

Verastem, Inc.
Form 424B5
January 20, 2015

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Filed Pursuant to Rule 424b(5)
Registration No. 333-192968

The information in this preliminary prospectus supplement and the accompanying prospectus is not complete and may be changed. A registration statement relating to the securities has become effective under the Securities Act of 1933, as amended. This preliminary prospectus supplement together with the accompanying prospectus is not an offer to sell the securities and it is not soliciting an offer to buy the securities in any jurisdiction where the offer or sale is not permitted.

Subject to Completion, Dated January 20, 2015

Preliminary Prospectus Supplement

(To Prospectus dated January 8, 2014)

\$40,000,000

Common Stock

We are offering _____ shares of our common stock. Our common stock is listed on The NASDAQ Global Market under the symbol "VSTM." On January 16, 2015, the last reported sale price of our common stock on The NASDAQ Global Market was \$8.43 per share.

We are an "emerging growth company" as defined under the federal securities laws and, as such, we may elect to comply with certain reduced public company reporting requirements.

Investing in our common stock involves a high degree of risk. Please read "Risk Factors" beginning on page S-11 of this prospectus supplement and in the documents incorporated by reference into this prospectus supplement.

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

Longwood Fund II, LP, an entity affiliated with Christoph Westphal, our Executive Chairman and one of our directors, and its affiliated entities, which we refer to collectively as the Longwood funds, and Timothy Barberich, one of our directors, have indicated an interest in purchasing approximately \$8 million and \$250,000, respectively, in shares of our common stock in this offering at the public offering price. However, because indications of interest are not binding agreements or commitments to purchase, the underwriters could determine to sell more, fewer or no shares to the Longwood funds and Mr. Barberich, and each of the Longwood funds and Mr. Barberich could determine to purchase more, fewer or no shares in this offering.

PER SHARE TOTAL

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| | | |
|--|----|----|
| Public offering price | \$ | \$ |
| Underwriting discounts and commissions | \$ | \$ |
| Proceeds to us (after expenses) | \$ | \$ |

Delivery of the shares of common stock is expected to be made on or about January , 2015. We have granted the underwriters an option for a period of 30 days to purchase up to an additional shares of our common stock. If the underwriters exercise the option in full, the total underwriting discounts and commissions payable by us will be \$, and the total proceeds to us, before expenses, will be \$.

Joint Book-Running Managers

Jefferies

Leerink Partners

Co-Lead Managers

Guggenheim Securities

Oppenheimer & Co.

Prospectus Supplement dated January , 2015

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ABOUT THIS PROSPECTUS SUPPLEMENT

This prospectus supplement and the accompanying prospectus relate to part of a registration statement that we filed with the Securities and Exchange Commission, or SEC, using a shelf registration process. Both this prospectus supplement and the accompanying prospectus include or incorporate by reference important information about us, our common stock and other information you should know before investing. You should read both this prospectus supplement and the accompanying prospectus as well as additional information described under "Where You Can Find More Information" in the accompanying prospectus before making an investment decision.

We have not authorized any dealer, agent or other person to give any information or to make any representation other than those contained or incorporated by reference in this prospectus supplement and the accompanying prospectus. You must not rely upon any information or representation not contained or incorporated by reference in this prospectus supplement or the accompanying prospectus. This prospectus supplement and the accompanying prospectus do not constitute an offer to sell or the solicitation of an offer to buy any securities other than the registered securities to which they relate, nor do this prospectus supplement and the accompanying prospectus constitute an offer to sell or the solicitation of an offer to buy securities in any jurisdiction to any person to whom it is unlawful to make such offer or solicitation in such jurisdiction. You should not assume that the information contained in this prospectus supplement and the accompanying prospectus is accurate on any date subsequent to the date set forth on the front of the document or that any information we have incorporated by reference is correct on any date subsequent to the date of the document incorporated by reference, even though this prospectus supplement and any accompanying prospectus is delivered or securities are sold on a later date.

This prospectus supplement may add to, update or change the information in the accompanying prospectus. If information in this prospectus supplement is inconsistent with information in the accompanying prospectus, this prospectus supplement will apply and will supersede that information in the accompanying prospectus.

Unless otherwise indicated or unless the context requires otherwise, all references in this prospectus supplement to "Verastem," "we," "us" and "our" refer to Verastem, Inc. and its consolidated subsidiary.

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PROSPECTUS SUPPLEMENT SUMMARY

This summary highlights selected information included or incorporated by reference in this prospectus supplement and the accompanying prospectus and does not contain all of the information that may be important to you. You should carefully review this entire prospectus supplement and the accompanying prospectus, including the risk factors and financial statements included and incorporated by reference in this prospectus supplement and the accompanying prospectus.

Company Overview

We are a biopharmaceutical company focused on discovering and developing drugs to treat cancer by the targeted killing of cancer stem cells. 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 tumors, their recurrence and metastasis. We have proprietary technology to create a stable population of cancer stem cells that we use to screen for and identify small molecule compounds that target cancer stem cells. Our most advanced programs target the Focal Adhesion Kinase, or FAK, and the PI3K/mTOR signaling pathways. Our lead FAK inhibitor, VS-6063, has been assigned defactinib as the United States Adopted Name. We have received orphan drug designation for use of VS-6063 in mesothelioma in the European Union and in the United States. VS-6063 is currently in a registration-directed trial (COMMAND) in patients with mesothelioma, a Phase 1b trial in combination with weekly paclitaxel for patients with ovarian cancer, a Phase 2 study in patients with non-small cell lung cancer and a Phase 2 trial preceding surgery in mesothelioma. In addition to VS-6063, both our FAK inhibitor VS-4718 and our dual mTORC1/2 and PI3K inhibitor VS-5584 are in Phase 1 clinical trials in patients with advanced cancers. We expect to conduct an interim analysis of COMMAND during the second quarter of 2015 and following this, we intend to communicate the specific patient population for the primary analysis. We also expect to update or announce results from the combination trial of VS-6063 and paclitaxel in patients with ovarian cancer and results from the Phase 2 study of VS-6063 in patients with non-small cell lung cancer in the second half of 2015. We also expect to report results from the Phase 1 trials of VS-4718 and VS-5584 in the second half of 2015. We expect to report preliminary data on the extended treatment cohort for the Phase 2 trial preceding surgery in mesothelioma in the first half of 2016.

Cancer is a group of diseases characterized by uncontrolled growth and spread of abnormal cells. The American Cancer Society estimated that in the United States in 2014, approximately 1.7 million new cases of cancer would be diagnosed and approximately 600,000 people would die from the disease. Current treatments for cancer include surgery, radiation therapy, chemotherapy, hormone therapy and targeted therapy. According to estimates by the National Institutes of Health, the direct medical cost of cancer of all types was projected to reach \$124.6 billion in the United States in 2010. IMS Health estimates that in the United States in 2014, approximately \$27.9 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.

We believe that a key reason for the ultimate failure of many current cancer therapies to achieve a durable clinical response is the presence of cancer stem cells, or CSCs, which are also sometimes referred to as tumor-initiating cells, within tumors. CSCs have been identified in many types of cancer, including mesothelioma, ovarian, lung, breast, pancreatic, colon, brain and leukemia. Following many cancer treatments, the tumor can remain with a high percentage of CSCs and become more aggressive and resistant to further treatment. In addition, patients who relapse often develop metastatic disease in which the cancer spreads to other sites in the body. Tumor metastasis to critical organs is the cause of more than 90% of cancer deaths. We believe that it is the drug resistance and ability of CSCs to spread to other sites in the body that may be the root causes of these therapies failing. Accordingly, our mission is to develop drugs targeting CSCs that either in combination with other cancer treatments or alone can target all of the cells comprising a tumor and, thus, create a durable clinical response.

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Clinical Trials

Our most advanced product candidates are VS-6063, VS-4718 and VS-5584. We are currently evaluating these compounds in both preclinical and clinical studies as potential therapies for certain cancers, including mesothelioma, ovarian and lung. We believe that these compounds may be especially beneficial as therapeutics in aggressive cancers driven by CSCs that have a poorer prognosis and lower overall survival rate than other types of cancer.

VS-6063

MESOTHELIOMA

COMMAND

We are conducting a randomized, double-blind, multi-center, multi-national study of VS-6063 in patients with malignant pleural mesothelioma who have achieved disease control consisting of at least stable disease post first-line therapy with pemetrexed and platinum. We have met with regulatory agencies in the United States and the United Kingdom and interacted with regulatory agencies in eleven other countries to discuss COMMAND and, based on these discussions, we believe that positive results, if obtained, from this trial may enable us to seek regulatory approval for VS-6063 in mesothelioma. The study is currently open in 13 countries and recruiting patients at 55 study centers. We have enrolled 180 patients as of January 8, 2015 and in total, we expect to enroll 350-400 patients into COMMAND.

Window-of-Opportunity

VS-6063 is currently in an open-label neoadjuvant study in subjects with malignant pleural mesothelioma who are eligible for surgery. Neoadjuvant refers to the administration of VS-6063 prior to surgery to remove the mesothelioma tumor. The purpose of this study is to assess biomarker responses from tumor tissue. The study is being conducted in two parts. In part one, 10 subjects were administered VS-6063 for 12 days. In part two, 10-15 subjects will receive VS-6063 for 35 days. Pre- and post-treatment biopsies and blood samples are being collected and PET/CT scans are being performed both pre- and post-treatment. The safety, pharmacokinetics, and tumor response rate to VS-6063 are also being assessed.

In October 2014, results from part one were presented at the International Mesothelioma Interest Group (iMig) meeting. Based upon biopsy results, treatment with VS-6063 for 12 days reduced FAK activity by an average of 70% in evaluable biopsies and decreases in a marker of cancer stem cells were observed in five of seven evaluable biopsies. In addition, the results of the pre- and post-treatment PET/CT scans, as measured by Response Evaluation Criteria in Solid Tumors, or RECIST, modified for mesothelioma, indicated that no disease progression was observed and that reductions in tumor size consistent with a partial response were observed in two patients. A waterfall plot of the tumor size measurements is presented in Figure 1.

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Figure 1. Measurement of tumor size from part one of the "Window of Opportunity" study

Part two of the study, where the treatment period is increased from 12 to 35 days, is currently ongoing.

Phase 1 Combination of VS-6063 and VS-5584

This clinical study is being conducted in patients with relapsed pleural or peritoneal mesothelioma and is comprised of two parts. Part one is a dose escalation of oral VS-5584 in addition to VS-6063, at 400 mg twice daily, or BID, to determine the recommended Phase 2 dose of VS-5584 in combination with VS-6063, and to assess the safety of the combination and pharmacokinetics. In part two, patients will be treated with the recommended Phase 2 doses of VS-5584 and VS-6063 in combination to assess the anti-cancer activity of the combination. Approximately 40 subjects are expected to be enrolled.

OVARIAN CANCER

Combination of VS-6063 and Paclitaxel

We are conducting a Phase 1/1b clinical trial of VS-6063 in combination with weekly paclitaxel in patients with ovarian cancer. The study, which has completed enrollment, is evaluating 22 patients at three sites in the United States.

This study is comprised of two parts. Part one is a dose escalation of oral VS-6063 BID in addition to the standard dose of weekly paclitaxel. The purpose of part one is to assess the safety, evaluate pharmacokinetic parameters and determine the recommended Phase 2 dose in combination with paclitaxel. Part two includes patients treated with the recommended Phase 2 dose of VS-6063 in combination with paclitaxel. The purpose of part two is to evaluate the pharmacodynamic effect, the biochemical and physiological effect of VS-6063 through measurement of biomarkers from tumor biopsies pre- and post-treatment and assess the anti-cancer activity of VS-6063 when administered in combination with paclitaxel according to RECIST guidelines.

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As of June 30, 2014, seventeen serious adverse events, or SAEs, were observed in 9 patients (41%). All but one SAE (Grade 3 dehydration, deemed possibly related) were deemed to be not related or unlikely

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related to study drug. In general, the combination of VS-6063 and paclitaxel did not significantly worsen the side effect profile of weekly paclitaxel alone. Data from the ongoing study are included in Figures 2, 3 and 4 below.

Figure 2. Safety profile of the combination of VS-6063 and paclitaxel treatment emergent events in $\geq 20\%$ patients, as reported on June 2, 2014 at the American Society of Clinical Oncology Annual Meeting.

As of December 15, 2014, 64% of patients have achieved a best overall response of at least stable disease of ≥ 8 weeks as per RECIST guidelines in this ongoing study. Biomarker data on biopsies obtained pre- and post-treatment with VS-6063 (400mg BID) as a single agent for 10 days shows reductions in FAK activity and decreases in cancer stem cells (Figure 3). In addition, of the twenty-two patients treated with the combination of VS-6063 and paclitaxel, three partial responses and two complete responses have been reported as of December 15, 2014. Five patients remained on study as of December 15, 2014 (Figure 4).

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Figure 3. Biomarker results from pre- and post-treatment biopsies in patients with ovarian cancer treated for 10 days with single-agent VS-6063

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Figure 4. Overall best response to the combination of VS-6063 and paclitaxel in patients with ovarian cancer

Overall Best Response of at least Stable Disease of ≥ 8 weeks: 64%

LUNG CANCER

We are conducting a Phase 2 open-label, multi-center, multi-cohort study of VS-6063 in patients with KRAS mutant non-small cell lung cancer (NSCLC). NSCLC with a KRAS mutation is required for study entry and subjects will be enrolled into one of four cohorts based on the status of their INK4a/Arf and p53 mutations. The purpose of this study is to determine the progression free survival rate within each cohort. The safety and tolerability of VS-6063, tumor response rate, progression free survival and overall survival will also be assessed. The study is expected to enroll up to 150 patients at nine clinical sites in the United States.

