Dage

Prospectus Supplement

(To Prospectus dated April 24, 2017)

7,166,666 shares



Common Stock

We are offering 7,166,666 shares of our common stock in this offering at a price of \$6.00 per share. The proceeds to us, before expenses, will be approximately \$43,000,000. Our common stock is listed on The Nasdaq Global Market under the symbol "VSTM." On June 13, 2018 the last reported sale price of our common stock on The Nasdaq Global Market was \$5.66 per share.

Investing in our common stock involves a high degree of risk. Before making an investment decision, you should carefully consider the information under the heading "Risk Factors" beginning on page S-5 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.

Prospectus Supplement dated June 14, 2018

Table of Contents

TABLE OF CONTENTS

PROSPECTUS SUPPLEMENT

	Page
About This Prospectus Supplement	S-1
Prospectus Supplement Summary	S-2
The Offering	S-4
Risk Factors	S-5
Forward-Looking Statements	S-6
<u>Use of Proceeds</u>	S-7
Plan of Distribution	S-8
Material United States Federal Income and Estate Tax Considerations for Non-U.S. Holders of Shares of our Common Stock	S-9
Incorporation of Certain Documents by Reference	S-13
<u>Legal Matters</u>	S-13
<u>Experts</u>	S-13
PROSPECTUS	

About this Prospectus	3
<u>Our Company</u>	4

Risk Factors	5
Forward-Looking Statements	6
<u>Use of Proceeds</u>	7
Ratio of Earnings to Fixed Charges	8
Plan of Distribution	9
Description of Common Stock	11
Description of Preferred Stock	13
<u>Description of Warrants</u>	14
<u>Description of Debt Securities</u>	15
Where You Can Find More Information	21
<u>Incorporation of Certain Documents by Reference</u>	22
<u>Legal Matters</u>	23
<u>Experts</u>	23

Table of Contents

ABOUT THIS PROSPECTUS SUPPLEMENT

S-i

This prospectus supplement and the accompanying prospectus relate to part of a registration statement on Form S-3 (File No. 333-217048) that we filed with the Securities and Exchange Commission, or SEC, using a shelf registration process and a related registration statement filed on June 14, 2018 pursuant to Rule 462(b) of the Securities Act of 1933, as amended. 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 or in any related free writing prospectus filed by us with the SEC. We have not authorized anyone to provide you with information that is different from or in addition to such information. 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 or the documents incorporated by reference herein. If information in this prospectus supplement is inconsistent with information in the accompanying prospectus or the documents incorporated by reference herein, this prospectus supplement will apply and will supersede that information in the accompanying prospectus or the documents incorporated by reference herein.

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.

S-1

Table of Contents

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 developing and commercializing drugs to improve the survival and quality of life of cancer patients. Our most advanced product candidates, duvelisib and defactinib, utilize a multi-faceted approach designed to treat cancers originating either in the blood or

major organ systems. We are currently evaluating these compounds in both preclinical and clinical studies as potential therapies for certain cancers, including leukemia, lymphoma, lung cancer, ovarian cancer, mesothelioma, and pancreatic cancer. We believe that these compounds may be beneficial as therapeutics either as single agents or when used in combination with immuno-oncology agents or other current and emerging standard of care treatments in aggressive cancers that are poorly served by currently available therapies.

Duvelisib targets the Phosphoinositide 3-kinase, or PI3K, signaling pathway. The PI3K signaling pathway plays a central role in cancer proliferation and survival. Duvelisib is an investigational oral therapy designed to attack both malignant B-cells and T-cells and disrupt the tumor microenvironment to help thwart their growth and proliferation through the dual inhibition of PI3K delta and gamma. Duvelisib is being developed for the treatment of patients with hematologic cancers including chronic lymphocytic leukemia and small lymphocytic lymphoma, or CLL/SLL, and indolent non-Hodgkin lymphoma, or iNHL, which includes follicular lymphoma, or FL, and other subtypes of lymphoma, including peripheral T-cell lymphoma, or PTCL. Duvelisib has U.S. Food and Drug Administration, or FDA, Fast Track Designation for patients with CLL or PTCL who have received at least one prior therapy and for patients with FL who have received at least two prior therapies. In addition, duvelisib has orphan drug designation for patients with CLL/SLL and FL in the United States and European Union. Our New Drug Application, or NDA, requesting the full approval of duvelisib for the treatment of patients with relapsed or refractory CLL/SLL and accelerated approval for the treatment of patients with relapsed or refractory FL was accepted for filing by the FDA with Priority Review and a target action date of October 5, 2018. Additionally, we plan to submit a marketing authorization application to the European Medicines Agency in 2019. We are currently building our U.S. commercial capabilities for our potential product launch in 2018, and we intend to enter into one or more partnerships or collaborations for the potential commercialization of duvelisib outside of the United States.

