaches that are the same as or similar to our approach, and

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others are based on entirely different approaches. Potential competitors also include academic institutions, government agencies and other public and private research organizations that conduct research, seek patent protection and establish collaborative arrangements for research, development, manufacturing and commercialization.

We are developing our product candidates for the treatment of cancer. There are a variety of available therapies marketed for cancer. In many cases, these drugs are administered in combination to enhance efficacy. Some of these drugs are branded and subject to patent protection, and others are available on a generic basis. Many of these approved drugs are well established therapies and are widely accepted by physicians, patients and third-party payors. Insurers and other third-party payors may also encourage the use of generic products. We expect that if our product candidates are approved, they will be priced at a significant premium over competitive generic products. This may make it difficult for us to achieve our business strategy of using our product candidates in combination with existing therapies or replacing existing therapies with our product candidates.

There are also a number of products in clinical development by third parties to treat cancer by targeting CSCs. These companies include divisions of large pharmaceutical companies, including Astellas Pharma US, Inc., Sanofi-Aventis US LLC, GlaxoSmithKline plc, Boehringer Ingelheim GmbH, Pfizer Inc. and others. There are also biotechnology companies of various size that are developing therapies against CSCs, including OncoMed Pharmaceuticals, Inc., Boston Biomedical, Inc. and Stemline Therapeutics, Inc. Our competitors may develop products that are more effective, safer, more convenient or less costly than any that we are developing or that would render our product candidates obsolete or non-competitive. In addition, our competitors may discover biomarkers that more efficiently measure CSCs than our methods, which may give them a competitive advantage in developing potential products. Our competitors may also obtain marketing approval from the FDA or other regulatory authorities for their products more rapidly than we may obtain approval for ours, which could result in our competitors establishing a strong market position before we are able to enter the market.

Many of our competitors have significantly greater financial resources and expertise in research and development, manufacturing, preclinical testing, conducting clinical trials, obtaining regulatory approvals and marketing approved products than we do. Mergers and acquisitions in the pharmaceutical and biotechnology industries may result in even more resources being concentrated among a smaller number of our competitors. Smaller and other early stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies. These third parties compete with us in recruiting and retaining qualified scientific and management personnel, establishing clinical trial sites and patient registration for clinical trials, as well as in acquiring technologies complementary to, or necessary for, our programs.

Even if we are able to commercialize any product candidates, the products may become subject to unfavorable pricing regulations, third-party reimbursement practices or healthcare reform initiatives, which would harm our business.

The regulations that govern marketing approvals, pricing and reimbursement for new drug products vary widely from country to country. In the United States, recently passed legislation may significantly change the approval requirements in ways that could involve additional costs and cause delays in obtaining approvals. Some countries require approval of the sale price of a drug before it can be marketed. In many countries, the pricing review period begins after marketing or product licensing approval is granted. In some foreign markets, prescription pharmaceutical pricing remains subject to continuing governmental control even after initial approval is granted. As a result, we might obtain marketing approval for a product in a particular country, but then be subject to price regulations that delay our commercial launch of the product, possibly for lengthy time periods, and negatively impact the revenues we are able to generate from the sale of the product in that country. Adverse pricing limitations may hinder our ability to recoup our investment in one or more product candidates, even if our product candidates obtain marketing approval.

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Risk factors

Our ability to commercialize any products successfully also will depend in part on the extent to which reimbursement for these products and related treatments will be available from government health administration authorities, private health insurers and other organizations. Government authorities and third-party payors, such as private health insurers and health maintenance organizations, decide which medications they will pay for and establish reimbursement levels. A primary trend in the U.S. healthcare industry and elsewhere is cost containment. Government authorities and third-party payors have attempted to control costs by limiting coverage and the amount of reimbursement for particular medications. Increasingly, third-party payors are requiring that drug companies provide them with predetermined discounts from list prices and are challenging the prices charged for medical products. We cannot be sure that reimbursement will be available for any product that we commercialize and, if reimbursement is available, the level of reimbursement. Reimbursement may impact the demand for, or the price of, any product candidate for which we obtain marketing approval. Obtaining reimbursement for our products may be particularly difficult because of the higher prices often associated with drugs administered under the supervision of a physician. If reimbursement is not available or is available only to limited levels, we may not be able to successfully commercialize any product candidate for which we obtain marketing approval.

There may be significant delays in obtaining reimbursement for newly approved drugs, and coverage may be more limited than the purposes for which the drug is approved by the FDA or similar regulatory authorities outside the United States. Moreover, eligibility for reimbursement does not imply that any drug will be paid for in all cases or at a rate that covers our costs, including research, development, manufacture, sale and distribution. Interim reimbursement levels for new drugs, if applicable, may also not be sufficient to cover our costs and may not be made permanent. Reimbursement rates may vary according to the use of the drug and the clinical setting in which it is used, may be based on reimbursement levels already set for lower cost drugs and may be incorporated into existing payments for other services. Net prices for drugs may be reduced by mandatory discounts or rebates required by government healthcare programs or private payors and by any future relaxation of laws that presently restrict imports of drugs from countries where they may be sold at lower prices than in the United States. Third-party payors often rely upon Medicare coverage policy and payment limitations in setting their own reimbursement policies. Our inability to promptly obtain coverage and profitable payment rates from both government-funded and private payors for any approved products that we develop could have a material adverse effect on our operating results, our ability to raise capital needed to commercialize products and our overall financial condition.

Product liability lawsuits against us could cause us to incur substantial liabilities and to limit commercialization of any products that we may develop.

We face an inherent risk of product liability exposure related to the testing of our product candidates in human clinical trials and will face an even greater risk if we commercially sell any products that we may develop. If we cannot successfully defend ourselves against claims that our product candidates or products caused injuries, we will incur substantial liabilities. Regardless of merit or eventual outcome, liability claims may result in:

- decreased demand for any product candidates or products that we may develop;
- injury to our reputation and significant negative media attention;
- withdrawal of clinical trial participants;
- significant costs to defend the related litigation;
- substantial monetary awards to trial participants or patients;
- loss of revenue; and
- the inability to commercialize any products that we may develop.