This study is divided into two stages. In stage one, up to 11 patients will be enrolled in each cohort and treated with VS-6063 400mg BID. If ≥ 4 patients in a cohort achieve disease control for ≥ 12 weeks, the cohort will become eligible to enroll an additional 23 patients. As of January 8, 2015, two of the cohorts had completed enrollment of stage one with ≥ 4 patients achieving disease control for ≥ 12 weeks. The remaining cohorts continue to enroll patients for stage one.

JAPAN

In November 2014, we reported data from a Phase 1 dose escalation study of VS-6063 as a single agent in Japanese subjects. The dose levels were 200, 400 or 600mg of VS-6063 BID. No dose limiting toxicities, or DLTs, or SAEs were observed at any dose cohort. All treatment emergent adverse events were generally mild or moderate in nature, or grade 1 or 2 as determined in accordance with commonly accepted terminology for adverse events, except for one subject in the 200mg BID cohort who exhibited an isolated Grade 3 increase in serum bilirubin, defined as between 3 and 10 times the value of the upper limit of the normal laboratory range. No associated increase in liver enzymes, AST or ALT, were observed in this subject.

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Data from the poster presented at the 2014 EORTC-NCI-AACR Symposium on Molecular Targets and Therapeutic are included in Figure 5 below.

Figure 5. Safety profile of VS-6063 in Japanese subjects

The study results showed that VS-6063 was generally well tolerated and side effects were consistent with previously reported results from our U.S. Phase 1 trial. One patient in the study had mesothelioma which had relapsed following frontline chemotherapy and was on VS-6063 for 5.6 months with best response of stable disease.

VS-4718

We are conducting a Phase 1, dose escalation clinical trial of our FAK inhibitor, VS-4718, in patients with advanced cancers. As of January 8, 2015, the Maximum Tolerated Dose (MTD) has not been reached. Three patients on the study have mesothelioma and two of these mesothelioma patients have had disease stabilization for at least five months.

VS-5584

We are conducting a Phase 1, dose escalation clinical trial of our dual mTORC1/2 and PI3K inhibitor, VS-5584, in patients with advanced cancers. As of January 8, 2015, the MTD has not been reached. Reductions in pharmacodynamic markers of PI3K and mTOR activity have been observed. Clinical activity has been observed in mesothelioma and other tumors. Disease control of at least six months has been observed in some patients. We have received orphan medicinal product designation from the European Commission for the use of VS-5584 in the treatment of mesothelioma. A Phase 1 clinical trial of VS-5584 in combination with VS-6063 for patients with relapsed mesothelioma is currently ongoing.

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Recent Developments

On December 20, 2013, we established an at-the-market equity offering program pursuant to which we are able to make sales of our common stock at then current market prices from time to time through Cantor Fitzgerald & Co., as sales agent. In the fourth quarter of 2014, we commenced sales under this program. To date, we have sold 1,623,339 shares of our common stock pursuant to this program and have received \$14.2 million, net of commissions paid.

We are currently finalizing our financial results for the fiscal year ended December 31, 2014. While complete financial information and operating data are not available, based on information currently available, we estimate that as of December 31, 2014 we had approximately \$92.7 million of cash and cash equivalents and investments available for sale, which includes approximately \$9.6 million of net proceeds from the sale of approximately 1.1 million shares of common stock under our at-the-market offering program. These preliminary estimates have been prepared by, and are the responsibility of, our management. Our independent registered public accounting firm, Ernst & Young LLP, has not audited or reviewed, and does not express an opinion with respect to, these estimates. Our actual cash and cash equivalents and investments available for sale as of December 31, 2014 may differ from these estimates due to the completion of our closing procedures with respect to the fiscal year ended December 31, 2014, final adjustments and other developments that may arise between now and the time the financial results for the fiscal year are finalized. We expect to complete our closing procedures with respect to the fiscal year ended December 31, 2014 after this offering is consummated. Accordingly, our consolidated financial statements as of and for the fiscal year ended December 31, 2014 will not be available until after this offering is completed.

Corporate information

We were incorporated under the laws of the State of Delaware in August 2010. We are headquartered in Needham, Massachusetts, and our principal offices are located at 117 Kendrick Street, Suite 500, Needham, Massachusetts and our telephone number is (781) 292-4200.

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THE OFFERING

| | |
|--|--|
| Common stock offered by us | Shares |
| Common stock to be outstanding after this offering | Shares |
| Use of proceeds | We intend to use the net proceeds from this offering as follows: for our registration-directed COMMAND study in mesothelioma and the initiation of associated studies in preparation for a possible NDA filing to the FDA and similar filings to other regulatory authorities; our other ongoing clinical trials with VS-6063, VS-4718 and VS-5584; and the balance, if any, for other general corporate purposes. |
| Risk factors | See "Risk Factors" beginning on page S-11 and other information included or incorporated by reference in this prospectus supplement and the accompanying prospectus for a discussion of factors you should carefully consider before deciding to invest in shares of our common stock. |
| Underwriters' option | The underwriters have an option for a period of 30 days to purchase additional shares of our common stock. |
| NASDAQ Global Market symbol | VSTM |
| The number of shares of our common stock to be outstanding after this offering as reflected above is based on 25,894,413 actual shares of our common stock outstanding as of September 30, 2014, including 15,995 shares of unvested restricted stock subject to repurchase by us. | |

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

4,224,858 shares of our common stock issuable upon the exercise of stock options outstanding as of September 30, 2014 at a weighted average price of \$10.36 per share;

572,441 shares of our common stock available for future issuance as of September 30, 2014 under our 2012 incentive plan, plus up to a maximum of 283,842 shares of our common stock subject to outstanding awards under our 2010 equity incentive plan that could expire, be terminated or otherwise be surrendered, cancelled, forfeited or repurchased, plus an additional 1,081,045 shares that became available on January 1, 2015 pursuant to the evergreen provision of our 2012 incentive plan;

314,694 shares of our common stock issuable pursuant to unvested restricted stock units outstanding as of September 30, 2014;

142,857 shares of our common stock issuable upon the exercise of an outstanding warrant, with an exercise price of \$17.16 per share; and

1,623,339 shares of our common stock issued to date pursuant to our at-the-market equity offering program since September 30, 2014.

The Longwood funds, entities affiliated with Christoph Westphal, our Executive Chairman and one of our directors, and Timothy Barberich, one of our directors, have indicated an interest in purchasing approximately \$8 million and \$250,000, respectively, in shares of our common stock in this offering at the public offering price. Assuming a public offering price of \$8.43 per share, which is the last reported sale price of our common stock on January 16, 2015, the Longwood funds and Mr. Barberich would purchase an aggregate of approximately 978,646 of the shares in this offering based on these indications of interest. However, because indications of interest are not binding agreements or commitments to purchase, the underwriters could determine to sell more, fewer or no shares to the Longwood funds and Mr. Barberich, and each of the Longwood funds and Mr. Barberich could determine to purchase more, fewer or no shares in this offering.

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RISK FACTORS

An investment in our common stock involves significant risks. For a discussion of the factors that you should carefully consider before deciding to purchase any of our common stock, please review the risk factors below and those included in the documents incorporated by reference in this prospectus supplement, including Item 1A. Risk Factors included in our Annual Report on Form 10-K for the year ended December 31, 2013. In addition, please read "Forward-Looking Statements" in this prospectus supplement, where we describe additional uncertainties associated with our business and the forward-looking statements included or incorporated by reference in this prospectus supplement and the accompanying prospectus. Please note that additional risks not currently known to us or that we currently deem immaterial may also impair our business and operations.

Additional Risks Related to This Offering

We may allocate the net proceeds from this offering in ways that you and other stockholders may not approve.

We currently intend to use the net proceeds of this offering for: our registration-directed COMMAND study in mesothelioma and the initiation of associated studies in preparation for a possible NDA filing to the FDA and similar filings to other regulatory authorities; our other ongoing clinical trials with VS-6063, VS-4718 and VS-5584; and the balance, if any, for other general corporate purposes. This expected use of the net proceeds from this offering represents our intentions based upon our current plans and business conditions. The amounts and timing of our actual expenditures may vary significantly depending on numerous factors, including the progress of our development efforts, the status of and results from clinical trials, as well as any collaborations that we may enter into with third parties for our product candidates, and any unforeseen cash needs. Because the number and variability of factors that will determine our use of the proceeds from this offering, their ultimate use may vary substantially from their currently intended use. As a result, our management will retain broad discretion over the allocation of the net proceeds from this offering and could spend the proceeds in ways that do not necessarily improve our operating results or enhance the value of our common stock. See "Use of Proceeds."

If you purchase our common stock in this offering, you will incur immediate and substantial dilution in the book value of your shares.

The public offering price of our common stock is substantially higher than the net tangible book value per share of our common stock. Therefore, if you purchase shares of our common stock in this offering, you will pay a price per share that substantially exceeds our net tangible book value per share after this offering. After giving effect to the sale of 4,744,958 shares of our common stock in this offering, assuming a public offering price of \$8.43 per share, which is the last reported sale price of our common stock on January 16, 2015, less the estimated underwriting discounts and commissions, and estimated offering expenses payable by us and based on a net tangible book value per share of our common stock of \$3.43 as of September 30, 2014, if you purchase shares in this offering, you will suffer immediate and substantial dilution of \$4.31 per share in the net tangible book value of common stock purchased. To the extent shares are issued under outstanding options, restricted stock units or the warrant issued to Encarta, Inc. or further sales are made pursuant to our controlled equity sales agreement with Cantor Fitzgerald & Co., you will incur further dilution. See "Dilution" for a more detailed description of the dilution to new investors in the offering.

Investors in this offering may experience future dilution.

In order to raise additional capital, we may in the future offer additional shares of our common stock or other securities convertible into, or exchangeable for, our common stock at prices that may not be the same as the price per share in this offering. We cannot assure you that we will be able to sell shares of our common stock or other related securities in any other offering at a price per share that is equal to or greater than the price per share paid by investors in this offering. If the price per share at which we sell additional shares of our common stock or related securities in future transactions is less than the price per share in

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this offering, investors who purchase our common stock in this offering will suffer a dilution in their investment.

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

Sales of a substantial number of shares of our common stock in the public market could occur at any time. These sales, or the perception in the market that the holders of a large number of shares intend to sell shares, could reduce the market price of our common stock.

Upon the completion of this offering, approximately 1,058,866 shares of our common stock beneficially owned by our officers and directors will be subject to lock-up agreements with the underwriters that prohibit, subject to certain exceptions, the disposal or pledge of, or the hedging against, any of their common stock or securities convertible into or exchangeable for shares of common stock for a period of 90 days after the date of this prospectus supplement. However, all of the shares sold in this offering and the remaining shares of our common stock outstanding prior to this offering will not be subject to lock-up agreements with the underwriters and, except to the extent such shares are held by our affiliates, will be freely tradable. In addition, the holders of a significant number of the shares outstanding, as of our initial public offering, have registration rights pursuant to which they may require us, upon request of holders of at least 30% of such shares, to register their securities for resale under the Securities Act of 1933 (including prior to the expiration of the 90-day lock up period referenced above). The market price of our common stock could decline as a result of sales by our stockholders in the market following completion of this offering or the perception that these sales could occur. These factors could also make it difficult for us to raise additional capital by selling stock.

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FORWARD-LOOKING STATEMENTS

This prospectus supplement, the accompanying prospectus and the other documents we have filed with the SEC that are incorporated by reference herein contain forward-looking statements that involve substantial risks and uncertainties. All statements, other than statements related to present facts or current conditions or of historical fact, contained in this prospectus supplement, the accompanying prospectus and the other documents we have filed with the SEC that are incorporated by reference herein, including statements regarding our strategy, future operations, future financial position, future revenues, projected costs, prospects, plans and objectives of management, are forward-looking statements. Such statements relate to, among other things, the development of our product candidates, including VS-6063, VS-4718 and VS-5584, and our FAK, PI3K/mTOR, Wnt and diagnostics programs generally, the timeline for clinical development and regulatory approval of our product candidates, the expected timing for the reporting of data from on-going trials and for the COMMAND interim analysis, the expected timing of completion of COMMAND enrollment, the structure of our planned or pending clinical trials, additional planned studies, our rights to develop or commercialize our product candidates and our ability to finance contemplated development activities and to fund operations for a specified period. The words "anticipate," "believe," "estimate," "expect," "intend," "may," "plan," "predict," "project," "target," "potential," "will," "would," "could," "should," "continue" and similar expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words.

Forward-looking statements are not guarantees of future performance and our actual results could differ materially from the results discussed in the forward-looking statements. Factors that could cause actual results to differ materially from those in the forward-looking statements include, but are not limited to, our ability to raise additional capital to support our clinical development programs and other operations, our ability to develop products of commercial value and to identify, discover and obtain rights to additional potential product candidates, our ability to protect and maintain our intellectual property and the ability of our licensors to obtain and maintain patent protection for the technology or products that we license from them, the fact that the preclinical and clinical testing of our product candidates and preliminary data from clinical trials may not be predictive of the results or success of ongoing or later clinical trials, that data may not be available when we expect it to be, that enrollment of clinical trials may take longer than expected, that our product candidates may cause unexpected safety events, that we will be unable to successfully initiate or complete the clinical development of our product candidates, including VS-6063, VS-4718, and VS-5584, that the development of our product candidates will take longer or cost more than planned, our reliance on third-parties, competitive developments, the effect of current and future legislation and regulation and regulatory actions, as well as other risks described in this prospectus supplement and under "Risk Factors" in our Annual Report on Form 10-K for the year ended December 31, 2013 incorporated by reference in this prospectus supplement.

As a result of these and other factors, we may not actually achieve the plans, intentions or expectations disclosed in our forward-looking statements, and you should not place undue reliance on our forward-looking statements. Our forward-looking statements do not reflect the potential impact of any future acquisitions, mergers, dispositions, joint ventures or investments we may make. We do not assume any obligation to update any forward-looking statements, whether as a result of new information, future events or otherwise, except as required by law.