Defactinib is a targeted inhibitor of the Focal Adhesion Kinase, or FAK, signaling pathway. FAK is a non-receptor tyrosine kinase encoded by the PTK-2 gene that is involved in cellular adhesion and, in cancer, metastatic capability. Similar to duvelisib, defactinib is also orally available and designed to be a potential therapy for patients to take at home under the advice of their physician. Defactinib has orphan drug designation in ovarian cancer in the United States and the European Union, and in mesothelioma in the United States, the European Union, and Australia.

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 2018, approximately 1.7 million new cases of cancer will be diagnosed and approximately 610,000 people will die from the disease. Current treatments for cancer include surgery, radiation therapy, chemotherapy, hormonal therapy, immunotherapy, and targeted therapy. Despite years of intensive research and clinical use, current treatments often fail to cure cancer. Cancer remains one of the world's most serious health problems and is the second most common cause of death in the United States after heart disease.

According to Decision Resources, the prevalence of CLL/SLL in the United States is approximately 197,000, and the prevalence of FL is approximately 141,000. The CLL/SLL and FL markets are projected to expand in the coming years, driven by the growing elderly population and the availability of new treatments. According to Decision Resources, the total value in global major markets is expected to grow at a compounded annual rate of over 14%, from \$6 billion in 2016 to \$24 billion in 2026. The use of targeted therapies for patients with CLL/SLL has recently increased due to the approval of novel agents and now encompasses approximately one third of first line treatment with an increasing share of use across lines of therapy. In contrast, targeted therapies are currently less utilized for treatment of patients with FL as fewer agents have demonstrated efficacy in the patient population, and chemotherapy still accounts for the majority of treatments administered. However, as new targeted therapies emerge for these diseases, it is expected that the share of chemotherapy use will decrease.

There are numerous factors to consider when determining the best course of treatment for any patient. For instance, approximately 20% of FL patients are relatively insensitive to first line chemotherapy, have a poor ongoing prognosis or no longer respond to treatment. While ibrutinib use in first line treatment for patients with CLL/SLL continues to increase, nearly a quarter of CLL/SLL patients discontinue ibrutinib after a median of seven months and ibrutinib has not been shown to be efficacious in FL. It is also important to note that 70% of the CLL/SLL and FL patient population are treated in community settings, away from major academic centers, and as many as 55% of oncology patients give equal importance to quality of life and survival.

Community oncologists treat a wide variety of lymphomas, including CLL/SLL and FL. When treating elderly patients, factors such as comorbidities, rate of progression, genetic risks as well as the patient's overall quality of life are some of the considerations. It is important to note that over 70% of elderly iNHL patients experience at least one major comorbidity that may limit existing treatment options. Additionally, approximately 20% of FL patients are "fast progressors" on chemotherapy, while approximately two-thirds of CLL/SLL patients have medium to high tumor burden, and greater than 30% have high risk genetic alterations, limiting their treatment options. Almost 60% of patients feel burdened by hospital visits, so a treatment that can be administered without infusions and at home may be of further benefit to patients.

With the application of new technologies and key discoveries, we believe that we are now entering an era of cancer research characterized by a more sophisticated understanding of the biology of cancer. We believe that the potential of oral, targeted therapies, along with the rapidly advancing field of immunotherapy, or using the body's immune system to fight cancer, are important new insights that present the opportunity to develop more effective cancer treatments. Our goal is to develop targeted agents that both specifically kill cancer cells and disrupt the tumor microenvironment to enhance the efficacy of cancer treatment.

S-2

Table of Contents

Recent Developments

The following is a summary of selected key developments affecting our business that have occurred since March 31, 2018.

Underwritten Public Offering

On May 16, 2018, we entered into an underwriting agreement with Cantor Fitzgerald & Co. pursuant to which we issued and sold in an underwritten offering 8,944,444 shares of our common stock, \$0.0001 par value per share, at a price to the public of \$4.50 per share. The aggregate gross proceeds to us from the offering was approximately \$40.2 million.