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We currently hold $3.0 million in product liability insurance coverage in the aggregate, with a per incident limit of $3.0 million, which may not be adequate to cover all liabilities that we may incur. We may need to increase our insurance coverage when we begin clinical trials or the commercialization of our product candidates, if ever. Insurance coverage is increasingly expensive. We may not be able to maintain insurance coverage at a reasonable cost or in an amount adequate to satisfy any liability that may arise.

If we fail to comply with environmental, health and safety laws and regulations, we could become subject to fines or penalties or incur costs that could have a material adverse effect on the success of our business.

We are subject to numerous environmental, health and safety laws and regulations, including those governing laboratory procedures and the handling, use, storage, treatment and disposal of hazardous materials and wastes. Our operations involve the use of hazardous and flammable materials, including chemicals and biological materials. Our operations also produce hazardous waste products. We generally contract with third parties for the disposal of these materials and wastes. We cannot eliminate the risk of contamination or injury from these materials. In the event of contamination or injury resulting from our use of hazardous materials, we could be held liable for any resulting damages, and any liability could exceed our resources. We also could incur significant costs associated with civil or criminal fines and penalties.

Although we maintain workers' compensation insurance to cover us for costs and expenses we may incur due to injuries to our employees resulting from the use of hazardous materials, this insurance may not provide adequate coverage against potential liabilities. We do not maintain insurance for environmental liability or toxic tort claims that may be asserted against us in connection with our storage or disposal of biological, hazardous or radioactive materials.

In addition, we may incur substantial costs in order to comply with current or future environmental, health and safety laws and regulations. These current or future laws and regulations may impair our research, development or production efforts. Failure to comply with these laws and regulations also may result in substantial fines, penalties or other sanctions.

RISKS RELATED TO OUR DEPENDENCE ON THIRD PARTIES

We expect to depend on collaborations with third parties for the development and commercialization of our product candidates. If those collaborations are not successful, we may not be able to capitalize on the market potential of these product candidates.

We may seek third-party collaborators for the development and commercialization of our product candidates. Our likely collaborators for any collaboration arrangements include large and mid-size pharmaceutical companies, regional and national pharmaceutical companies and biotechnology companies. If we do enter into any such arrangements with any third parties, we will likely have limited control over the amount and timing of resources that our collaborators dedicate to the development or commercialization of our product candidates. Our ability to generate revenues from these arrangements will depend on our collaborators' abilities to successfully perform the functions assigned to them in these arrangements.

Collaborations involving our product candidates would pose the following risks to us:

> collaborators have significant discretion in determining the efforts and resources that they will apply to these collaborations;

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- collaborators may not pursue development and commercialization of our product candidates or may elect not to continue or renew development or commercialization programs based on clinical trial results, changes in the collaborator's strategic focus or available funding or external factors such as an acquisition that diverts resources or creates competing priorities;

- collaborators may delay clinical trials, provide insufficient funding for a clinical trial program, stop a clinical trial or abandon a product candidate, repeat or conduct new clinical trials or require a new formulation of a product candidate for clinical testing;

- collaborators could independently develop, or develop with third parties, products that compete directly or indirectly with our products or product candidates if the collaborators believe that competitive products are more likely to be successfully developed or can be commercialized under terms that are more economically attractive than ours;

- a collaborator with marketing and distribution rights to one or more products may not commit sufficient resources to the marketing and distribution of such product or products;

- collaborators may not properly maintain or defend our intellectual property rights or may use our proprietary information in such a way as to invite litigation that could jeopardize or invalidate our proprietary information or expose us to potential litigation;

- disputes may arise between the collaborators and us that result in the delay or termination of the research, development or commercialization of our products or product candidates or that result in costly litigation or arbitration that diverts management attention and resources; and

- collaborations may be terminated and, if terminated, may result in a need for additional capital to pursue further development or commercialization of the applicable product candidates.

Collaboration agreements may not lead to development or commercialization of product candidates in the most efficient manner or at all. If a present or future collaborator of ours were to be involved in a business combination, the continued pursuit and emphasis on our product development or commercialization program could be delayed, diminished or terminated.

If we are not able to establish collaborations, we may have to alter our development and commercialization plans.

Our drug development programs and the potential commercialization of our product candidates will require substantial additional cash to fund expenses. For some of our product candidates, we may decide to collaborate with pharmaceutical and biotechnology companies for the development and potential commercialization of those product candidates.

We face significant competition in seeking appropriate collaborators. Whether we reach a definitive agreement for a collaboration will depend, among other things, upon our assessment of the collaborator's resources and expertise, the terms and conditions of the proposed collaboration and the proposed collaborator's evaluation of a number of factors. Those factors may include the design or results of clinical trials, the likelihood of approval by the FDA or similar regulatory authorities outside the United States, the potential market for the subject product candidate, the costs and complexities of manufacturing and delivering such product candidate to patients, the potential of competing products, the existence of uncertainty with respect to our ownership of technology, which can exist if there is a challenge to such ownership without regard to the merits of the challenge and industry and market conditions generally. The collaborator may also consider alternative product candidates or technologies for similar indications that may be available to collaborate on and whether such a collaboration could be more attractive than the one with us for our product candidate. We may also be restricted under existing license agreements from entering into agreements on certain terms with potential collaborators.

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Risk factors

Collaborations are complex and time-consuming to negotiate and document. In addition, there have been a significant number of recent business combinations among large pharmaceutical companies that have resulted in a reduced number of potential future collaborators.