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USE OF PROCEEDS

We estimate that the net proceeds we will receive from this offering will be approximately \$ _____ million, after deducting the estimated underwriting discounts and commissions and estimated offering expenses payable by us. If the underwriters exercise their option to purchase additional shares in full, we estimate that the net proceeds from this offering will be approximately \$ _____ million.

We intend to use the net proceeds from this offering to:

Continue the registration-directed COMMAND study in mesothelioma and initiate associated studies in preparation for a possible NDA filing to the FDA and similar filings to other regulatory authorities.

Continue our other ongoing clinical trials with VS-6063, VS-4718 and VS-5584.

We intend to use any remaining amounts for general corporate purposes.

We believe that the net proceeds from this offering, together with our existing cash and cash equivalents and investments, will be sufficient to fund our projected operating expenses and capital expenditures into 2017, allowing us to obtain the primary efficacy read-out of the COMMAND trial. Our expected use of the net proceeds from this offering represents our intentions based upon our current plans and business conditions. The amounts and timing of our actual expenditures may vary significantly depending on numerous factors, including the progress of our development efforts, the status of and results from clinical trials, as well as any collaborations that we may enter into with third parties for our product candidates, and any unforeseen cash needs. As a result, our management will retain broad discretion over the allocation of the net proceeds from this offering. We have no current understandings, agreements or commitments for any material acquisitions or licenses of any compounds, product candidates or technology.

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

Table of Contents**DILUTION**

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

Our historical net tangible book value as of September 30, 2014 was \$88.8 million, or \$3.43 per share of our common stock. Historical net tangible book value per share represents the amount of our total tangible assets less total liabilities, divided by 25,878,418 shares of our common stock outstanding, which excludes 15,995 shares of unvested restricted stock subject to repurchase by us.

After giving effect to the sale of 4,744,958 shares of common stock by us, assuming a public offering price of \$8.43 per share, which is the last reported sale price of our common stock on January 16, 2015, less the estimated underwriting discounts and commissions and estimated offering expenses payable by us, our pro forma net tangible book value as of September 30, 2014 would have been approximately \$126.3 million, or approximately \$4.12 per share. This represents an immediate increase in pro forma net tangible book value per share of \$0.69 to existing stockholders and immediate dilution of \$4.31 in pro forma net tangible book value per share to new investors purchasing common stock in this offering.

Dilution per share to new investors is determined by subtracting pro forma net tangible book value per share after this offering from the assumed public offering price per share paid by new investors. The following table illustrates this dilution on a per share basis.

| | | |
|---|----|------|
| Assumed public offering price per share | \$ | 8.43 |
| Net tangible book value per share as of September 30, 2014 | \$ | 3.43 |
| Increase in net tangible book value per share attributable to new investors | \$ | 0.69 |
| | | |
| Pro forma net tangible book value per share after this offering | \$ | 4.12 |
| | | |
| Dilution per share to new investors | \$ | 4.31 |

The number of shares of our common stock to be outstanding upon completion of this offering as reflected in the foregoing dilution calculations excludes:

4,224,858 shares of our common stock issuable upon the exercise of stock options outstanding as of September 30, 2014 at a weighted average price of \$10.36 per share;

572,441 shares of our common stock available for future issuance as of September 30, 2014 under our 2012 incentive plan, plus up to a maximum of 283,842 shares of our common stock subject to outstanding awards under our 2010 equity incentive plan that could expire, be terminated or otherwise be surrendered, cancelled, forfeited or repurchased, plus an additional 1,081,045 shares that became available on January 1, 2015 pursuant to the evergreen provision of our 2012 incentive plan;

314,694 shares of our common stock issuable pursuant to unvested restricted stock units outstanding as of September 30, 2014;

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142,857 shares of our common stock issuable upon the exercise of an outstanding warrant, with an exercise price of \$17.16 per share; and

1,623,339 shares of our common stock issued to date pursuant to our at-the-market equity offering program since September 30, 2014.

If the underwriters exercise their option to purchase additional shares or if any additional shares are issued in connection with the above transactions, you will experience further dilution.

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UNDERWRITING

Subject to the terms and conditions set forth in the Underwriting Agreement, dated January _____, 2015, between us and Jefferies LLC and Leerink Partners LLC, as the representatives of the underwriters named below and the joint book-running managers of this offering, we have agreed to sell to the underwriters, and each of the underwriters has agreed, severally and not jointly, to purchase from us, the respective number of shares of common stock shown opposite its name below:

| Underwriter | Number of Shares |
|----------------------------|---------------------------------|
| Jefferies LLC | |
| Leerink Partners LLC | |
| Guggenheim Securities, LLC | |
| Oppenheimer & Co. Inc. | |
| Total | |

The Underwriting Agreement provides that the obligations of the several underwriters are subject to certain conditions precedent such as the receipt by the underwriters of officers' certificates and legal opinions and approval of certain legal matters by their counsel. The Underwriting Agreement provides that the underwriters will purchase all of the shares of common stock if any of them are purchased. If an underwriter defaults, the Underwriting Agreement provides that the purchase commitments of the nondefaulting underwriters may be increased or the Underwriting Agreement may be terminated. We have agreed to indemnify the underwriters and certain of their controlling persons against certain liabilities, including liabilities under the Securities Act, and to contribute to payments that the underwriters may be required to make in respect of those liabilities.

The underwriters have advised us that, following the completion of this offering, they currently intend to make a market in the common stock as permitted by applicable laws and regulations. However, the underwriters are not obligated to do so, and the underwriters may discontinue any market-making activities at any time without notice in their sole discretion. Accordingly, no assurance can be given as to the liquidity of the trading market for the common stock, that you will be able to sell any of the common stock held by you at a particular time or that the prices that you receive when you sell will be favorable.

The underwriters are offering the shares of common stock subject to their acceptance of the shares of common stock from us and subject to prior sale. The underwriters reserve the right to withdraw, cancel or modify offers to the public and to reject orders in whole or in part.

The Longwood funds, entities affiliated with Christoph Westphal, our Executive Chairman and one of our directors, and Timothy Barberich, one of our directors, have indicated an interest in purchasing approximately \$8 million and \$250,000, respectively, in shares of our common stock in this offering at the public offering price. However, because indications of interest are not binding agreements or commitments to purchase, the underwriters could determine to sell more, fewer or no shares to the Longwood funds and Mr. Barberich, and each of the Longwood funds and Mr. Barberich could determine to purchase more, fewer or no shares in this offering.

Table of Contents**Commission and Expenses**

The underwriters have advised us that they propose to offer the shares of common stock to the public at the public offering price set forth on the cover page of this prospectus supplement and to certain dealers, which may include the underwriters, at that price less a concession not in excess of \$ _____ per share of common stock. After the offering, the public offering price, concession and reallowance to dealers may be reduced by the representatives. No such reduction will change the amount of proceeds to be received by us as set forth on the cover page of this prospectus supplement.

The underwriting fee is equal to the public offering price per share of common stock less the amount paid by the underwriters to us per share of common stock. The underwriting fee is \$ _____ per share. The following table shows the public offering price, the underwriting discounts and commissions that we are to pay the underwriters and the proceeds, after expenses, to us in connection with this offering. Such amounts are shown assuming both no exercise and full exercise of the underwriters' option to purchase additional shares.

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

We estimate our expenses in connection with this offering, other than the underwriting discounts and commissions referred to above, will be approximately \$150,000, including up to \$10,000 for certain expenses relating to clearance of this offering with the Financial Industry Regulatory Authority that we have agreed to pay.

Listing

Our common stock is listed on The NASDAQ Global Market under the trading symbol "VSTM".

Option to Purchase Additional Shares

We have granted to the underwriters an option, exercisable for 30 days from the date of this prospectus supplement, to purchase, from time to time, in whole or in part, up to an aggregate of _____ additional shares of common stock from us at the public offering price set forth on the cover page of this prospectus supplement, less underwriting discounts and commissions. If the underwriters exercise this option, each underwriter will be obligated, subject to specified conditions, to purchase a number of additional shares of common stock proportionate to that underwriter's initial purchase commitment as indicated in the table above.

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No Sales of Similar Securities

We, our executive officers and directors have agreed, subject to specified exceptions, not to directly or indirectly:

sell, offer, contract or grant any option to sell (including any short sale), pledge, transfer, establish an open "put equivalent position" within the meaning of Rule 16a-1(h) under the Securities Exchange Act of 1934, as amended, or

otherwise dispose of any shares of common stock, options or warrants to acquire shares of common stock, or securities exchangeable or exercisable for or convertible into shares of common stock currently or hereafter owned either of record or beneficially, or

publicly announce an intention to do any of the foregoing for a period of 90 days after the date of this prospectus supplement without the prior written consent of the representatives.

These restrictions terminate after the close of trading of the common stock on and including the 90th day after the date of this prospectus supplement.

The representatives may, in their sole discretion and at any time or from time to time before the termination of the 90-day period, release all or any portion of the securities subject to lock-up agreements. There are no existing agreements between the underwriters and any of our shareholders who will execute a lock-up agreement, providing consent to the sale of shares prior to the expiration of the lock-up period.

Not all of our shares of common stock outstanding prior to this offering will be subject to the lock-up agreements described above. In addition, certain holders of our common stock have registration rights pursuant to which they may request that we register their securities for resale under the Securities Act of 1933 (including prior to the expiration of the 90-day lock-up period). See "Risk Factors A significant portion of our total outstanding shares may be sold into the market at any time, which could cause the market price of our common stock to drop significantly, even if our business is doing well."

Stabilization

The underwriters have advised us that, pursuant to Regulation M under the Securities Exchange Act of 1934, as amended, certain persons participating in the offering may engage in short sale transactions, stabilizing transactions, syndicate covering transactions or the imposition of penalty bids in connection with this offering. These activities may have the effect of stabilizing or maintaining the market price of the common stock at a level above that which might otherwise prevail in the open market. Establishing short sales positions may involve either "covered" short sales or "naked" short sales.

"Covered" short sales are sales made in an amount not greater than the underwriters' option to purchase additional shares of our common stock in this offering. The underwriters may close out any covered short position by either exercising their option to purchase additional shares of our common stock or purchasing shares of our common stock in the open market. In determining the source of shares to close out the covered short position, the underwriters will consider, among other things, the price of shares of common stock available for purchase in the open market as compared to the price at which they may purchase shares through the option to purchase additional shares.

"Naked" short sales are sales in excess of the option to purchase additional shares of our common stock. The underwriters must close out any naked short position by purchasing shares in the open market. A naked short position is more likely to be created if the underwriters are concerned that there may be downward pressure on the price of the shares of our common stock in the open market after pricing that could adversely affect investors who purchase in this offering.

A stabilizing bid is a bid for the purchase of shares of common stock on behalf of the underwriters for the purpose of fixing or maintaining the price of the common stock. A syndicate covering transaction is the bid for or the purchase of shares of common stock on behalf of the underwriters to reduce a short position

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incurred by the underwriters in connection with the offering. Similar to other purchase transactions, the underwriters' purchases to cover the syndicate short sales may have the effect of raising or maintaining the market price of our common stock or preventing or retarding a decline in the market price of our common stock. As a result, the price of our common stock may be higher than the price that might otherwise exist in the open market. A penalty bid is an arrangement permitting the underwriters to reclaim the selling concession otherwise accruing to a syndicate member in connection with the offering if the common stock originally sold by such syndicate member are purchased in a syndicate covering transaction and therefore have not been effectively placed by such syndicate member.

Neither we, nor any of the underwriters make any representation or prediction as to the direction or magnitude of any effect that the transactions described above may have on the price of our common stock. The underwriters are not obligated to engage in these activities and, if commenced, any of the activities may be discontinued at any time.

The underwriters may also engage in passive market-making transactions in our common stock on The NASDAQ Global Market in accordance with Rule 103 of Regulation M during a period before the commencement of offers or sales of shares of our common stock in this offering and extending through the completion of distribution. A passive market maker must display its bid at a price not in excess of the highest independent bid of that security. However, if all independent bids are lowered below the passive market maker's bid, that bid must then be lowered when specified purchase limits are exceeded.

Electronic Distribution

This prospectus supplement and the accompanying prospectus in electronic format may be made available by e-mail or on the web sites or through online services maintained by one or more of the underwriters or their affiliates. In those cases, prospective investors may view offering terms online and may be allowed to place orders online. The underwriters may agree with us to allocate a specific number of shares of common stock for sale to online brokerage account holders. Any such allocation for online distributions will be made by the underwriters on the same basis as other allocations. Other than this prospectus supplement and the accompanying prospectus in electronic format, the information on the underwriters' web sites and any information contained in any other web site maintained by any of the underwriters is not part of this prospectus supplement or the accompanying prospectus, has not been approved and/or endorsed by us or the underwriters and should not be relied upon by investors.

Other Activities and Relationships

The underwriters and certain of their affiliates are full service financial institutions engaged in various activities, which may include securities trading, commercial and investment banking, financial advisory, investment management, investment research, principal investment, hedging, financing and brokerage activities. The underwriters and certain of their affiliates have, from time to time, performed, and may in the future perform, various commercial and investment banking and financial advisory services for us and our affiliates, for which they received or will receive customary fees and expenses.

In the ordinary course of their various business activities, the underwriters and certain of their affiliates may make or hold a broad array of investments and actively traded debt and equity securities (or related derivative securities) and financial instruments (including bank loans) for their own account and for the accounts of their customers, and such investment and securities activities may involve securities and/or instruments issued by us and our affiliates. The underwriters and certain of their respective affiliates may also communicate independent investment recommendations, market color or trading ideas and/or publish or express independent research views in respect of such securities or instruments and may at any time hold, or recommend to clients that they acquire, long and/or short positions in such securities and instruments.