Duvelisib NDA Accepted by FDA with Priority Review

In April 2018, we announced that the FDA accepted the duvelisib NDA for filing with Priority Review, and with a target action date of October 5, 2018. In the accepted NDA, we are seeking full approval for duvelisib, our investigational oral dual inhibitor of PI3K-delta and PI3K-gamma, for the treatment of relapsed or refractory CLL/SLL and accelerated approval for the treatment of relapsed or refractory FL. The duvelisib NDA is supported by clinical data

from the randomized Phase 3 DUOTM study evaluating duvelisib as a monotherapy in patients with relapsed or refractory CLL/SLL, as well as the Phase 2 DYNAMOTM study evaluating patients with indolent non-Hodgkin lymphoma that are double-refractory to both rituximab and chemotherapy or radioimmunotherapy. Both DUO and DYNAMO achieved their primary endpoints.

At-the-Market Offering Program

On March 30, 2017, we entered into a Controlled Equity OfferingSM Sales Agreement with Cantor Fitzgerald & Co., as sales agent, which we amended on August 28, 2017. Under the sales agreement, as amended, we are permitted, from time to time, to issue and sell shares of our common stock, \$0.0001 par value per share, having up to an aggregate offering price of \$75.0 million through an "at-the-market offering" program. From April 1, 2018 to May 9, 2018, we sold 6,314,410 shares of our common stock pursuant to this program and received proceeds of approximately \$23.7 million, net of commissions paid. There have been no sales under this program since May 9, 2018.

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.

S-3

Table of Contents

THE OFFERING

Common stock offered by us 7,166,666 shares

Common stock to be outstanding after

this offering 73,393,493 shares

Use of proceeds We intend to use the net proceeds from this offering for commercial preparation and launch costs, pending

successful development and a favorable regulatory outcome for our lead product candidate duvelisib, for the continued clinical development of our lead product candidates and to fund working capital, capital expenditures and other general corporate purposes, which may include the acquisition or in-license of additional compounds,

product candidates or technology. See "Use of Proceeds" on page S-7.

Risk factors You should read the "Risk Factors" section of this prospectus supplement and in the documents 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.

The 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 50,967,973 shares of our common stock outstanding as of March 31, 2018, plus:

- · 8,944,444 shares of our common stock issued pursuant to a shelf registration statement filed with the SEC that became effective on April 24, 2017 (Registration No. 333-217048) and a related prospectus supplement filed with the SEC and dated May 16, 2018; and
- 6,314,410 shares of our common stock issued pursuant to our at-the-market equity offering program since March 31, 2018.

The number of shares of our common stock outstanding after this offering as reflected above does not include:

- 10,818,454 shares of our common stock issuable upon the exercise of stock options outstanding under our equity incentive plans, as of March 31, 2018, at a weighted average price of \$4.79 per share;
- · 166,250 shares of our common stock issuable pursuant to unvested restricted stock units outstanding as of March 31, 2018; and
- · 702,118 shares of our common stock available for future issuance as of March 31, 2018 under our 2012 equity incentive plan, plus up to a maximum of 68,591 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.

Unless otherwise stated, all information in this prospectus supplement excludes the shares referenced in the bullets immediately above.

S-4

Table of Contents

RISK FACTORS

An investment in our common stock involves significant risks. Before making an investment in our common stock, you should carefully read all of the information contained in this prospectus supplement, the accompanying prospectus and in the documents incorporated by reference herein. For a discussion of risks that you should carefully consider before deciding to purchase any of our common stock, please review the risk factors disclosed below, together with the other information in this prospectus supplement, the accompanying prospectus, and the information and documents incorporated by reference herein and

therein, including "Item 1A. Risk Factors" included in our Annual Report on Form 10-K for the year ended December 31, 2017. Any of these risks, as well as additional risks not currently known to us or that we currently deem immaterial, may adversely affect our business, financial condition, results of operations, and prospects, resulting in a decline in the trading price of our common stock and loss of all or part of your investment.

Additional Risks Related to This Offering and Our Common Stock

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 commercial preparation and launch costs, pending successful development and a favorable regulatory outcome for our lead product candidate duvelisib, for the continued clinical development of our lead product candidates and to fund working capital, capital expenditures and other general corporate purposes, which may include the acquisition or in-license of additional compounds, product candidates or technology. 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 of 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."

Investors who purchase the common stock sold 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 this offering, any investor who purchases 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 and could also make it difficult for us to raise additional capital by selling stock.