We may not be able to negotiate collaborations on a timely basis, on acceptable terms, or at all. If we are unable to do so, we may have to curtail the development of such product candidate, reduce or delay its development program or one or more of our other development programs, delay its potential commercialization or reduce the scope of any sales or marketing activities, or increase our expenditures and undertake development or commercialization activities at our own expense. If we elect to increase our expenditures to fund development or commercialization activities on our own, we may need to obtain additional capital, which may not be available to us on acceptable terms or at all. If we do not have sufficient funds, we may not be able to further develop our product candidates or bring them to market and generate product revenue.

We expect to rely on third parties to conduct our clinical trials and some aspects of our compound formulation research and preclinical testing, and those third parties may not perform satisfactorily, including failing to meet deadlines for the completion of such trials, research or testing.

We do not plan to independently conduct clinical trials of our product candidates. In addition, we do not expect to independently conduct all aspects of our compound formulation research or preclinical testing of our product candidates. We expect to rely on third parties, such as contract research organizations, clinical data management organizations, medical institutions and clinical investigators, to conduct our clinical trials. We currently rely and expect to continue to rely on third parties to conduct some aspects of our compound formulation research and preclinical testing. For example, we currently rely on third parties in the development of various formulations of VS-507, VS-4718 and VS-5095. We cannot finish preclinical testing and initiate clinical trials of these product candidates until the development of a formulation is complete. Any of these third parties may terminate their engagements with us at any time. If we need to enter into alternative arrangements, it would delay our product development activities.

Our reliance on these third parties for research and development activities will reduce our control over these activities but will not relieve us of our responsibilities. For example, we will remain responsible for ensuring that each of our clinical trials is conducted in accordance with the general investigational plan and protocols for the trial. Moreover, the FDA requires us to comply with standards, commonly referred to as Good Clinical Practices, for conducting, recording and reporting the results of clinical trials to assure that data and reported results are credible and accurate and that the rights, integrity and confidentiality of trial participants are protected. We also are required to register ongoing clinical trials and post the results of completed clinical trials on a government-sponsored database, ClinicalTrials.gov, within certain timeframes. Failure to do so can result in fines, adverse publicity and civil and criminal sanctions.

Furthermore, these third parties may also have relationships with other entities, some of which may be our competitors. If these third parties do not successfully carry out their contractual duties, meet expected deadlines or conduct our clinical trials in accordance with regulatory requirements or our stated protocols, we will not be able to obtain, or may be delayed in obtaining, marketing approvals for our product candidates and will not be able to, or may be delayed in our efforts to, successfully commercialize our product candidates.

We also expect to rely on other third parties to store and distribute drug supplies for our clinical trials. Any performance failure on the part of our distributors could delay clinical development or marketing

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approval of our product candidates or commercialization of our products, producing additional losses and depriving us of potential product revenue.

We contract with third parties for the manufacture of our product candidates for preclinical testing and expect to continue to do so for clinical trials and for commercialization. This reliance on third parties increases the risk that we will not have sufficient quantities of our product candidates or products or such quantities at an acceptable cost, which could delay, prevent or impair our development or commercialization efforts.

We do not have any manufacturing facilities or personnel. We currently rely, and expect to continue to rely, on third-party manufacturers for the manufacture of our product candidates for preclinical testing, other than small amounts of compounds that we may synthesize ourselves for such purpose. To date, we have obtained starting materials for our supply of the cGMP bulk drug substance for our product candidates from one third-party manufacturer. We do not have a long term supply agreement with this third-party manufacturer, and we purchase our required drug supply on a purchase order basis.

We expect to rely on third-party manufacturers or third-party collaborators for the manufacture of our product candidates for clinical trials and for commercial supply of any of these product candidates for which we or our collaborators obtain marketing approval. We may be unable to establish any agreements with third-party manufacturers or to do so on acceptable terms. Even if we are able to establish agreements with third-party manufacturers, reliance on third-party manufacturers entails additional risks, including:

- reliance on the third party for regulatory compliance and quality assurance;
- the possible breach of the manufacturing agreement by the third party; and
- the possible termination or nonrenewal of the agreement by the third party at a time that is costly or inconvenient for us.

Third-party manufacturers may not be able to comply with current good manufacturing practices, or cGMP, regulations or similar regulatory requirements outside the United States. Our failure, or the failure of our third-party manufacturers, to comply with applicable regulations could result in sanctions being imposed on us, including fines, injunctions, civil penalties, delays, suspension or withdrawal of approvals, license revocation, seizures or recalls of product candidates or products, operating restrictions and criminal prosecutions, any of which could significantly and adversely affect supplies of our products and harm our business and results of operations.

Any products that we may develop may compete with other product candidates and products for access to manufacturing facilities. There are a limited number of manufacturers that operate under cGMP regulations and that might be capable of manufacturing for us.

Any performance failure on the part of our existing or future manufacturers could delay clinical development or marketing approval. We do not currently have arrangements in place for redundant supply or a second source for bulk drug substance. If our current contract manufacturer cannot perform as agreed, we may be required to replace that manufacturer. Although we believe that there are several potential alternative manufacturers who could manufacture our product candidates, we may incur added costs and delays in identifying and qualifying any such replacement.

Our current and anticipated future dependence upon others for the manufacture of our product candidates or products may adversely affect our future profit margins and our ability to commercialize any products that receive marketing approval on a timely and competitive basis.

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Risk factors

RISKS RELATED TO OUR INTELLECTUAL PROPERTY

If we fail to comply with our obligations under our intellectual property licenses with third parties, we could lose license rights that are important to our business.