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NOTICE TO INVESTORS

Australia

This prospectus supplement is not a disclosure document for the purposes of Australia's Corporations Act 2001 (Cth) of Australia, or Corporations Act, has not been lodged with the Australian Securities & Investments Commission and is only directed to the categories of exempt persons set out below. Accordingly, if you receive this prospectus supplement in Australia:

A.

You confirm and warrant that you are either:

a "sophisticated investor" under section 708(8)(a) or (b) of the Corporations Act;

a "sophisticated investor" under section 708(8)(c) or (d) of the Corporations Act and that you have provided an accountant's certificate to the company which complies with the requirements of section 708(8)(c)(i) or (ii) of the Corporations Act and related regulations before the offer has been made; or

a "professional investor" within the meaning of section 708(11)(a) or (b) of the Corporations Act.

To the extent that you are unable to confirm or warrant that you are an exempt sophisticated investor or professional investor under the Corporations Act, any offer made to you under this prospectus supplement is void and incapable of acceptance.

B.

You warrant and agree that you will not offer any of the shares issued to you pursuant to this prospectus supplement for resale in Australia within 12 months of those shares being issued unless any such resale offer is exempt from the requirement to issue a disclosure document under section 708 of the Corporations Act.

European Economic Area

In relation to each Member State of the European Economic Area which has implemented the Prospectus Directive (each, a "Relevant Member State"), an offer to the public of any Ordinary Shares may not be made in that Relevant Member State, except that the Ordinary Shares may be offered to the public in that Relevant Member State at any time under the following exemptions under the Prospectus Directive, if it has been implemented in that Relevant Member State:

a)

to legal entities which are "qualified investors" as defined in the Prospectus Directive;

b)

to fewer than 100, or, if the Relevant Member State has implemented the relevant provisions of the 2010 PD Amending Directive, 150, natural or legal persons (other than "qualified investors" as defined in the Prospectus Directive) as permitted under the Prospectus Directive; or

c)

in any other circumstances falling within Article 3(2) of the Prospectus Directive,

provided that no such offer of Ordinary Shares shall result in a requirement for, the publication by the Company or either of the Joint Sponsors of a Prospectus pursuant to Article 3 of the Prospectus Directive, or supplementing a Prospectus pursuant to Article 16 of the Prospectus Directive, and each person who initially acquires Ordinary Shares or to whom any offer is made will be deemed to have represented, warranted to and agreed with the Joint Sponsors and the Company that it is a "qualified investor" within the meaning of the law in that Relevant Member State implementing Article 2(1)(e) of the Prospectus Directive.

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For the purposes of this provision, the expression an "offer to the public" in relation to any Ordinary Shares in any Relevant Member State means the communication in any form and by any means of sufficient information on the terms of the offer and the Ordinary Shares to be offered so as to enable an investor to decide to purchase any Ordinary Shares, as the same may be varied in that Member State by any measure

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implementing the Prospectus Directive in that Member State and the expression "Prospectus Directive" means Directive 2003/71/EC (and amendments thereto, including the 2010 PD Amending Directive, to the extent implemented in the Relevant Member State) and includes any relevant implementing measure in each Relevant Member State and the expression "2010 PD Amending Directive" means Directive 2010/73/EU.

Hong Kong

No securities have been offered or sold, and no securities may be offered or sold, in Hong Kong, by means of any document, other than to persons whose ordinary business is to buy or sell shares or debentures, whether as principal or agent; or to "professional investors" as defined in the Securities and Futures Ordinance (Cap. 571) of Hong Kong and any rules made under that Ordinance; or in other circumstances which do not result in the document being a "prospectus" as defined in the Companies Ordinance (Cap. 32) of Hong Kong or which do not constitute an offer to the public within the meaning of the Companies Ordinance (Cap. 32) of Hong Kong. No document, invitation or advertisement relating to the securities has been issued or may be issued or may be in the possession of any person for the purpose of issue (in each case whether in Hong Kong or elsewhere), which is directed at, or the contents of which are likely to be accessed or read by, the public of Hong Kong (except if permitted under the securities laws of Hong Kong) other than with respect to securities which are or are intended to be disposed of only to persons outside Hong Kong or only to "professional investors" as defined in the Securities and Futures Ordinance (Cap. 571) of Hong Kong and any rules made under that Ordinance.

This prospectus supplement has not been registered with the Registrar of Companies in Hong Kong. Accordingly, this prospectus supplement may not be issued, circulated or distributed in Hong Kong, and the securities may not be offered for subscription to members of the public in Hong Kong. Each person acquiring the securities will be required, and is deemed by the acquisition of the securities, to confirm that he is aware of the restriction on offers of the securities described in this prospectus supplement and the relevant offering documents and that he is not acquiring, and has not been offered any securities in circumstances that contravene any such restrictions.

Japan

The offering has not been and will not be registered under the Financial Instruments and Exchange Law of Japan (Law No. 25 of 1948 of Japan, as amended), or FIEL, and the underwriters will not offer or sell any securities, directly or indirectly, in Japan or to, or for the benefit of, any resident of Japan (which term as used herein means, unless otherwise provided herein, any person resident in Japan, including any corporation or other entity organized under the laws of Japan), or to others for re-offering or resale, directly or indirectly, in Japan or to a resident of Japan, except pursuant to an exemption from the registration requirements of, and otherwise in compliance with, the FIEL and any other applicable laws, regulations and ministerial guidelines of Japan.

Singapore

This prospectus supplement has not been and will not be lodged or registered with the Monetary Authority of Singapore. Accordingly, this prospectus supplement and any other document or material in connection with the offer or sale, or the invitation for subscription or purchase of the securities may not be issued, circulated or distributed, nor may the securities be offered or sold, or be made the subject of an invitation for subscription or purchase, whether directly or indirectly, to the public or any member of the public in Singapore other than (i) to an institutional investor under Section 274 of the Securities and Futures Act, Chapter 289 of Singapore, or the SFA, (ii) to a relevant person as defined under Section 275(2), or any person pursuant to Section 275(1A) of the SFA, and in accordance with the conditions, specified in Section 275 of the SFA, or (iii) otherwise pursuant to, and in accordance with the conditions of any other

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applicable provision of the SFA. Where the securities are subscribed or purchased under Section 275 of the SFA by a relevant person which is:

- a) a corporation (which is not an accredited investor as defined under Section 4A of the SFA) the sole business of which is to hold investments and the entire share capital of which is owned by one or more individuals, each of whom is an accredited investor; or
- b) a trust (where the trustee is not an accredited investor) whose sole purpose is to hold investments and each beneficiary is an accredited investor, shares, debentures and units of shares and debentures of that corporation or the beneficiaries' rights and interest in that trust shall not be transferable for six months after that corporation or that trust has acquired such securities under Section 275 of the SFA except:
 - i) to an institutional investor under Section 274 of the SFA or to a relevant person defined in Section 275(2) of the SFA, or to any person pursuant to an offer that is made on terms that such shares, debentures and units of shares and debentures of that corporation or such rights and interest in that trust are acquired at a consideration of not less than \$200,000 (or its equivalent in a foreign currency) for each transaction, whether such amount is to be paid for in cash or by exchange of securities or other assets, and further for corporations, in accordance with the conditions, specified in Section 275 of the SFA;
 - ii) where no consideration is given for the transfer; or
 - iii) where the transfer is by operation of law.

Switzerland

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

Neither this prospectus supplement nor any other offering or marketing material relating to the offering, the Company or the securities have been or will be filed with or approved by any Swiss regulatory authority. In particular, this prospectus supplement will not be filed with, and the offer of securities will not be supervised by, the Swiss Financial Market Supervisory Authority, or FINMA, and the offer of securities has not been and will not be authorized under the Swiss Federal Act on Collective Investment Schemes, or CISA. The investor protection afforded to acquirers of interests in collective investment schemes under the CISA does not extend to acquirers of securities.

United Kingdom

This prospectus supplement is only being distributed to, and is only directed at, persons in the United Kingdom that are qualified investors within the meaning of Article 2(1)(e) of the Prospectus Directive that are also (i) investment professionals falling within Article 19(5) of the Financial Services and Markets Act 2000 (Financial Promotion) Order 2005, as amended, which is referred to as the Order, and/or (ii) high net worth entities falling within Article 49(2)(a) to (d) of the Order and other persons to whom it may lawfully be communicated, each such person being referred to as a relevant person.

This prospectus supplement and its contents are confidential and should not be distributed, published or reproduced (in whole or in part) or disclosed by recipients to any other persons in the United Kingdom. Any person in the United Kingdom that is not a relevant person should not act or rely on this document or any of its contents.

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**MATERIAL UNITED STATES FEDERAL INCOME AND ESTATE TAX CONSIDERATIONS
FOR NON-U.S. HOLDERS OF SHARES OF OUR COMMON STOCK**

The following is a summary of certain material United States federal income and estate tax considerations relating to the purchase, ownership, and disposition of shares of our common stock by a non-U.S. holder (as defined below) that acquires our common stock in this offering and holds it as a capital asset within the meaning of Section 1221 of the Internal Revenue Code of 1986, as amended (the "Code"). For purposes of this summary, a "non-U.S. holder" is a beneficial owner of our common stock that, for United States federal income tax purposes, is an individual, corporation, estate or trust other than:

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

a corporation, or any other organization taxable as a corporation for United States federal income tax purposes, that is created or organized under the laws of the United States, any state thereof, or the District of Columbia;

an estate the income of which is subject to United States federal income taxation regardless of its source; or

a trust if (1) a court within the United States is able to exercise primary supervision over the trust's administration and one or more United States persons (as defined in the Code) have the authority to control all substantial decisions of that trust, or (2) the trust has in effect a valid election under the applicable Treasury regulations to be treated as a United States person.

A modified definition of "non-U.S. holder" applies for United States federal estate tax purposes (as discussed below).

This summary is based upon the Code, Treasury regulations promulgated or proposed thereunder, judicial decisions, rulings, and administrative interpretations thereof, all as of the date hereof and all of which are subject to change, possibly with retroactive effect. The foregoing are subject to differing interpretations which could affect the tax consequences described herein. This summary does not purport to be a complete analysis of all the potential tax considerations relevant to non-U.S. holders of our common stock. In addition, this summary does not address all aspects of United States federal income and estate taxation that may be applicable to non-U.S. holders in light of their particular circumstances or status, nor does it address specific tax considerations that may be relevant to particular persons (including, for example, financial institutions, broker-dealers, insurance companies, partnerships or other pass-through entities, certain United States expatriates, tax-exempt organizations, pension plans, "controlled foreign corporations," "passive foreign investment companies," corporations that accumulate earnings to avoid United States federal income tax, persons in special situations, such as those who have elected to mark securities to market or those who hold shares of our common stock as part of a straddle, hedge, conversion transaction, synthetic security or other integrated investment, persons that have a "functional currency" other than the U.S. dollar, or holders subject to the alternative minimum tax or the unearned income Medicare contribution tax). In addition, except as explicitly addressed herein with respect to estate tax, this summary does not address certain estate and any gift tax considerations or considerations under the tax laws of any state, local or non-United States jurisdiction.

If a partnership (including any entity or arrangement treated as a partnership for United States federal income tax purposes) owns our common stock, the tax treatment of a person treated as a partner in the partnership for United States federal income tax purposes generally will depend upon the status of the partner and the activities of the partnership. Partnerships and other entities that are treated as partnerships for United States federal income tax purposes and persons holding our common stock through a partnership or other entity treated as a partnership for United States federal income tax purposes should consult their tax advisors.

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There can be no assurance that the Internal Revenue Service ("IRS") will not challenge one or more of the tax consequences described herein, and we have not obtained, nor do we intend to obtain, a ruling from the IRS or an opinion of counsel with respect to the United States federal income or estate tax consequences to a non-U.S. holder of the purchase, ownership or disposition of our common stock.

THIS SUMMARY IS FOR GENERAL INFORMATION ONLY AND IS NOT INTENDED TO BE TAX ADVICE. YOU ARE URGED TO CONSULT YOUR TAX ADVISOR REGARDING THE UNITED STATES FEDERAL INCOME AND ESTATE TAXATION, STATE, LOCAL, AND NON-UNITED STATES TAXATION AND OTHER TAX CONSEQUENCES OF THE PURCHASE, OWNERSHIP, AND DISPOSITION OF OUR COMMON STOCK, INCLUDING THE CONSEQUENCES UNDER ANY APPLICABLE TAX TREATY.

Distributions on our shares of our common stock

We do not currently expect to pay dividends. In the event we do make a distribution of cash or property with respect to our common stock, any such distributions generally will constitute dividends for United States federal income tax purposes to the extent of our current or accumulated earnings and profits, as determined under United States federal income tax principles, and will be subject to withholding as described in the next paragraph below. If a distribution exceeds our current and accumulated earnings and profits, the excess will be treated as a tax-free return of the non-U.S. holder's investment, up to such holder's adjusted tax basis in shares of our common stock. Any remaining excess will be treated as capital gain, subject to the tax treatment described below in "Gain on Sale, exchange or other taxable disposition of our common stock." Any distribution described in this paragraph would also be subject to the discussion below in "Additional withholding and reporting requirements."

Any dividends paid to a non-U.S. holder with respect to shares of our common stock generally will be subject to withholding of United States federal tax at a 30% rate unless such non-U.S. holder provides us or our agent, as the case may be, with the appropriate IRS Form W-8 prior to the payment of dividends, such as:

IRS Form W-8BEN or W-8BEN-E, as applicable (or successor form), certifying, under penalties of perjury, that such non-U.S. holder is entitled to a reduction in withholding under an applicable income tax treaty, or

IRS Form W-8ECI (or successor form) certifying, under penalties of perjury that a dividend paid on our common stock is not subject to withholding tax because it is effectively connected with the conduct of a trade or business in the United States of the non-U.S. holder (and, if required by an applicable income tax treaty, is attributable to a permanent establishment or fixed base maintained in the U.S.) (in which case such dividend generally will be subject to graduated United States federal income tax rates on a net income basis as described below).