S-5

Table of Contents

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 about our strategy, future operations, future financial position, future plans and prospects, including statements regarding the development and activity of our investigational product candidates, including duvelisib and defactinib, and our PI3K and FAK programs generally, the structure of our planned or pending clinical trials, the timeline and indications for clinical development and regulatory approval of our product candidates, the expected timing for the reporting of data from ongoing trials, additional planned studies, our rights to develop or commercialize our product candidates and our ability to finance contemplated development and commercialization activities and fund operations for a specified period. The words "anticipate," "believe," "estimate," "expect," "intend," "may," "plan," "predict," "project," "target," "potential," "will," "would," "could," "continue," and similar expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words. Each forward-looking statement is subject to risks and uncertainties that could cause actual results to differ materially from those expressed or implied in such statement. Applicable risks and uncertainties include the risks that approval of our New Drug Application for duvelisib will not occur on the expected timeframe or at all, including by the U.S. Food and Drug Administration's target action date; that a filing of a marketing authorization application to the European Medicines Agency may not be achieved in fiscal year 2019 or at all; that we may not enter into any partnerships or collaborations for the potential commercialization of duvelisib outside of the United States; that the full data from the Phase 3 DUOTM study will not be consistent with the previously presented results of the study; that the preclinical testing of our product candidates and preliminary or interim 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 expected, including for the Phase 3 DUO study; that even if data from clinical trials is positive, regulatory authorities may require additional studies for approval or may approve for indications or patient populations that are not as broad as intended and the product may not prove to be safe and effective or may require labeling with use or distribution restrictions; that the degree of market acceptance of product candidates, if approved, may be lower than expected; that the timing, scope and rate of reimbursement for our product candidates is uncertain; that there may be competitive developments affecting our product candidates; that data may not be available when expected; that enrollment of clinical trials may take longer than expected; that our product candidates will cause unexpected safety events or result in an unmanageable safety profile as compared to their level of efficacy; that duvelisib will be ineffective at treating patients with lymphoid malignancies; that we will be unable to successfully initiate or complete the clinical development and eventual commercialization of our product candidates; that the development and commercialization of our product candidates will take longer or cost more than planned; that we may not have sufficient cash to fund our contemplated operations; that we or Infinity Pharmaceuticals, Inc. will fail to fully perform under the duvelisib license agreement; that we may be unable to make additional draws under our debt facility or obtain adequate financing in the future through product licensing, co-promotional arrangements, public or private equity, debt financing or otherwise; that we will not pursue or submit regulatory filings for our product candidates, including for duvelisib in patients with CLL/SLL or iNHL; and that our product candidates will not receive regulatory approval, become commercially successful products, or result in new treatment options being offered to patients.

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 we make. In particular, you should consider the numerous risks described in the "Risk Factors" section of this prospectus supplement and the accompanying prospectus.

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

S-6

Table of Contents

USE OF PROCEEDS

We estimate that the net proceeds we will receive from this offering will be approximately \$42.8 million, after deducting estimated offering expenses payable by us.

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

- · commercial preparation and launch costs, pending successful development and a favorable regulatory outcome for our lead product candidate duvelisib;
- · the continued clinical development of our lead product candidates; and
- the balance to fund working capital, capital expenditures and other general corporate purposes, which may include the acquisition or in-license of additional compounds, product candidates or technology.

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 2019. 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.

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.

S-7

Table of Contents

PLAN OF DISTRIBUTION

We have agreed to sell directly to Consonance Capital Master Account L.P. and P Consonance Opportunities Ltd. 7,166,666 shares of our common stock at a price of \$6.00 per share. No underwriters or agents were engaged by us for this transaction. We estimate the total expenses of this offering that will be payable by us to be approximately \$0.2 million.

We have entered into a purchase agreement directly with the investors in connection with this offering. The purchase agreement contains customary representations, warranties and covenants for transactions of this type. These representations, warranties and covenants were made solely for purposes of the purchase agreement and should not be relied upon by any of our investors who are not parties to the agreement, nor should any such investor rely upon any descriptions thereof as characterizations of the actual state of facts or conditions. Such investors are not third party beneficiaries under the purchase agreement.

We expect to deliver the shares of common stock being offered pursuant to this prospectus supplement on or about June 18, 2018.

S-8

Table of Contents

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, persons subject to special tax accounting rules as a result of any item of gross income with respect to our common stock being taken into account in an applicable financial statement 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 and certain determinations made at the partner level. 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.

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.

S-9

Table of Contents

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" and "Information reporting and backup withholding."