We are a party to a number of intellectual property license agreements with third parties, including the Whitehead Institute and Poniard Pharmaceuticals, Inc., or Poniard, and expect to enter into additional license agreements in the future. Our existing license agreements impose, and we expect that future license agreements will impose, various diligence, milestone payment, royalty, insurance and other obligations on us. For example, under our license agreements with the Whitehead Institute and Poniard, we are required to use commercially reasonable efforts to develop and commercialize licensed products under the agreement and to satisfy other specified obligations. If we fail to comply with our obligations under these licenses, our licensors may have the right to terminate these license agreements, in which event we might not be able to market any product that is covered by these agreements, or to convert the exclusive licenses to non-exclusive licenses, which could materially adversely affect the value of the product candidate being developed under these license agreements. Termination of these license agreements or reduction or elimination of our licensed rights may result in our having to negotiate new or reinstated licenses with less favorable terms. If the Whitehead Institute were to terminate its drug discovery platform license agreement with us for any reason, we would lose access to the EMT technology and the ability to use the stable population of CSCs for high-throughput screening. If Poniard were to terminate its license agreement with us for any reason, we would lose our rights to VS-4718 and VS-5095.

If we are unable to obtain and maintain patent protection for our technology and products, or if our licensors are unable to obtain and maintain patent protection for the technology or products that we license from them, or if the scope of the patent protection obtained is not sufficiently broad, our competitors could develop and commercialize technology and products similar or identical to ours, and our ability to successfully commercialize our technology and products may be adversely affected.

Our success depends in large part on our and our licensors' ability to obtain and maintain patent protection in the United States and other countries with respect to our proprietary technology and products. We and our licensors seek to protect our proprietary position by filing patent applications in the United States and abroad related to our novel technologies and products that are important to our business. To date, one U.S. patent has issued that covers an aspect of our proprietary technology, with claims covering certain methods of predicting the likelihood that a tumor will metastasize. However, no patents have issued that cover our proprietary EMT technology or our product candidates, and we cannot be certain that any patents will issue with claims that cover our proprietary EMT technology or product candidates.

The patent prosecution process is expensive and time-consuming, and we may not be able to file and prosecute all necessary or desirable patent applications at a reasonable cost or in a timely manner. It is also possible that we will fail to identify patentable aspects of our research and development output before it is too late to obtain patent protection. Moreover, in some circumstances, we do not have the right to control the preparation, filing and prosecution of patent applications, or to maintain the patents, covering technology or products that we license from third parties and are reliant on our licensors. For example, we do not control the prosecution of the patent applications licensed to us under our agreements with the Whitehead Institute or those patent applications owned by The Scripps Research Institute, or Scripps, licensed to us under our agreement with Poniard. Therefore, we cannot be certain that these patents and applications will be prosecuted and enforced in a manner consistent with the best interests of our business. If such licensors fail to maintain such patents, or lose rights to those patents, the rights we have licensed may be reduced or eliminated.

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Risk factors

The patent position of biotechnology and pharmaceutical companies generally is highly uncertain, involves complex legal and factual questions and has in recent years been the subject of much litigation. As a result, the issuance, scope, validity, enforceability and commercial value of our and our licensors' patent rights are highly uncertain. Our and our licensors' pending and future patent applications may not result in patents being issued which protect our technology or products or which effectively prevent others from commercializing competitive technologies and products. Changes in either the patent laws or interpretation of the patent laws in the United States and other countries may diminish the value of our patents or narrow the scope of our patent protection.

The laws of foreign countries may not protect our rights to the same extent as the laws of the United States. Publications of discoveries in the scientific literature often lag behind the actual discoveries, and patent applications in the United States and other jurisdictions are typically not published until 18 months after filing, or in some cases not at all. Therefore we cannot be certain that we or our licensors were the first to make the inventions claimed in our owned or licensed patents or pending patent applications, or that we or our licensors were the first to file for patent protection of such inventions.

Assuming the other requirements for patentability are met, currently, in the United States, the first to make the claimed invention is entitled to the patent, while outside the United States, the first to file a patent application is entitled to the patent. In March 2013, the United States will transition to a first inventor to file system in which, assuming the other requirements for patentability are met, the first inventor to file a patent application will be entitled to the patent. We may be subject to a third party preissuance submission of prior art to the U.S. Patent and Trademark Office, or become involved in opposition, derivation, reexamination, *inter parties* review or interference proceedings challenging our patent rights or the patent rights of others. An adverse determination in any such submission, proceeding or litigation could reduce the scope of, or invalidate, our patent rights, allow third parties to commercialize our technology or products and compete directly with us, without payment to us, or result in our inability to manufacture or commercialize products without infringing third-party patent rights.

Even if our owned and licensed patent applications issue as patents, they may not issue in a form that will provide us with any meaningful protection, prevent competitors from competing with us or otherwise provide us with any competitive advantage. Our competitors may be able to circumvent our owned or licensed patents by developing similar or alternative technologies or products in a non-infringing manner. For example, although we expect to file patent applications with respect to our product candidate VS-507 with claims directed to its formulation and method of use, patent protection is not available for composition of matter claims directed to its active pharmaceutical ingredient. Because VS-507 lacks composition of matter protection for its active pharmaceutical ingredient, competitors will be able to offer and sell products with the same active pharmaceutical ingredient so long as these competitors do not infringe any other patents that we may obtain covering this drug.

The issuance of a patent is not conclusive as to its inventorship, scope, validity or enforceability, and our owned and licensed patents may be challenged in the courts or patent offices in the United States and abroad. Such challenges may result in loss of exclusivity or freedom to operate or in patent claims being narrowed, invalidated or held unenforceable, which could limit our ability to stop others from using or commercializing similar or identical technology and products, or limit the duration of the patent protection of our technology and products. Given the amount of time required for the development, testing and regulatory review of new product candidates, patents protecting such candidates might expire before or shortly after such candidates are commercialized. As a result, our owned and licensed patent portfolio may not provide us with sufficient rights to exclude others from commercializing products similar or identical to ours.

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Risk factors

We may become involved in lawsuits to protect or enforce our patents, which could be expensive, time consuming and unsuccessful.

Competitors may infringe our patents. To counter infringement or unauthorized use, we may be required to file infringement claims, which can be expensive and time consuming. In addition, in an infringement proceeding, a court may decide that a patent of ours is invalid or unenforceable, or may refuse to stop the other party from using the technology at issue on the grounds that our patents do not cover the technology in question. An adverse result in any litigation proceeding could put one or more of our patents at risk of being invalidated or interpreted narrowly. Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation, there is a risk that some of our confidential information could be compromised by disclosure during this type of litigation. In addition, our licensors may have rights to file and prosecute such claims and we are reliant on them.