The certification requirement described above also may require a non-U.S. holder that provides an IRS form or that claims treaty benefits to provide its United States taxpayer identification number.

Each non-U.S. holder is urged to consult its own tax advisor about the specific methods for satisfying these requirements. A claim for exemption will not be valid if the person receiving the applicable form has actual knowledge or reason to know that the statements on the form are false.

If dividends are "effectively connected" with the conduct of a trade or business in the United States of a non-U.S. holder (and, if required by an applicable income tax treaty, are attributable to a permanent establishment or fixed base maintained by such non-U.S. holder in the United States), the non-U.S. holder, although exempt from the withholding tax described above (provided that the certifications described above are satisfied), will generally be subject to United States federal income tax on such dividends on a net income basis in the same manner as if it were a resident of the United States. In addition, if the non-U.S. holder is taxable as a corporation for United States federal income tax purposes, such holder may, under

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certain circumstances, be subject to an additional "branch profits tax" equal to 30% (unless reduced by an applicable income tax treaty) of its effectively connected earnings and profits for the taxable year.

If a non-U.S. holder is eligible for a reduced rate of United States federal withholding tax pursuant to an applicable income tax treaty, such holder may obtain a refund or credit of any amounts withheld in excess of that rate by timely filing an appropriate refund claim with the IRS.

Gain on sale, exchange or other taxable disposition of shares of our common stock

Subject to the discussion below under "Additional withholding and reporting requirements," a non-U.S. holder generally will not be subject to United States federal income tax or withholding tax on gain realized upon a sale, exchange or other taxable disposition of shares of our common stock (including a redemption, but only if the redemption would be treated as a sale or exchange rather than a distribution for United States federal income tax purposes) unless:

- (1) the gain is "effectively connected" with the conduct of a trade or business of the non-U.S. holder in the United States (and, if required by an applicable income tax treaty, the gain is attributable to a permanent establishment or fixed base maintained in the United States);
- (2) the non-U.S. holder is an individual who is present in the United States for 183 or more days in the taxable year of the disposition and meets certain other conditions; or
- (3) we are or have been a "United States real property holding corporation" ("USRPHC") for United States federal income tax purposes at any time within the shorter of the five-year period preceding the disposition and the non-U.S. holder's holding period for our common stock (the "relevant period").

If the first exception applies, the non-U.S. holder generally will be subject to United States federal income tax on a net income basis with respect to such gain in the same manner as if such holder were a resident of the United States. In addition, if the non-U.S. holder is a corporation for United States federal income tax purposes, such gains may, under certain circumstances, also be subject to an additional "branch profits tax" at a 30% rate (or at a lower rate under an applicable income tax treaty).

If the second exception applies, the non-U.S. holder generally will be subject to United States federal income tax at a rate of 30% (unless an applicable income tax treaty provides otherwise) on the amount by which such non-U.S. holder's capital gains allocable to United States sources exceed capital losses allocable to United States sources during the taxable year of the disposition.

With respect to the third exception above, although there can be no assurances, we believe we currently are not, and we do not anticipate becoming, a USRPHC for United States federal income tax purposes. However, because the determination of whether we are a USRPHC depends on the fair market value of our United States real property interests relative to the fair market value of our other trade or business assets and our foreign real property interests, there can be no assurance that we will not become a USRPHC in the future. Generally, a corporation is a USRPHC only if the fair market value of its United States real property interests (as defined in the Code) equals or exceeds 50% of the sum of the fair market value of its worldwide real property interests plus its other assets used or held for use in a trade or business. Even if we are or become a USRPHC, a non-U.S. holder would not be subject to U.S. federal income tax on a sale, exchange or other taxable disposition of our common stock by reason of our status as a USRPHC so long as (i) our common stock continues to be regularly traded on an established securities market (within the meaning of Section 897(c)(3) of the Code) during the calendar year in which such disposition occurs and (ii) such non-U.S. holder does not own and is not deemed to own (directly, indirectly or constructively) more than 5% of our common stock at any time during the relevant period. If we are a USRPHC and the requirements of (i) or (ii) are not met, gain on the disposition of shares of our common stock generally will be taxed in the same manner as gain that is effectively connected with the conduct of a U.S. trade or business, except that the "branch profits tax" will not apply.

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Additional withholding and reporting requirements

Legislation (commonly referred to as "FATCA") imposes United States federal withholding at a rate of 30% on payments to certain non-U.S. entities (including financial intermediaries), including dividends on and the gross proceeds from dispositions of our common stock, unless various information reporting and due diligence requirements, which are different from and in addition to the certification requirements described elsewhere in this discussion, have been satisfied (generally relating to ownership by U.S. persons of interests in or accounts with those entities). The withholding rules applicable to payments of dividends on our common stock apply beginning July 1, 2014. The withholding rules will apply to gross proceeds from dispositions of our common stock beginning January 1, 2017. Although Treasury regulations implementing FATCA have been finalized, certain aspects of these rules remain unclear and subject to change. An intergovernmental agreement between the United States and a foreign country where a holder or intermediary is located may modify the requirements in this paragraph. Non-U.S. holders should consult their tax advisors regarding the possible implications of FATCA on their investment in our common stock.

Information reporting and backup withholding

We must report annually to the IRS and to each non-U.S. holder the gross amount of the distributions on our common stock paid to such holder and the tax withheld, if any, with respect to such distributions, regardless of whether withholding was required. A non-U.S. holder will generally be subject to backup withholding on dividends paid to such holder unless such holder furnishes a valid IRS Form W-8BEN or W-8BEN-E, as applicable (or such other applicable form and documentation as required by the Code or the Treasury regulations), certifying under penalties of perjury that it is a non-U.S. holder (and the payor does not have actual knowledge or reason to know that such holder is a United States person as defined under the Code), or such holder otherwise establishes an exemption. Dividends paid to non-U.S. holders subject to the United States federal withholding tax, as described above in "Distributions on shares of our common stock," generally will be exempt from U.S. backup withholding.

Information reporting and, depending on the circumstances, backup withholding will apply to the payment of the proceeds of a sale or other disposition of shares of our common stock by a non-U.S. holder effected by or through the United States office of any broker, United States or foreign, unless the holder certifies that it is not a United States person (as defined under the Code) and satisfies certain other requirements, or otherwise establishes an exemption. Generally, information reporting and backup withholding will not apply to a payment of disposition proceeds to a non-U.S. holder where the transaction is effected outside the United States through a non-United States office of a broker. However, for information reporting purposes, dispositions effected through a non-United States office of a broker with substantial United States ownership or operations generally will be treated in a manner similar to dispositions effected through a United States office of a broker. Prospective investors should consult their own tax advisors regarding the application of the information reporting and backup withholding rules to them.

Copies of the information returns may be made available to the tax authorities in the country in which the non-U.S. holder resides or is incorporated under the provisions of an applicable treaty or agreement.

Backup withholding is not an additional tax. Any amounts withheld under the backup withholding rules may be allowed as a credit against a non-U.S. holder's United States federal income tax liability, if any, and may entitle such holder to a refund, provided that an appropriate claim is timely filed with the IRS.

Federal estate taxes

Shares of our common stock held (or treated as held) by an individual who is not a United States citizen or resident (as specifically determined for United States federal estate tax purposes) at the time of such individual's death generally will be included in the holder's gross estate for United States federal estate tax purposes, unless an applicable estate tax or other treaty provides otherwise, and, therefore, may be subject to United States federal estate tax.

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INCORPORATION OF CERTAIN DOCUMENTS BY REFERENCE

The SEC allows us to "incorporate by reference" into this prospectus supplement the information we file with it, which means that we can disclose important information to you by referring you to those documents. The information incorporated by reference is considered to be part of this prospectus supplement, and information in documents that we file later with the SEC will automatically update and supersede information in this prospectus supplement. We incorporate by reference into this prospectus supplement the documents listed below and any future filings made by us with the SEC under Section 13(a), 13(c), 14 or 15(d) of the Exchange Act, except for information "furnished" under Items 2.02, 7.01 or 9.01 on Form 8-K or other information "furnished" to the SEC which is not deemed filed and not incorporated in this prospectus supplement, until the termination of the offering of securities described in the applicable prospectus supplement. We hereby incorporate by reference the following documents:

Our Annual Report on Form 10-K for the year ended December 31, 2013, as filed with the SEC on March 6, 2014;

Our Quarterly Reports on Form 10-Q for the quarterly period ended March 31, 2014, as filed with the SEC on May 8, 2014, the quarterly period ended June 30, 2014, as filed with the SEC on August 7, 2014, and the quarterly period ended September 30, 2014, as filed with the SEC on October 30, 2014;

Our Definitive Proxy Statement on Schedule 14A, filed with the SEC on April 7, 2014, (excluding those portions that are not incorporated by reference into our Annual Report on Form 10-K for the year ended December 31, 2013);

Our Current Reports on Form 8-K filed with the SEC on February 25, 2014, March 11, 2014, April 18, 2014, May 8, 2014, May 12, 2014, September 16, 2014, December 18, 2014 and January 8, 2015; and

Description of our common stock, which is contained in the Registration Statement on Form 8-A, as filed with the SEC on January 23, 2012, as supplemented by the Description of Common Stock found on page 9 of the accompanying prospectus and including any amendments or reports filed for the purpose of updating such description.

You may request a copy of these filings, at no cost, by writing or telephoning us at the following address:

Investor Relations
Verastem, Inc.
117 Kendrick Street, Suite 500
Needham, Massachusetts 02494
(781) 292-4200

Copies of these filings are also available, without charge, on the SEC's website at www.sec.gov and on our website at www.verastem.com as soon as reasonably practicable after they are filed electronically with the SEC. The information contained on our website is not a part of this prospectus supplement.

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LEGAL MATTERS

The validity of the shares of common stock offered hereby is being passed upon for us by Ropes & Gray LLP, Boston, Massachusetts. Gibson, Dunn & Crutcher LLP, New York, New York will pass upon certain legal matters relating to this offering for the underwriters.

EXPERTS

The consolidated financial statements of Verastem, Inc. appearing in Verastem, Inc.'s Annual Report on Form 10-K for the year ended December 31, 2013 have been audited by Ernst & Young LLP, independent registered public accounting firm, as set forth in their report thereon, included therein, and incorporated herein by reference. Such consolidated financial statements are incorporated herein by reference in reliance upon such report given on the authority of such firm as experts in accounting and auditing.

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PROSPECTUS

\$150,000,000

**Common Stock
Preferred Stock
Warrants
Debt Securities**

We may offer and sell from time to time, in one or more series or issuances and on terms that we will determine at the time of the offering, any combination of the securities described in this prospectus, up to an aggregate amount of \$150,000,000.

We will provide specific terms of any offering in a supplement to this prospectus. Any prospectus supplement may also add, update, or change information contained in this prospectus. You should carefully read this prospectus and the applicable prospectus supplement as well as the documents incorporated or deemed to be incorporated by reference in this prospectus before you purchase any of the securities offered hereby.

These securities may be offered and sold in the same offering or in separate offerings; to or through underwriters, dealers, and agents; or directly to purchasers. The names of any underwriters, dealers, or agents involved in the sale of our securities and their compensation will be described in the applicable prospectus supplement.

Our common stock is traded on the Nasdaq Global Market under the symbol "VSTM." On December 18, 2013, the closing price of our common stock was \$12.52.

Investing in our securities involves risks. See "Risk Factors" on page 3.

Neither the Securities and Exchange Commission nor any state securities commission has approved or disapproved of these securities or passed upon the adequacy or accuracy of this prospectus. Any representation to the contrary is a criminal offense.

Prospectus dated January 8, 2014

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ABOUT THIS PROSPECTUS

This prospectus is a part of a registration statement that we filed with the Securities and Exchange Commission (the "SEC") using a "shelf" registration process. Under this shelf registration process, we may offer to sell any combination of the securities described in this prospectus in one or more offerings up to a total dollar amount of \$150,000,000. Each time we sell securities under this shelf registration, we will provide a prospectus supplement that will contain specific information about the terms of that offering. The prospectus supplement may also add, update or change information contained in this prospectus. You should read both this prospectus and the applicable prospectus supplement, including all documents incorporated herein and therein by reference, together with additional information described under "Where You Can Find More Information" below.

This prospectus does not include all of the information that is in the registration statement. We omitted certain parts of the registration statement from this prospectus as permitted by the SEC. We refer you to the registration statement and its exhibits for additional information about us and the securities that may be sold under this prospectus.

We have not authorized any dealer, agent or other person to give any information or to make any representation other than those contained or incorporated by reference in this prospectus and any accompanying prospectus supplement. You must not rely upon any information or representation not contained or incorporated by reference in this prospectus or an accompanying prospectus supplement. This prospectus and the accompanying prospectus supplement, if any, do not constitute an offer to sell or the solicitation of an offer to buy any securities other than the registered securities to which they relate, nor do this prospectus and the accompanying prospectus supplement constitute an offer to sell or the solicitation of an offer to buy securities in any jurisdiction to any person to whom it is unlawful to make such offer or solicitation in such jurisdiction. You should not assume that the information contained in this prospectus and the accompanying prospectus supplement, if any, is accurate on any date subsequent to the date set forth on the front of the document or that any information we have incorporated by reference is correct on any date subsequent to the date of the document incorporated by reference, even though this prospectus and any accompanying prospectus supplement is delivered or securities are sold on a later date.

References in this prospectus to "Verastem," the "Company," "we," "us," "our" and similar terms refer to Verastem, Inc. and our subsidiary on a consolidated basis, as appropriate, unless we state otherwise or the context otherwise requires.