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 the then applicable 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 certain circumstances, be subject to an additional "branch profits tax" at the then applicable rate (unless reduced by an applicable income tax treaty) on 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" and "Information reporting and backup withholding," 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);

S-10

Table of Contents

- (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 non-U.S. holder may, under certain circumstances, also be subject to an additional "branch profits tax" at the then applicable rate (or at a lower rate under an applicable income tax treaty) on its effectively connected earnings and profits.

If the second exception applies, the non-U.S. holder generally will be subject to United States federal income tax at the then applicable rate (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.

Additional withholding and reporting requirements

Legislation (commonly referred to as "FATCA") imposes United States federal withholding tax 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 have been satisfied (generally relating to ownership by U.S. persons of interests in or accounts with those entities) or an exemption applies. The withholding rules applicable to payments of dividends on our common stock currently apply. The withholding rules will apply to gross proceeds from dispositions of our common stock beginning January 1, 2019. 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

S-11

Table of Contents

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.

S-12

Table of Contents

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 later file 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 this prospectus supplement. We hereby incorporate by reference the following documents:

- · Our Annual Report on Form 10-K for the year ended December 31, 2017, as filed with the SEC on March 13, 2018;
- · Our Quarterly Report on Form 10-Q for the quarterly period ended March 31, 2018, as filed with the SEC on May 3, 2018;
- · Our Definitive Proxy Statement on Schedule 14A, filed with the SEC on April 10, 2018 (excluding those portions that are not incorporated by reference into our Annual Report on Form 10-K for the year ended December 31, 2017);
- · Our Current Reports on Form 8-K filed with the SEC on January 4, 2018, May 18, 2018, May 22, 2018, June 1, 2018, and June 8, 2018; and
- · The 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 13 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 or the accompanying prospectus.

LEGAL MATTERS

The validity of the shares of common stock offered hereby is being passed upon for us by, Ropes & Gray LLP, Boston, Massachusetts.

EXPERTS

The consolidated financial statements of Verastem, Inc. appearing in Verastem, Inc.'s Annual Report (Form 10-K) for the year ended December 31, 2017 and the effectiveness of Verastem, Inc.'s internal control over financial reporting as of December 31, 2017 have been audited by Ernst & Young LLP, independent registered public accounting firm, as set forth in their reports thereon (which contain an explanatory paragraph describing conditions that raise substantial doubt about the Company's ability to continue as a going concern as described in Note 1 to the consolidated financial statements), appearing elsewhere therein, and incorporated herein by reference. Such consolidated financial statements are incorporated herein by reference upon such reports given on the authority of such firm as experts in accounting and auditing.

S-13



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.

Investing in our securities involves a high degree of risk. Before making an investment decision, please read the information under the heading "Risk Factors" beginning on page 7 of this prospectus and in the documents incorporated by reference into this prospectus.

Our common stock is listed on The NASDAQ Global Market under the symbol "VSTM." On March 29, 2017, the last reported sale price of our common stock was \$2.05 per share.

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 April 24, 2017

Table of Contents

TABLE OF CONTENTS

	Page
About this Prospectus	3
<u>Our Company</u>	4
Risk Factors	5
Forward-Looking Statements	6
<u>Use of Proceeds</u>	7
Ratio of Earnings to Fixed Charges	8
Plan of Distribution	9
Description of Common Stock	11
Description of Preferred Stock	13
Description of Warrants	14
Description of Debt Securities	15
Where You Can Find More Information	21

<u>Legal Matters</u>	23
<u>Experts</u>	23

i

22

Table of Contents

Incorporation of Certain Documents by Reference

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 prospectus, 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.

3

Table of Contents

OUR COMPANY

We are a biopharmaceutical company focused on discovering and developing drugs to improve outcomes for patients with cancer. Our most advanced product candidates, duvelisib and defactinib (VS-6063), utilize a multi-faceted approach to treat cancers originating either in the blood or major organ systems. We are currently evaluating these compounds in both preclinical and clinical studies as potential therapies for certain cancers, including leukemia, lymphoma, lung cancer, ovarian cancer, mesothelioma, and pancreatic cancer. We believe that these compounds may be beneficial as therapeutics either as single agents or when used in combination with immuno-oncology agents or other current and emerging standard of care treatments in aggressive cancers that are poorly served by currently available therapies.