Third parties may initiate legal proceedings alleging that we are infringing their intellectual property rights, the outcome of which would be uncertain and could have a material adverse effect on the success of our business.

Our commercial success depends upon our ability and the ability of our collaborators to develop, manufacture, market and sell our product candidates and use our proprietary technologies without infringing the proprietary rights of third parties. We have yet to conduct comprehensive freedom-to-operate searches to determine whether our use of certain of the patent rights licensed to us would infringe patents issued to third parties. We may become party to, or threatened with, future adversarial proceedings or litigation regarding intellectual property rights with respect to our products and technology, including interference proceedings before the U.S. Patent and Trademark Office. Third parties may assert infringement claims against us based on existing patents or patents that may be granted in the future. If we are found to infringe a third party's intellectual property rights, we could be required to obtain a license from such third party to continue developing and marketing our products and technology. However, we may not be able to obtain any required license on commercially reasonable terms or at all. Even if we were able to obtain a license, it could be non-exclusive, thereby giving our competitors access to the same technologies licensed to us. We could be forced, including by court order, to cease commercializing the infringing technology or product. In addition, we could be found liable for monetary damages. A finding of infringement could prevent us from commercializing our product candidates or force us to cease some of our business operations, which could materially harm our business. Claims that we have misappropriated the confidential information or trade secrets of third parties could have a similar negative impact on our business.

For example, we are aware of a U.S. patent application filed by a third party almost one year after the priority date of the U.S. patent application filed by Scripps and licensed to us by Poniard, which has pending generic claims that, if issued as written, potentially cover VS-4718 and VS-5095. The third-party patent application also specifically discloses VS-4718. Although the Scripps patent application has a priority date that is earlier than the priority date of the third-party application, we cannot be sure which party was the first to make the claimed invention. Because the United States currently uses a first to invent standard to determine priority, if a patent issues under the third-party patent application covering the composition of matter of VS-4718 or VS-5095 and such third party was determined to be the first to make the claimed invention, we would need to obtain a license to the patented technology to commercialize VS-4718 or VS-5095 in the United States, which would cause us to incur licensing related costs. However, a license to this patent might not be available on commercially reasonable terms, or at all. Our failure to obtain a license to any such patent could delay or prevent our potential commercialization of VS-4718 or VS-5095 in the United States.

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We may be subject to claims that our employees have wrongfully used or disclosed alleged trade secrets of their former employers.

Many of our employees were previously employed at universities or other biotechnology or pharmaceutical companies, including our competitors or potential competitors. Although we try to ensure that our employees do not use the proprietary information or know-how of others in their work for us, we may be subject to claims that we or these employees have used or disclosed intellectual property, including trade secrets or other proprietary information, of any such employee's former employer. Litigation may be necessary to defend against these claims. If we fail in defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights or personnel. Even if we are successful in defending against such claims, litigation could result in substantial costs and be a distraction to management.

Intellectual property litigation could cause us to spend substantial resources and distract our personnel from their normal responsibilities.

Even if resolved in our favor, litigation or other legal proceedings relating to intellectual property claims may cause us to incur significant expenses, and could distract our technical and management personnel from their normal responsibilities. In addition, there could be public announcements of the results of hearings, motions or other interim proceedings or developments and if securities analysts or investors perceive these results to be negative, it could have a substantial adverse effect on the price of our common stock. Such litigation or proceedings could substantially increase our operating losses and reduce the resources available for development activities or any future sales, marketing or distribution activities. We may not have sufficient financial or other resources to adequately conduct such litigation or proceedings. Some of our competitors may be able to sustain the costs of such litigation or proceedings more effectively than we can because of their greater financial resources. Uncertainties resulting from the initiation and continuation of patent litigation or other proceedings could have a material adverse effect on our ability to compete in the marketplace.

If we are unable to protect the confidentiality of our trade secrets, our business and competitive position would be harmed.

In addition to seeking patents for some of our technology and products, we also rely on trade secrets, including unpatented know-how, technology and other proprietary information, to maintain our competitive position. We seek to protect these trade secrets, in part, by entering into non-disclosure and confidentiality agreements with parties who have access to them, such as our employees, corporate collaborators, outside scientific collaborators, contract manufacturers, consultants, advisors and other third parties. We also enter into confidentiality and invention or patent assignment agreements with our employees and consultants. Despite these efforts, any of these parties may breach the agreements and disclose our proprietary information, including our trade secrets, and we may not be able to obtain adequate remedies for such breaches. Enforcing a claim that a party illegally disclosed or misappropriated a trade secret is difficult, expensive and time-consuming, and the outcome is unpredictable. In addition, some courts inside and outside the United States are less willing or unwilling to protect trade secrets. If any of our trade secrets were to be lawfully obtained or independently developed by a competitor, we would have no right to prevent them from using that technology or information to compete with us. If any of our trade secrets were to be disclosed to or independently developed by a competitor, our competitive position would be harmed.

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Risk factors

RISKS RELATED TO REGULATORY APPROVAL OF OUR PRODUCT CANDIDATES AND OTHER LEGAL COMPLIANCE MATTERS

If we are not able to obtain, or if there are delays in obtaining, required regulatory approvals, we will not be able to commercialize our product candidates, and our ability to generate revenue will be materially impaired.