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OUR COMPANY

We are a biopharmaceutical company focused on discovering and developing drugs to treat cancer by the targeted killing of cancer stem cells. 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 tumors, their recurrence and metastasis. We have proprietary technology to create a stable population of cancer stem cells that we use to screen for and identify small molecule compounds that target cancer stem cells. Our most advanced programs target the Focal Adhesion Kinase, or FAK, and the PI3K/mTOR signaling pathways. Our lead FAK inhibitor, VS-6063, has been assigned defactinib as the United States Adopted Name (USAN). We have received orphan drug designation for the use of VS-6063 in mesothelioma in the European Union and in the United States. VS-6063 is currently in a registration-directed trial (COMMAND) in patients with mesothelioma, a Phase 1b trial in combination with weekly paclitaxel for patients with ovarian cancer, a Phase 2 study in patients with non-small cell lung cancer and a Phase 1 trial in Japan. In addition to VS-6063, both our FAK inhibitor VS-4718 and our dual mTORC1/2 and PI3K inhibitor VS-5584 are in Phase 1 clinical trials in patients with advanced cancers.

Cancer is a group of diseases characterized by uncontrolled growth and spread of abnormal cells. The American Cancer Society estimated that in the United States in 2011, approximately 1.6 million new cases of cancer would be diagnosed and nearly 600,000 people would die from the 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.

We believe that a key reason for the ultimate failure of many current cancer therapies to achieve a durable clinical response is the presence of cancer stem cells, or CSCs, which are also sometimes referred to as tumor-initiating cells, within tumors. CSCs have been identified in many types of cancer, including mesothelioma, ovarian, breast, pancreatic, colon, brain, lung and leukemia. Following many cancer treatments, the tumor can remain with a high percentage of CSCs and become more aggressive and resistant to further treatment. In addition, patients who relapse often develop metastatic disease in which the cancer spreads to other sites in the body. Tumor metastasis to critical organs is the cause of more than 90% of cancer deaths. We believe that it is the drug resistance and ability of CSCs to spread to other sites in the body that may be the root causes of these therapies failing. Accordingly, our mission is to develop drugs targeting CSCs that either in combination with other cancer treatments or alone can target all of the cells comprising a tumor and, thus, create a durable clinical response.

Our most advanced product candidates are VS-6063, VS-4718 and VS-5584. We are currently evaluating these compounds in both preclinical and clinical studies as potential therapies for certain cancers, including mesothelioma, ovarian and lung. We believe that these compounds may be especially beneficial as therapeutics in aggressive cancers driven by CSCs that have a poorer prognosis and lower overall survival rate than other types of cancer.

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. We plan to use these diagnostics as part of a personalized medicine approach to identify patients that we believe will benefit most from our therapies. We also believe that our diagnostics may be used to monitor patients' progress on therapy and aid physicians' ongoing treatment decisions.

We are headquartered in Cambridge, Massachusetts, and our principal offices are located at 215 First Street, Suite 440, Cambridge, Massachusetts and our telephone number is (617) 252-9300.

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RISK FACTORS

Investing in our securities involves a high degree of risk. See "Item 1A Risk Factors" in our most recent Annual Report on Form 10-K incorporated by reference in this prospectus and in any subsequent Quarterly Report on Form 10-Q and the "Risk Factors" section in the applicable prospectus supplement for a discussion of the factors you should carefully consider before deciding to purchase our securities. Before you invest in our securities, you should carefully consider these risks as well as other information we include or incorporate by reference into this prospectus and the applicable prospectus supplement. The risks and uncertainties we have described are not the only ones facing our company. Additional risks and uncertainties not presently known to us or that we currently deem immaterial may also affect our business operations. The occurrence of any of these risks might cause you to lose all or part of your investment in the offered securities. The discussion of risks includes or refers to forward-looking statements; you should read the explanation of the qualifications and limitations on such forward-looking statements discussed elsewhere in this prospectus.

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FORWARD-LOOKING STATEMENTS

This prospectus, any prospectus supplement and the other documents we have filed with the SEC that are incorporated herein by reference contain forward-looking statements that involve substantial risks and uncertainties. All statements, other than statements related to present facts or current conditions or of historical facts, including statements regarding our strategy, future operations, future financial position, future revenues, projected costs, prospects, plans and objectives of management, are forward-looking statements. The words "anticipate," "believe," "estimate," "expect," "intend," "may," "plan," "predict," "project," "target," "potential," "will," "would," "could," "should," "continue," and similar expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words. We may not actually achieve the plans, intentions or expectations disclosed in our forward-looking statements, and you should not place undue reliance on our forward-looking statements. Actual results or events could differ materially from the plans, intentions and expectations disclosed in the forward-looking statements we make. In particular, you should consider the numerous risks described in our Annual Report on Form 10-K for the year ended December 31, 2012 and any subsequent Quarterly Reports on Form 10-Q, each incorporated by reference in this prospectus, and in the "Risk Factors" section in the applicable prospectus supplement. See "Where You Can Find More Information."

Although we believe the expectations reflected in the forward-looking statements are reasonable, we cannot guarantee future results, level of activity, performance or achievements. You should not rely upon forward-looking statements as predictions of future events. Unless required by law, we will not undertake and we specifically disclaim any obligation to release publicly the result of any revisions which may be made to any forward-looking statements to reflect events or circumstances after the date of such statements or to reflect the occurrence of events, whether or not anticipated. In that respect, we wish to caution readers not to place undue reliance on any such forward-looking statements, which speak only as of the date they are made.

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USE OF PROCEEDS

Except as otherwise provided in the applicable prospectus supplement, we intend to use the net proceeds we receive from our sale of the securities covered by this prospectus for general corporate purposes, which may include, working capital, capital expenditures, research and development expenditures, clinical trial expenditures, commercial expenditures, and possible acquisitions. Additional information on the use of net proceeds we receive from the sale of securities covered by this prospectus may be set forth in the prospectus supplement relating to the specific offering.

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The following table sets forth, for each of the periods presented, our ratio of earnings to fixed charges. You should read this table in conjunction with the financial statements and notes incorporated by reference in this prospectus.

| | Nine Months Ended | | | Period from August 4, 2010 (inception) to December 31, 2010 | Period from August 4, 2010 (inception) to September 30, 2013 |
|------------------------------------|---------------------------|--------------------------|--------------------------|--|---|
| | September 30, 2013 | December 31, 2012 | December 31, 2011 | 31, 2010 | 30, 2013 |
| Ratio of earnings to fixed charges | N/A | N/A | N/A | N/A | N/A |

For purposes of calculating the ratio above, earnings consist of income before income taxes plus fixed charges. Fixed charges include interest expense, non-cash interest expense, and an estimate of the interest expense within rental expense.

We did not record earnings for the nine months ended September 30, 2013, the year ended December 31, 2012, the year ended December 31, 2011, the period from August 4, 2010 (inception) to December 31, 2010 or for the period from August 4, 2010 (inception) to September 30, 2013. Accordingly, our earnings were insufficient to cover fixed charges for such periods and we are unable to disclose a ratio of earnings to fixed charges for such periods. The dollar amount of the deficiency in earnings available for fixed charges for the nine months ended September 30, 2013, the year ended December 31, 2012, the year ended December 31, 2011, the period from August 4, 2010 (inception) to December 31, 2010 and the period from August 4, 2010 (inception) to September 30, 2013 was approximately \$29.9 million, \$32.0 million, \$13.7 million, \$784,000, and \$76.3 million, respectively.

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PLAN OF DISTRIBUTION

We may sell securities in any of the ways described below or in any combination:

to or through underwriters or dealers;

through one or more agents; or

directly to purchasers or to a single purchaser.

The distribution of the securities by us may be effected from time to time in one or more transactions:

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

at market prices prevailing at the time of sale;

at prices related to such prevailing market prices; or

at negotiated prices.

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

The prospectus supplement will describe the terms of the offering of the securities, including the following:

the name or names of any underwriters, dealers or agents and the amounts of securities underwritten or purchased by each of them;

the public offering price of the securities and the proceeds to us and any discounts, commissions or concessions allowed or reallocated or paid to dealers; and

any securities exchanges on which the securities may be listed.

Any offering price and any discounts or concessions allowed or reallocated or paid to dealers will be specified in the applicable prospectus supplement and may be changed from time to time.

Only the agents or underwriters named in each prospectus supplement are agents or underwriters in connection with the securities being offered thereby.

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

solicitation of these contracts.

Agents, underwriters and other third parties described above may be entitled to indemnification by us against certain civil liabilities, including liabilities under the Securities Act of 1933, as amended (the "Securities Act"), or to contribution from us with respect to payments which the agents, underwriters or other third parties may be required to make in respect thereof. Agents, underwriters and such other third parties may be customers of, engage in transactions with, or perform services for us in the ordinary course of business. We may also use underwriters or such other third parties with whom we

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have a material relationship. We will describe the nature of any such relationship in the applicable prospectus supplement.

One or more firms, referred to as "remarketing firms," may also offer or sell the securities, if a prospectus supplement so indicates, in connection with a remarketing arrangement upon their purchase. Remarketing firms will act as principals for their own accounts or as our agents. These remarketing firms will offer or sell the securities in accordance with the terms of the securities. Each prospectus supplement will identify and describe any remarketing firm and the terms of its agreement, if any, with us and will describe the remarketing firm's compensation. Remarketing firms may be deemed to be underwriters in connection with the securities they remarket. Remarketing firms may be entitled under agreements that may be entered into with us to indemnification by us against certain civil liabilities, including liabilities under the Securities Act, and may engage in transactions with or perform services for us in the ordinary course of business.

Certain underwriters may use this prospectus and any accompanying prospectus supplement for offers and sales related to market-making transactions in the securities. These underwriters may act as principal or agent in these transactions, and the sales will be made at prices related to prevailing market prices at the time of sale. Any underwriters involved in the sale of the securities may qualify as "underwriters" within the meaning of Section 2(a)(11) of the Securities Act. In addition, the underwriters' commissions, discounts or concessions may qualify as underwriters' compensation under the Securities Act and the rules of the Financial Industry Regulatory Authority.

Our common stock is listed on the NASDAQ Global Market. Underwriters may make a market in our common stock, but will not be obligated to do so and may discontinue any market making at any time without notice. We can make no assurance as to the development, maintenance or liquidity of any trading market for the securities.

Certain persons participating in an offering may engage in overallotment, stabilizing transactions, short covering transactions and penalty bids in accordance with rules and regulations under the Securities Exchange Act of 1934, as amended (the "Exchange Act"). Overallotment involves sales in excess of the offering size, which create a short position. Stabilizing transactions permit bids to purchase the underlying security so long as the stabilizing bids do not exceed a specified maximum. Short covering transactions involve purchases of the securities in the open market after the distribution is completed to cover short positions. Penalty bids permit the underwriters to reclaim a selling concession from a dealer when the securities originally sold by the dealer are purchased in a short covering transaction to cover short positions. Those activities may cause the price of the securities to be higher than it would otherwise be. If commenced, the underwriters may discontinue any of the activities at any time.

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DESCRIPTION OF COMMON STOCK

The following summary of the terms of our common stock does not purport to be complete. You should refer to our certificate of incorporation and bylaws, both of which are on file with the SEC as exhibits to previous filings. The summary below is also qualified by provisions of applicable law.

General

Under our certificate of incorporation, we have authority to issue up to 100,000,000 shares of common stock, par value \$0.0001 per share. As of September 30, 2013, we had 25,647,732 shares of common stock outstanding.

Holders of our common stock are entitled to one vote for each share held on all matters submitted to a vote of stockholders and do not have cumulative voting rights. An election of directors by our stockholders shall be determined by a plurality of the votes cast by the stockholders entitled to vote on the election. Holders of common stock are entitled to receive proportionately any dividends as may be declared by our board of directors, subject to any preferential dividend rights of outstanding preferred stock.

In the event of our liquidation or dissolution, the holders of common stock are entitled to receive proportionately all assets available for distribution to stockholders after the payment of all debts and other liabilities and subject to the prior rights of any outstanding preferred stock. Holders of common stock have no preemptive, subscription, redemption or conversion rights. The rights, preferences and privileges of holders of common stock are subject to and may be adversely affected by the rights of the holders of shares of any series of preferred stock that we may designate and issue in the future.

Delaware Anti-Takeover Law and Certain Charter and Bylaw Provisions

Delaware law

We are subject to Section 203 of the Delaware General Corporation Law. Subject to certain exceptions, Section 203 prevents a publicly-traded Delaware corporation from engaging in a "business combination" with any "interested stockholder" for three years following the date that the person became an interested stockholder, unless either the interested stockholder attained such status with the approval of our board of directors, the business combination is approved by our board of directors and stockholders in a prescribed manner or the interested stockholder acquired at least 85% of our outstanding voting stock in the transaction in which it became an interested stockholder. A "business combination" includes, among other things, a merger or consolidation involving us and the "interested stockholder" and the sale of more than 10% of our assets. In general, an "interested stockholder" is any entity or person beneficially owning 15% or more of our outstanding voting stock and any entity or person affiliated with or controlling or controlled by such entity or person.

Staggered board

Our certificate of incorporation and our bylaws divide our board of directors into three classes with staggered three-year terms. In addition, our certificate of incorporation and our bylaws provide that directors may be removed only for cause and only by the affirmative vote of the holders of 75% of our shares of capital stock present in person or by proxy and entitled to vote. Under our certificate of incorporation and bylaws, any vacancy on our board of directors, including a vacancy resulting from an enlargement of our board of directors, may be filled only by vote of a majority of our directors then in office. Furthermore, our certificate of incorporation provides that the authorized number of directors may be changed only by the resolution of our board of directors. The classification of our board of directors and the limitations on the ability of our stockholders to remove directors, change the

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authorized number of directors and fill vacancies could make it more difficult for a third party to acquire, or discourage a third party from seeking to acquire, control of our company.