Our product candidates and the activities associated with their development and commercialization, including their design, testing, manufacture, safety, efficacy, recordkeeping, labeling, storage, approval, advertising, promotion, sale and distribution, are subject to comprehensive regulation by the FDA and other regulatory agencies in the United States and by comparable authorities in other countries. Failure to obtain marketing approval for a product candidate will prevent us from commercializing the product candidate. We have not received approval to market any of our product candidates from regulatory authorities in any jurisdiction. We have only limited experience in filing and supporting the applications necessary to gain marketing approvals and expect to rely on third-party contract research organizations to assist us in this process. Securing FDA approval requires the submission of extensive preclinical and clinical data and supporting information to the FDA for each therapeutic indication to establish the product candidate's safety and efficacy. Securing FDA approval also requires the submission of information about the product manufacturing process to, and inspection of manufacturing facilities by, the FDA. Our product candidates may not be effective, may be only moderately effective or may prove to have undesirable or unintended side effects, toxicities or other characteristics that may preclude our obtaining marketing approval or prevent or limit commercial use.

The process of obtaining marketing approvals, both in the United States and abroad, is expensive, may take many years if additional clinical trials are required, if approval is obtained at all, and can vary substantially based upon a variety of factors, including the type, complexity and novelty of the product candidates involved. Changes in marketing approval policies during the development period, changes in or the enactment of additional statutes or regulations, or changes in regulatory review for each submitted product application, may cause delays in the approval or rejection of an application. The FDA has substantial discretion in the approval process and may refuse to accept any application or may decide that our data is insufficient for approval and require additional preclinical, clinical or other studies. In addition, varying interpretations of the data obtained from preclinical and clinical testing could delay, limit or prevent marketing approval of a product candidate. Any marketing approval we ultimately obtain may be limited or subject to restrictions or post-approval commitments that render the approved product not commercially viable.

If we experience delays in obtaining approval or if we fail to obtain approval of our product candidates, the commercial prospects for our product candidates may be harmed and our ability to generate revenues will be materially impaired.

Failure to obtain marketing approval in international jurisdictions would prevent our product candidates from being marketed abroad.

In order to market and sell our products in the European Union and many other jurisdictions, we or our third-party collaborators must obtain separate marketing approvals and comply with numerous and varying regulatory requirements. The approval procedure varies among countries and can involve additional testing. The time required to obtain approval may differ substantially from that required to obtain FDA approval. The regulatory approval process outside the United States generally includes all of the risks associated with obtaining FDA approval. In addition, in many countries outside the United States, it is required that the product be approved for reimbursement before the product can be approved for sale in that country. We or these third parties may not obtain approvals from regulatory

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authorities outside the United States on a timely basis, if at all. Approval by the FDA does not ensure approval by regulatory authorities in other countries or jurisdictions, and approval by one regulatory authority outside the United States does not ensure approval by regulatory authorities in other countries or jurisdictions or by the FDA. We may not be able to file for marketing approvals and may not receive necessary approvals to commercialize our products in any market.

Any product candidate for which we obtain marketing approval could be subject to restrictions or withdrawal from the market and we may be subject to penalties if we fail to comply with regulatory requirements or if we experience unanticipated problems with our products, when and if any of them are approved.

Any product candidate for which we obtain marketing approval, along with the manufacturing processes, post-approval clinical data, labeling, advertising and promotional activities for such product, will be subject to continual requirements of and review by the FDA and other regulatory authorities. These requirements include submissions of safety and other post-marketing information and reports, registration and listing requirements, cGMP requirements relating to quality control, quality assurance and corresponding maintenance of records and documents, requirements regarding the distribution of samples to physicians and recordkeeping. Even if marketing approval of a product candidate is granted, the approval may be subject to limitations on the indicated uses for which the product may be marketed or to the conditions of approval, or contain requirements for costly post-marketing testing and surveillance to monitor the safety or efficacy of the product. The FDA closely regulates the post-approval marketing and promotion of drugs to ensure drugs are marketed only for the approved indications and in accordance with the provisions of the approved labeling. The FDA imposes stringent restrictions on manufacturers' communications regarding off-label use and if we do not market our products for their approved indications, we may be subject to enforcement action for off-label marketing.

In addition, later discovery of previously unknown problems with our products, manufacturers or manufacturing processes, or failure to comply with regulatory requirements, may yield various results, including:

- restrictions on such products, manufacturers or manufacturing processes;
- restrictions on the labeling or marketing of a product;
- restrictions on product distribution or use;
- requirements to conduct post-marketing clinical trials;
- warning or untitled letters;
- withdrawal of the products from the market;
- refusal to approve pending applications or supplements to approved applications that we submit;
- recall of products;
- fines, restitution or disgorgement of profits or revenue;
- suspension or withdrawal of marketing approvals;
-

refusal to permit the import or export of our products;

> product seizure; or

> injunctions or the imposition of civil or criminal penalties.

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Risk factors

Our relationships with customers and third-party payors will be subject to applicable anti-kickback, fraud and abuse and other healthcare laws and regulations, which could expose us to criminal sanctions, civil penalties, contractual damages, reputational harm and diminished profits and future earnings.

Healthcare providers, physicians and third-party payors play a primary role in the recommendation and prescription of any product candidates for which we obtain marketing approval. Our future arrangements with third-party payors and customers may expose us to broadly applicable fraud and abuse and other healthcare laws and regulations that may constrain the business or financial arrangements and relationships through which we market, sell and distribute our products for which we obtain marketing approval. Restrictions under applicable federal and state healthcare laws and regulations, include the following:

> the federal healthcare anti-kickback statute prohibits, among other things, persons from knowingly and willfully soliciting, offering, receiving or providing remuneration, directly or indirectly, in cash or in kind, to induce or reward either the referral of an individual for, or the purchase, order or recommendation of, any good or service, for which payment may be made under federal and state healthcare programs such as Medicare and Medicaid;

> the federal False Claims Act imposes criminal and civil penalties, including civil whistleblower or *qui tam* actions, against individuals or entities for knowingly presenting, or causing to be presented, to the federal government, claims for payment that are false or fraudulent or making a false statement to avoid, decrease or conceal an obligation to pay money to the federal government;

> the federal Health Insurance Portability and Accountability Act of 1996, as amended by the Health Information Technology for Economic and Clinical Health Act, imposes criminal and civil liability for executing a scheme to defraud any healthcare benefit program and also imposes obligations, including mandatory contractual terms, with respect to safeguarding the privacy, security and transmission of individually identifiable health information;

> the federal false statements statute prohibits knowingly and willfully falsifying, concealing or covering up a material fact or making any materially false statement in connection with the delivery of or payment for healthcare benefits, items or services;

> the federal transparency requirements under the Health Care Reform Law requires manufacturers of drugs, devices, biologics and medical supplies to report to the Department of Health and Human Services information related to physician payments and other transfers of value and physician ownership and investment interests; and

> analogous state laws and regulations, such as state anti-kickback and false claims laws, may apply to sales or marketing arrangements and claims involving healthcare items or services reimbursed by non-governmental third-party payors, including private insurers, and some state laws require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government in addition to requiring drug manufacturers to report information related to payments to physicians and other health care providers or marketing expenditures.

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Risk factors

Efforts to ensure that our business arrangements with third parties will comply with applicable healthcare laws and regulations will involve substantial costs. It is possible that governmental authorities will conclude that our business practices may not comply with current or future statutes, regulations or case law involving applicable fraud and abuse or other healthcare laws and regulations. If our operations are found to be in violation of any of these laws or any other governmental regulations that may apply to us, we may be subject to significant civil, criminal and administrative penalties, damages, fines, exclusion from government funded healthcare programs, such as Medicare and Medicaid, and the curtailment or restructuring of our operations. If any of the physicians or other providers or entities with whom we expect to do business are found to be not in compliance with applicable laws, they may be subject to criminal, civil or administrative sanctions, including exclusions from government funded healthcare programs.

Recently enacted and future legislation may increase the difficulty and cost for us to obtain marketing approval of and commercialize our product candidates and affect the prices we may obtain.

In the United States and some foreign jurisdictions, there have been a number of legislative and regulatory changes and proposed changes regarding the healthcare system that could prevent or delay marketing approval of our product candidates, restrict or regulate post-approval activities and affect our ability to profitably sell any product candidates for which we obtain marketing approval.

In the United States, the Medicare Prescription Drug, Improvement, and Modernization Act of 2003, or Medicare Modernization Act, changed the way Medicare covers and pays for pharmaceutical products. The legislation expanded Medicare coverage for drug purchases by the elderly and introduced a new reimbursement methodology based on average sales prices for physician administered drugs. In addition, this legislation provided authority for limiting the number of drugs that will be covered in any therapeutic class. Cost reduction initiatives and other provisions of this legislation could decrease the coverage and price that we receive for any approved products. While the Medicare Modernization Act applies only to drug benefits for Medicare beneficiaries, private payors often follow Medicare coverage policy and payment limitations in setting their own reimbursement rates. Therefore, any reduction in reimbursement that results from the Medicare Modernization Act may result in a similar reduction in payments from private payors.

More recently, in March 2010, President Obama signed into law the Health Care Reform Law, a sweeping law intended to broaden access to health insurance, reduce or constrain the growth of healthcare spending, enhance remedies against fraud and abuse, add new transparency requirements for health care and health insurance industries, impose new taxes and fees on the health industry and impose additional health policy reforms. Effective October 1, 2010, the Health Care Reform Law revises the definition of "average manufacturer price" for reporting purposes, which could increase the amount of Medicaid drug rebates to states. Further, the new law imposes a significant annual fee on companies that manufacture or import branded prescription drug products. Substantial new provisions affecting compliance have also been enacted, which may affect our business practices with health care practitioners. We will not know the full effects of the Health Care Reform Law until applicable federal and state agencies issue regulations or guidance under the new law. Although it is too early to determine the effect of the Health Care Reform Law, the new law appears likely to continue the pressure on pharmaceutical pricing, especially under the Medicare program, and may also increase our regulatory burdens and operating costs.

Legislative and regulatory proposals have been made to expand post-approval requirements and restrict sales and promotional activities for pharmaceutical products. We cannot be sure whether additional legislative changes will be enacted, or whether the FDA regulations, guidance or interpretations will be

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changed, or what the impact of such changes on the marketing approvals of our product candidates, if any, may be. In addition, increased scrutiny by the U.S. Congress of the FDA's approval process may significantly delay or prevent marketing approval, as well as subject us to more stringent product labeling and post-marketing testing and other requirements.

RISKS RELATED TO EMPLOYEE MATTERS AND MANAGING GROWTH

Our future success depends on our ability to retain our president and chief executive officer and other key executives and to attract, retain and motivate qualified personnel.

We are highly dependent on Christoph Westphal, our President and Chief Executive Officer, Robert Forrester, our Chief Operating Officer, and Jonathan Pachter, our Vice President, Head of Research, as well as the other principal members of our management and scientific teams, including our scientific co-founders, Robert Weinberg, Eric Lander and Piyush Gupta. Although we have formal employment agreements with Robert Forrester and Jonathan Pachter, these agreements do not prevent them from terminating their employment with us at any time. We do not have an employment agreement with Christoph Westphal. We do not maintain "key person" insurance for any of our executives or other employees. The loss of the services of any of these persons could impede the achievement of our research, development and commercialization objectives.

In addition to his role as Chairman of the board of directors and President and Chief Executive Officer of our company, Dr. Westphal also serves as a general partner of Longwood Fund, LP, a venture capital investment fund and one of our principal stockholders. We and Dr. Westphal anticipate that he will transition to an executive Chairman role at our company in the future based on our having meaningfully advanced our discovery, research and development efforts, the overall growth of our company and our identifying and hiring a suitable successor. In connection with Dr. Westphal's transition to this role, we will need to recruit and hire a new principal executive officer. Our inability to hire a suitable executive to assume this position in a timely fashion could delay the execution of our business plans or disrupt our operations.