Stockholder action; special meeting of stockholders; advance notice requirements for stockholder proposals and director nominations

Our certificate of incorporation and our bylaws provide that any action required or permitted to be taken by our stockholders at an annual meeting or special meeting of stockholders may only be taken if it is properly brought before such meeting and may not be taken by written action in lieu of a meeting. Our certificate of incorporation and our bylaws also provide that, except as otherwise required by law, special meetings of the stockholders can only be called by our chairman of the board, our president or chief executive officer or our board of directors. In addition, our bylaws establish an advance notice procedure for stockholder proposals to be brought before an annual meeting of stockholders, including proposed nominations of candidates for election to our board of directors. Stockholders at an annual meeting may only consider proposals or nominations specified in the notice of meeting or brought before the meeting by or at the direction of our board of directors, or by a stockholder of record on the record date for the meeting who is entitled to vote at the meeting and who has delivered timely written notice in proper form to our secretary of the stockholder's intention to bring such business before the meeting. These provisions could have the effect of delaying until the next stockholder meeting stockholder actions that are favored by the holders of a majority of our outstanding voting securities. These provisions also could discourage a third party from making a tender offer for our common stock, because even if it acquired a majority of our outstanding voting stock, it would be able to take action as a stockholder, such as electing new directors or approving a merger, only at a duly called stockholders meeting and not by written consent.

Super-majority voting

The Delaware General Corporation Law provides generally that the affirmative vote of a majority of the shares entitled to vote on any matter is required to amend a corporation's certificate of incorporation or bylaws, unless a corporation's certificate of incorporation or bylaws, as the case may be, requires a greater percentage. Our bylaws may be amended or repealed by a majority vote of our board of directors or the affirmative vote of the holders of at least 75% of the votes that all our stockholders would be entitled to cast in any annual election of directors. In addition, the affirmative vote of the holders of at least 75% of the votes that all our stockholders would be entitled to cast in any election of directors is required to amend or repeal or to adopt any provisions inconsistent with any of the provisions of our certificate of incorporation described above.

Transfer Agent and Registrar

The transfer agent and registrar for our common stock is Computershare Trust Company, N.A.

Listing

Our common stock is listed on the NASDAQ Global Market under the symbol "VSTM."

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DESCRIPTION OF PREFERRED STOCK

Under the terms of our certificate of incorporation, our board of directors is authorized to issue up to 5,000,000 shares of our preferred stock, par value \$0.0001 per share, in one or more series without stockholder approval. Our board of directors has the discretion to determine the rights, preferences, privileges and restrictions, including voting rights, dividend rights, conversion rights, redemption privileges and liquidation preferences, of each series of preferred stock. As of September 30, 2013, we had no shares of preferred stock outstanding. It is not possible to state the actual effect of the issuance of any shares of preferred stock upon the rights of the holders of common stock until the board of directors determines the specific rights of the holders of preferred stock. However, effects of the issuance of preferred stock include restricting dividends on common stock, diluting the voting power of common stock, impairing the liquidation rights of common stock, and making it more difficult for a third party to acquire us, which could have the effect of discouraging a third party from acquiring, or deterring a third party from paying a premium to acquire, a majority of our outstanding voting stock.

If we offer a specific class or series of preferred stock under this prospectus, we will describe the terms of the preferred stock in the prospectus supplement for such offering and will file a copy of the certificate establishing the terms of the preferred stock with the SEC. To the extent required, this description will include:

the title and stated value;

the number of shares offered, the liquidation preference per share and the purchase price;

the dividend rate(s), period(s) and/or payment date(s), or method(s) of calculation for such dividends;

whether dividends will be cumulative or non-cumulative and, if cumulative, the date from which dividends will accumulate;

the procedures for any auction and remarketing, if any;

the provisions for a sinking fund, if any;

the provisions for redemption, if applicable;

any listing of the preferred stock on any securities exchange or market;

whether the preferred stock will be convertible into our common stock, and, if applicable, the conversion price (or how it will be calculated) and conversion period;

whether the preferred stock will be exchangeable into debt securities, and, if applicable, the exchange price (or how it will be calculated) and exchange period;

voting rights, if any, of the preferred stock;

a discussion of any material U.S. federal income tax considerations applicable to the preferred stock;

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the relative ranking and preferences of the preferred stock as to dividend rights and rights upon liquidation, dissolution or winding up of the affairs of the Company; and

any material limitations on issuance of any class or series of preferred stock ranking senior to or on a parity with the series of preferred stock as to dividend rights and rights upon liquidation, dissolution or winding up of the Company.

The preferred stock offered by this prospectus, when issued, will not have, or be subject to, any preemptive or similar rights.

Transfer Agent and Registrar

The transfer agent and registrar for any series or class of preferred stock will be set forth in each applicable prospectus supplement.

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DESCRIPTION OF WARRANTS

We have agreed to issue a warrant for the purchase of 142,857 shares of our common stock with an exercise price of \$17.16 per share to Encarta, Inc. We may issue warrants to purchase shares of our common stock, preferred stock and/or debt securities in one or more series together with other securities or separately, as described in each applicable prospectus supplement. Below is a description of certain general terms and provisions of the warrants that we may offer. Particular terms of the warrants will be described in the applicable warrant agreements and the applicable prospectus supplement for the warrants.

The applicable prospectus supplement will contain, where applicable, the following terms of and other information relating to the warrants:

the specific designation and aggregate number of, and the price at which we will issue, the warrants;

the currency or currency units in which the offering price, if any, and the exercise price are payable;

the designation, amount and terms of the securities purchasable upon exercise of the warrants;

if applicable, the exercise price for shares of our common stock and the number of shares of common stock to be received upon exercise of the warrants;

if applicable, the exercise price for shares of our preferred stock, the number of shares of preferred stock to be received upon exercise, and a description of that class or series of our preferred stock;

if applicable, the exercise price for our debt securities, the amount of our debt securities to be received upon exercise, and a description of that series of debt securities;

the date on which the right to exercise the warrants will begin and the date on which that right will expire or, if the warrants may not be continuously exercised throughout that period, the specific date or dates on which the warrants may be exercised;

whether the warrants will be issued in fully registered form or bearer form, in definitive or global form or in any combination of these forms, although, in any case, the form of a warrant included in a unit will correspond to the form of the unit and of any security included in that unit;

any applicable material U.S. federal income tax consequences;

the identity of the warrant agent for the warrants and of any other depositaries, execution or paying agents, transfer agents, registrars or other agents;

the proposed listing, if any, of the warrants or any securities purchasable upon exercise of the warrants on any securities exchange;

if applicable, the date from and after which the warrants and the common stock, preferred stock and/or debt securities will be separately transferable;

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if applicable, the minimum or maximum amount of the warrants that may be exercised at any one time;

information with respect to book-entry procedures, if any;

the anti-dilution provisions of the warrants, if any;

any redemption or call provisions;

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whether the warrants are to be sold separately or with other securities as parts of units; and

any additional terms of the warrants, including terms, procedures and limitations relating to the exchange and exercise of the warrants.

Transfer Agent and Registrar

The transfer agent and registrar for any warrants will be set forth in the applicable prospectus supplement.

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DESCRIPTION OF DEBT SECURITIES

We will issue the debt securities offered by this prospectus and any accompanying prospectus supplement under an indenture to be entered into between us and the trustee identified in the applicable prospectus supplement. The terms of the debt securities will include those stated in the indenture and those made part of the indenture by reference to the Trust Indenture Act of 1939, as in effect on the date of the indenture. We have filed a copy of the form of indenture as an exhibit to the registration statement in which this prospectus is included. The indenture will be subject to and governed by the terms of the Trust Indenture Act of 1939.

We may offer under this prospectus debt securities that, unless otherwise specified in the applicable prospectus supplement, will represent direct, unsecured obligations of the Company and will rank equally with all of our other unsecured indebtedness.

The following statements relating to the debt securities and the indenture are summaries, qualified in their entirety by reference to the detailed provisions of the indenture.

General

We may issue the debt securities in one or more series with the same or various maturities, at par, at a premium, or at a discount. We will describe the particular terms of each series of debt securities in a prospectus supplement relating to that series, which we will file with the SEC.

The prospectus supplement will set forth, to the extent required, the following terms of the debt securities in respect of which the prospectus supplement is delivered:

the title of the series;

the aggregate principal amount;

the issue price or prices, expressed as a percentage of the aggregate principal amount of the debt securities;

any limit on the aggregate principal amount;

the date or dates on which principal is payable;

the interest rate or rates (which may be fixed or variable) or, if applicable, the method used to determine such rate or rates;

the date or dates from which interest, if any, will be payable and any regular record date for the interest payable;

the place or places where principal and, if applicable, premium and interest, is payable;

the terms and conditions upon which we may, or the holders may require us to, redeem or repurchase the debt securities;

the denominations in which such debt securities may be issuable, if other than denominations of \$1,000 or any integral multiple of that number;

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whether the debt securities are to be issuable in the form of certificated securities (as described below) or global securities (as described below);

the portion of principal amount that will be payable upon declaration of acceleration of the maturity date if other than the principal amount of the debt securities;

the currency of denomination;

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the designation of the currency, currencies or currency units in which payment of principal and, if applicable, premium and interest, will be made;

if payments of principal and, if applicable, premium or interest, on the debt securities are to be made in one or more currencies or currency units other than the currency of denomination, the manner in which the exchange rate with respect to such payments will be determined;

if amounts of principal and, if applicable, premium and interest may be determined by reference to an index based on a currency or currencies or by reference to a commodity, commodity index, stock exchange index or financial index, then the manner in which such amounts will be determined;

the provisions, if any, relating to any collateral provided for such debt securities;

any addition to or change in the covenants and/or the acceleration provisions described in this prospectus or in the indenture;

any events of default, if not otherwise described below under "Events of Default";

the terms and conditions, if any, for conversion into or exchange for shares of our common stock or preferred stock;

any depositaries, interest rate calculation agents, exchange rate calculation agents or other agents; and

the terms and conditions, if any, upon which the debt securities shall be subordinated in right of payment to other indebtedness of the Company.

We may issue discount debt securities that provide for an amount less than the stated principal amount to be due and payable upon acceleration of the maturity of such debt securities in accordance with the terms of the indenture. We may also issue debt securities in bearer form, with or without coupons. If we issue discount debt securities or debt securities in bearer form, we will describe material U.S. federal income tax considerations and other material special considerations which apply to these debt securities in the applicable prospectus supplement.

We may issue debt securities denominated in or payable in a foreign currency or currencies or a foreign currency unit or units. If we do, we will describe the restrictions, elections, and general tax considerations relating to the debt securities and the foreign currency or currencies or foreign currency unit or units in the applicable prospectus supplement.

Exchange and/or Conversion Rights

We may issue debt securities which can be exchanged for or converted into shares of our common stock or preferred stock. If we do, we will describe the terms of exchange or conversion in the prospectus supplement relating to these debt securities.

Transfer and Exchange

We may issue debt securities that will be represented by either:

"book-entry securities," which means that there will be one or more global securities registered in the name of a depositary or a nominee of a depositary; or

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"certificated securities," which means that they will be represented by a certificate issued in definitive registered form.

We will specify in the prospectus supplement applicable to a particular offering whether the debt securities offered will be book-entry or certificated securities.

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Certificated Debt Securities

If you hold certificated debt securities, you may transfer or exchange such debt securities at the trustee's office or at the paying agent's office or agency in accordance with the terms of the indenture. You will not be charged a service charge for any transfer or exchange of certificated debt securities but may be required to pay an amount sufficient to cover any tax or other governmental charge payable in connection with such transfer or exchange.

You may effect the transfer of certificated debt securities and of the right to receive the principal of, premium, and/or interest, if any, on the certificated debt securities only by surrendering the certificate representing the certificated debt securities and having us or the trustee issue a new certificate to the new holder.

Global Securities

If we decide to issue debt securities in the form of one or more global securities, then we will register the global securities in the name of the depository for the global securities or the nominee of the depository, and the global securities will be delivered by the trustee to the depository for credit to the accounts of the holders of beneficial interests in the debt securities.

The prospectus supplement will describe the specific terms of the depository arrangement for debt securities of a series that are issued in global form. None of our Company, the trustee, any payment agent or the security registrar will have any responsibility or liability for any aspect of the records relating to or payments made on account of beneficial ownership interests in a global debt security or for maintaining, supervising or reviewing any records relating to these beneficial ownership interests.

No Protection in the Event of Change of Control

The indenture does not have any covenants or other provisions providing for a put or increased interest or otherwise that would afford holders of our debt securities additional protection in the event of a recapitalization transaction, a change of control of the Company, or a highly leveraged transaction. If we offer any covenants or provisions of this type with respect to any debt securities covered by this prospectus, we will describe them in the applicable prospectus supplement.

Covenants

Unless otherwise indicated in this prospectus or the applicable prospectus supplement, our debt securities will not have the benefit of any covenants that limit or restrict our business or operations, the pledging of our assets or the incurrence by us of indebtedness. We will describe in the applicable prospectus supplement any material covenants in respect of a series of debt securities.

Consolidation, Merger and Sale of Assets

We have agreed in the indenture that we will not consolidate with or merge into any other person or convey, transfer, sell or lease our properties and assets substantially as an entirety to any person, unless:

the person formed by the consolidation or into or with which we are merged or the person to which our properties and assets are conveyed, transferred, sold or leased, is a corporation organized and existing under the laws of the U.S., any state or the District of Columbia or a corporation or comparable legal entity organized under the laws of a foreign jurisdiction and, if we are not the surviving person, the surviving person has expressly assumed all of our obligations, including the payment of the principal of and, premium, if any, and interest on the debt securities and the performance of the other covenants under the indenture; and

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immediately before and immediately after giving effect to the transaction, no event of default, and no event which, after notice or lapse of time or both, would become an event of default, has occurred and is continuing under the indenture.