Recruiting and retaining qualified scientific, clinical, manufacturing and sales and marketing personnel will also be critical to our success. We may not be able to attract and retain these personnel on acceptable terms given the competition among numerous pharmaceutical and biotechnology companies for similar personnel. We also experience competition for the hiring of scientific and clinical personnel from universities and research institutions. In addition, we rely on consultants and advisors, including scientific and clinical advisors, to assist us in formulating our research and development and commercialization strategy. Our consultants and advisors, including our scientific co-founders, may be employed by employers other than us and may have commitments under consulting or advisory contracts with other entities that may limit their availability to us.

We expect to expand our development, regulatory and future sales and marketing capabilities, and as a result, we may encounter difficulties in managing our growth, which could disrupt our operations.

We expect to experience significant growth in the number of our employees and the scope of our operations, particularly in the areas of drug development, regulatory affairs and sales and marketing. To manage our anticipated future growth, we must continue to implement and improve our managerial, operational and financial systems, expand our facilities and continue to recruit and train additional qualified personnel. Due to our limited financial resources and the limited experience of our management team in managing a company with such anticipated growth, we may not be able to

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effectively manage the expansion of our operations or recruit and train additional qualified personnel. The physical expansion of our operations may lead to significant costs and may divert our management and business development resources. Any inability to manage growth could delay the execution of our business plans or disrupt our operations.

RISKS RELATED TO OUR COMMON STOCK AND THIS OFFERING

After this offering, our executive officers, directors and principal stockholders will maintain the ability to control all matters submitted to stockholders for approval.

Upon the closing of this offering, our executive officers, directors and stockholders who owned more than 5% of our outstanding common stock before this offering will, in the aggregate, beneficially own shares representing approximately 55.7% of our capital stock, excluding any shares of our common stock that our existing principal stockholders may purchase in this offering. Based on the initial public offering price of $10.00 per share, if our principal stockholders purchase all the shares they have indicated interests in purchasing in this offering, the number of shares of our common stock beneficially owned by our executive officers, directors and stockholders who owned more than 5% of our outstanding common stock before this offering will, in the aggregate, increase to 61.4% of our capital stock. As a result, if these stockholders were to choose to act together, they would be able to control all matters submitted to our stockholders for approval, as well as our management and affairs. For example, these persons, if they choose to act together, would control the election of directors and approval of any merger, consolidation or sale of all or substantially all of our assets. This concentration of voting power could delay or prevent an acquisition of our company on terms that other stockholders may desire.

Provisions in our corporate charter documents and under Delaware law could make an acquisition of us, which may be beneficial to our stockholders, more difficult and may prevent attempts by our stockholders to replace or remove our current management.

Provisions in our corporate charter and our bylaws that will become effective upon the closing of this offering may discourage, delay or prevent a merger, acquisition or other change in control of us that stockholders may consider favorable, including transactions in which you might otherwise receive a premium for your shares. These provisions could also limit the price that investors might be willing to pay in the future for shares of our common stock, thereby depressing the market price of our common stock. In addition, because our board of directors is responsible for appointing the members of our management team, these provisions may frustrate or prevent any attempts by our stockholders to replace or remove our current management by making it more difficult for stockholders to replace members of our board of directors. Among other things, these provisions:

- establish a classified board of directors such that not all members of the board are elected at one time;
- allow the authorized number of our directors to be changed only by resolution of our board of directors;
- limit the manner in which stockholders can remove directors from the board;
- establish advance notice requirements for stockholder proposals that can be acted on at stockholder meetings and nominations to our board of directors;
- require that stockholder actions must be effected at a duly called stockholder meeting and prohibit actions by our stockholders by written consent;

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- limit who may call stockholder meetings;
- authorize our board of directors to issue preferred stock without stockholder approval, which could be used to institute a "poison pill" that would work to dilute the stock ownership of a potential hostile acquirer, effectively preventing acquisitions that have not been approved by our board of directors; and
- require the approval of the holders of at least 75% of the votes that all our stockholders would be entitled to cast to amend or repeal certain provisions of our charter or bylaws.

Moreover, because we are incorporated in Delaware, we are governed by the provisions of Section 203 of the Delaware General Corporation Law, which prohibits a person who owns in excess of 15% of our outstanding voting stock from merging or combining with us for a period of three years after the date of the transaction in which the person acquired in excess of 15% of our outstanding voting stock, unless the merger or combination is approved in a prescribed manner.

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

The initial public offering price of our common stock is substantially higher than the net tangible book value per share of our common stock. Therefore, if you purchase shares of our common stock in this offering, you will pay a price per share that substantially exceeds our net tangible book value per share after this offering. To the extent shares are issued under outstanding options or the restricted stock units granted effective upon the closing of this offering or the warrant issuable pursuant to our license agreement with Poniard, you will incur further dilution. Based on the initial public offering price of $10.00 per share, you will experience immediate dilution of $4.12 per share, representing the difference between our pro forma net tangible book value per share after giving effect to this offering and the initial public offering price. In addition, purchasers of common stock in this offering will have contributed approximately 45% of the aggregate price paid by all purchasers of our stock but will own only approximately 29% of our common stock outstanding after this offering.

An active trading market for our common stock may not develop.

Prior to this offering, there has been no public market for our common stock. The initial public offering price for our common stock was determined through negotiations with the underwriters. Although our common stock has been approved for listing on The NASDAQ Global Market, an active trading market for our shares may never develop or be sustained following this offering. If an active market for our common stock does not develop, it may be difficult for you to sell shares you purchase in this offering without depressing the market price for the shares or at all.

If our stock price is volatile, purchasers of our common stock could incur substantial losses.

Our stock price is likely to be volatile. The stock market in general and the market for biopharmaceutical companies in particular have experienced extreme volatility that has often been unrelated to the operating performance of particular companies. As a result of this volatility, you may not be able to sell your common stock at or above the initial public offering price. The market price for our common stock may be influenced by many factors, including:

- the success of competitive products or technologies;
- results of clinical trials of our product candidates or those of our competitors;