Events of Default

Unless otherwise specified in the applicable prospectus supplement, the following events will be events of default under the indenture with respect to debt securities of any series:

we fail to pay any principal or premium, if any, when it becomes due;

we fail to pay any interest within 30 days after it becomes due;

we fail to observe or perform any other covenant in the debt securities or the indenture for 60 days after written notice specifying the failure from the trustee or the holders of not less than 25% in aggregate principal amount of the outstanding debt securities of that series; and

certain events involving bankruptcy, insolvency or reorganization of Verastem or any of our significant subsidiaries.

The trustee may withhold notice to the holders of the debt securities of any series of any default, except in payment of principal or premium, if any, or interest on the debt securities of a series, if the trustee considers it to be in the best interest of the holders of the debt securities of that series to do so.

If an event of default (other than an event of default resulting from certain events of bankruptcy, insolvency or reorganization) occurs, and is continuing, then the trustee or the holders of not less than 25% in aggregate principal amount of the outstanding debt securities of any series may accelerate the maturity of the debt securities. If this happens, the entire principal amount, plus the premium, if any, of all the outstanding debt securities of the affected series plus accrued interest to the date of acceleration will be immediately due and payable. At any time after the acceleration, but before a judgment or decree based on such acceleration is obtained by the trustee, the holders of a majority in aggregate principal amount of outstanding debt securities of such series may rescind and annul such acceleration if:

all events of default (other than nonpayment of accelerated principal, premium or interest) have been cured or waived;

all lawful interest on overdue interest and overdue principal has been paid; and

the rescission would not conflict with any judgment or decree.

In addition, if the acceleration occurs at any time when we have outstanding indebtedness which is senior to the debt securities, the payment of the principal amount of outstanding debt securities may be subordinated in right of payment to the prior payment of any amounts due under the senior indebtedness, in which case the holders of debt securities will be entitled to payment under the terms prescribed in the instruments evidencing the senior indebtedness and the indenture.

If an event of default resulting from certain events of bankruptcy, insolvency or reorganization occurs, the principal, premium and interest amount with respect to all of the debt securities of any series will be due and payable immediately without any declaration or other act on the part of the trustee or the holders of the debt securities of that series.

The holders of a majority in principal amount of the outstanding debt securities of a series will have the right to waive any existing default or compliance with any provision of the indenture or the debt securities of that series and to direct the time, method and place of conducting any proceeding for any remedy available to the trustee, subject to certain limitations specified in the indenture.

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No holder of any debt security of a series will have any right to institute any proceeding with respect to the indenture or for any remedy under the indenture, unless:

the holder gives to the trustee written notice of a continuing event of default;

the holders of at least 25% in aggregate principal amount of the outstanding debt securities of the affected series make a written request and offer reasonable indemnity to the trustee to institute a proceeding as trustee;

the trustee fails to institute a proceeding within 60 days after such request; and

the holders of a majority in aggregate principal amount of the outstanding debt securities of the affected series do not give the trustee a direction inconsistent with such request during such 60-day period.

These limitations do not, however, apply to a suit instituted for payment on debt securities of any series on or after the due dates expressed in the debt securities.

We will periodically deliver certificates to the trustee regarding our compliance with our obligations under the indenture.

Modification and Waiver

From time to time, we and the trustee may, without the consent of holders of the debt securities of one or more series, amend the indenture or the debt securities of one or more series, or supplement the indenture, for certain specified purposes, including:

to provide that the surviving entity following a change of control of Verastem permitted under the indenture will assume all of our obligations under the indenture and debt securities;

to provide for certificated debt securities in addition to uncertificated debt securities;

to comply with any requirements of the SEC under the Trust Indenture Act of 1939;

to provide for the issuance of and establish the form and terms and conditions of debt securities of any series as permitted by the indenture;

to cure any ambiguity, defect or inconsistency, or make any other change that does not materially and adversely affect the rights of any holder; and

to appoint a successor trustee under the indenture with respect to one or more series.

From time to time we and the trustee may, with the consent of holders of at least a majority in principal amount of an outstanding series of debt securities, amend or supplement the indenture or the debt securities series, or waive compliance in a particular instance by us with any provision of the indenture or the debt securities. We may not, however, without the consent of each holder affected by such action, modify or supplement the indenture or the debt securities or waive compliance with any provision of the indenture or the debt securities in order to:

reduce the amount of debt securities whose holders must consent to an amendment, supplement, or waiver to the indenture or such debt security;

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reduce the rate of or change the time for payment of interest or reduce the amount of or postpone the date for payment of sinking fund or analogous obligations;

reduce the principal of or change the stated maturity of the debt securities;

make any debt security payable in money other than that stated in the debt security;

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change the amount or time of any payment required or reduce the premium payable upon any redemption, or change the time before which no such redemption may be made;

waive a default in the payment of the principal of, premium, if any, or interest on the debt securities or a redemption payment;

waive a redemption payment with respect to any debt securities or change any provision with respect to redemption of debt securities; or

take any other action otherwise prohibited by the indenture to be taken without the consent of each holder affected by the action.

Defeasance of Debt Securities and Certain Covenants in Certain Circumstances

The indenture permits us, at any time, to elect to discharge our obligations with respect to one or more series of debt securities by following certain procedures described in the indenture. These procedures will allow us either:

to defease and be discharged from any and all of our obligations with respect to any debt securities except for the following obligations (which discharge is referred to as "legal defeasance"):

- (1) to register the transfer or exchange of such debt securities;
- (2) to replace temporary or mutilated, destroyed, lost or stolen debt securities;
- (3) to compensate and indemnify the trustee; or
- (4) to maintain an office or agency in respect of the debt securities and to hold monies for payment in trust; or

to be released from our obligations with respect to the debt securities under certain covenants contained in the indenture, as well as any additional covenants which may be contained in the applicable supplemental indenture (which release is referred to as "covenant defeasance").

In order to exercise either defeasance option, we must deposit with the trustee or other qualifying trustee, in trust for that purpose:

money;

U.S. Government Obligations (as described below) or Foreign Government Obligations (as described below) which through the scheduled payment of principal and interest in accordance with their terms will provide money; or

a combination of money and/or U.S. Government Obligations and/or Foreign Government Obligations sufficient in the written opinion of a nationally-recognized firm of independent accountants to provide money;

which in each case specified above, provides a sufficient amount to pay the principal of, premium, if any, and interest, if any, on the debt securities of the series, on the scheduled due dates or on a selected date of redemption in accordance with the terms of the indenture.

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In addition, defeasance may be effected only if, among other things:

in the case of either legal or covenant defeasance, we deliver to the trustee an opinion of counsel, as specified in the indenture, stating that as a result of the defeasance neither the trust nor the trustee will be required to register as an investment company under the Investment Company Act of 1940;

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in the case of legal defeasance, we deliver to the trustee an opinion of counsel stating that we have received from, or there has been published by, the Internal Revenue Service a ruling to the effect that, or there has been a change in any applicable federal income tax law with the effect that (and the opinion shall confirm that), the holders of outstanding debt securities will not recognize income, gain or loss for U.S. federal income tax purposes solely as a result of such legal defeasance and will be subject to U.S. federal income tax on the same amounts, in the same manner, including as a result of prepayment, and at the same times as would have been the case if legal defeasance had not occurred;

in the case of covenant defeasance, we deliver to the trustee an opinion of counsel to the effect that the holders of the outstanding debt securities will not recognize income, gain or loss for U.S. federal income tax purposes as a result of covenant defeasance and will be subject to U.S. federal income tax on the same amounts, in the same manner and at the same times as would have been the case if covenant defeasance had not occurred; and

certain other conditions described in the indenture are satisfied.

If we fail to comply with our remaining obligations under the indenture and applicable supplemental indenture after a covenant defeasance of the indenture and applicable supplemental indenture, and the debt securities are declared due and payable because of the occurrence of any undefeased event of default, the amount of money and/or U.S. Government Obligations and/or Foreign Government Obligations on deposit with the trustee could be insufficient to pay amounts due under the debt securities of the affected series at the time of acceleration. We will, however, remain liable in respect of these payments.

The term "U.S. Government Obligations" as used in the above discussion means securities which are direct obligations of or non-callable obligations guaranteed by the United States of America for the payment of which obligation or guarantee the full faith and credit of the United States of America is pledged.

The term "Foreign Government Obligations" as used in the above discussion means, with respect to debt securities of any series that are denominated in a currency other than U.S. dollars (1) direct obligations of the government that issued or caused to be issued such currency for the payment of which obligations its full faith and credit is pledged or (2) obligations of a person controlled or supervised by or acting as an agent or instrumentality of such government the timely payment of which is unconditionally guaranteed as a full faith and credit obligation by that government, which in either case under clauses (1) or (2), are not callable or redeemable at the option of the issuer.

Regarding the Trustee

We will identify the trustee with respect to any series of debt securities in the prospectus supplement relating to the applicable debt securities. You should note that if the trustee becomes a creditor of Verastem, the indenture and the Trust Indenture Act of 1939 limit the rights of the trustee to obtain payment of claims in certain cases, or to realize on certain property received in respect of any such claim, as security or otherwise. The trustee and its affiliates may engage in, and will be permitted to continue to engage in, other transactions with us and our affiliates. If, however, the trustee acquires any "conflicting interest" within the meaning of the Trust Indenture Act of 1939, it must eliminate such conflict or resign.

The holders of a majority in principal amount of the then outstanding debt securities of any series may direct the time, method and place of conducting any proceeding for exercising any remedy available to the trustee. If an event of default occurs and is continuing, the trustee, in the exercise of its rights and powers, must use the degree of care and skill of a prudent person in the conduct of his or her own affairs. Subject to that provision, the trustee will be under no obligation to exercise any of its rights or powers under the indenture at the request of any of the holders of the debt securities, unless they have offered to the trustee reasonable indemnity or security.

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WHERE YOU CAN FIND MORE INFORMATION

We have filed a registration statement on Form S-3 with the SEC for the securities offered by this prospectus. This prospectus does not include all of the information contained in the registration statement. You should refer to the registration statement and its exhibits for additional information.

We are required to file annual and quarterly reports, current reports, proxy statements, and other information with the SEC. We make these documents publicly available, free of charge, on our website at www.verastem.com as soon as reasonably practicable after filing such documents with the SEC. The information contained on our website is not part of this prospectus. You can read our SEC filings, including the registration statement, on the SEC's website at <http://www.sec.gov>. You also may read and copy any document we file with the SEC at its public reference facility at:

Public Reference Room
100 F Street N.E.
Washington, DC 20549.

Please call the SEC at 1-800-732-0330 for further information on the operation of the public reference facilities.

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INCORPORATION OF CERTAIN DOCUMENTS BY REFERENCE

The SEC allows us to "incorporate by reference" into this prospectus the information we file with it, which means that we can disclose important information to you by referring you to those documents. The information incorporated by reference is considered to be part of this prospectus, and information in documents that we file later with the SEC will automatically update and supersede information in this prospectus. We incorporate by reference into this prospectus the documents listed below and any future filings made by us with the SEC under Section 13(a), 13(c), 14 or 15(d) of the Exchange Act, except for information "furnished" under Items 2.02, 7.01 or 9.01 on Form 8-K or other information "furnished" to the SEC which is not deemed filed and not incorporated in this prospectus, until the termination of the offering of securities described in the applicable prospectus supplement. We hereby incorporate by reference the following documents:

Our Annual Report on Form 10-K for the year ended December 31, 2012, as filed with the SEC on March 26, 2013;

The information specifically incorporated by reference into our Annual Report on Form 10-K for the year ended December 31, 2012 from our definitive proxy statement on Schedule 14A, as filed with the SEC on April 25, 2013;

Our Quarterly Reports on Form 10-Q for the quarterly periods ended March 31, 2013, as filed with the SEC on May 9, 2013, June 30, 2013, as filed with the SEC on August 13, 2013, and September 30, 2013, as filed with the SEC on November 12, 2013 (in each case, other than information furnished rather than filed with the SEC);

Our Current Reports on Form 8-K filed with the SEC on January 22, 2013, March 6, 2013, May 14, 2013, June 6, 2013, June 17, 2013, July 17, 2013, and November 27, 2013; and

Description of our common stock, which is contained in the Registration Statement on Form 8-A, as filed with the SEC on January 23, 2012, as supplemented by the Description of Common Stock found on page 9 of this prospectus and including any amendments or reports filed for the purpose of updating such description.

You may request a copy of these filings, at no cost, by writing or telephoning us at the following address:

Investor Relations
Verastem, Inc.
215 First Street, Suite 440
Cambridge, Massachusetts 02142
(617) 252-9300

Copies of these filings are also available, without charge, on the SEC's website at www.sec.gov and on our website at www.verastem.com as soon as reasonably practicable after they are filed electronically with the SEC. The information contained on our website is not a part of this prospectus.

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LEGAL MATTERS

The validity of the issuance of the securities offered pursuant to this prospectus will be passed upon for us by Ropes & Gray LLP, Boston, Massachusetts. The validity of any securities will be passed upon for any underwriters or agents by counsel that we will name in the applicable prospectus supplement.

EXPERTS

The consolidated financial statements of Verastem, Inc. appearing in Verastem, Inc.'s Annual Report on Form 10-K for the year ended December 31, 2012 have been audited by Ernst & Young LLP, independent registered public accounting firm, as set forth in their report thereon, included therein, and incorporated herein by reference. Such consolidated financial statements are incorporated herein by reference in reliance upon such report given on the authority of such firm as experts in accounting and auditing.

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\$40,000,000

Common Stock

PROSPECTUS SUPPLEMENT

Joint Book-Running Managers

**Jefferies
Leerink Partners**

Co-Lead Managers

**Guggenheim Securities
Oppenheimer & Co.**