Duvelisib targets the Phosphoinositide 3-kinase (PI3K) and defactinib targets the Focal Adhesion Kinase ("FAK") signaling pathways. The PI3K signaling pathway plays a central role in cancer proliferation and survival. Duvelisib is an investigational oral therapy designed to attack both malignant B-cells and T-cells and disrupt the tumor microenvironment to help thwart their growth and proliferation for patients with lymphatic cancers through the dual inhibition of PI3K delta and gamma. FAK is a non-receptor tyrosine kinase encoded by the PTK-2 gene that is involved in cellular adhesion and, in cancer, metastatic capability. Defactinib is a targeted inhibitor of the FAK signaling pathway. Similar to duvelisib, defactinib is also orally available and designed to be a potential therapy for patients to take at home under the advice of their physician.

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 2017, 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, hormonal therapy, immunotherapy, and targeted therapy. The cancer death rate in the United States has only decreased modestly since the early 1990s. Despite years of intensive research and clinical use, current treatments often fail to cure

With the application of new technologies and key discoveries, we believe that we are now entering an era of cancer research characterized by a more sophisticated understanding of the biology of cancer. We believe that the potential of oral, targeted therapies, along with the rapidly advancing field of immunotherapy, or using the body's immune system to fight cancer, are important new insights that present the opportunity to develop more effective cancer treatments. Our goal is to develop targeted agents that both specifically kill cancer cells and disrupt the tumor microenvironment to enhance the efficacy of cancer treatment.

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.

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.

5

Table of Contents

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 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. Such statements relate to, among other things, the development of our product candidates, including duvelisib, defactinib (VS-6063), VS-4718 and VS-5584, and our FAK, PI3K, and mTOR 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, 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 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 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, 2016 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."

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.

6

Table of Contents

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.

7

Table of Contents

RATIO OF EARNINGS TO FIXED CHARGES

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.

	December 31,				
	2016	2015	2014	2013	2012
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 any of the years ended December 31, 2016, 2015, 2014, 2013 or 2012. 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 year ended December 31, 2016, the year ended December 31, 2015, the year ended December 31, 2014, the year ended December 31, 2013, and the year ended December 31, 2012

was approximately \$36.4 million, \$57.9 million, \$53.4 million, \$41.2 million, and \$32.0 million, respectively.

Table of Contents

PLAN OF DISTRIBUTION

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

- · through one or more underwriters;
- through dealers, who may act as agents or principal (including a block trade in which a broker or dealer so engaged will attempt to sell the shares as agent but may position and resell a portion of the block as principal to facilitate the transaction);
- through one or more agents;
- through registered direct offerings;
- · as part of a collaboration with a third party;
- · as part of an acquisition or merger with a third party;
- through at-the-market issuances;
- in privately negotiated transactions; 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, as applicable:

- · the terms of the securities being offered, including the public offering price of the securities and the proceeds to us;
- · the name or names of any underwriters, dealers or agents and the amounts of securities underwritten or purchased by each of them;
- · any underwriting discounts and commissions or agency fees and other items constituting underwriters' or agents' compensation;
- · any options under which underwriters may purchase additional securities from us;
- · any discounts or concessions allowed or reallowed or paid to dealers; and
- · any securities exchanges on which the securities may be listed.

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 a specified date in the future. 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.

9

Table of Contents

We may indemnify agents, underwriters, dealers, or other third parties who participate in the distribution of securities against certain liabilities, including liabilities under the Securities Act, and agree to contribute to payments which these agents, underwriters, dealers, or other third parties may be required to make. Agents, underwriters, dealers 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 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.

10

Table of Contents

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 March 15, 2017, we had 36,992,418 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 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.

11

Table of Contents

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."

12

Table of Contents

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 March 15, 2017, 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;
- 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.

13

Table of Contents

DESCRIPTION OF WARRANTS

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;
- \cdot 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;
- \cdot the anti-dilution provisions of the warrants, if any;
- · any redemption or call provisions;
- \cdot 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.

14

Table of Contents

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, are 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;
- · 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;
- 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;

15

Table of Contents

- 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
- · "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.

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 depositary for the global securities or the nominee of the depositary, and the global securities will be delivered by the trustee to the depositary for credit to the accounts of the holders of beneficial interests in the debt securities.

16

Table of Contents

The prospectus supplement will describe the specific terms of the depositary 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
- · 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 of 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

17

Table of Contents

· 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.

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;

18

Table of Contents

- · 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;
- · 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 an 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.

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;
- 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

Table of Contents

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 any applicable supplemental indenture after a covenant defeasance of the indenture and any 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.

20

Table of Contents

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.

21

Table of Contents

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, 2016, as filed with the SEC on March 23, 2017;
- · Our Current Report on Form 8-K filed with the SEC on November 2, 2016, as amended on January 11, 2017; 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 13 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. 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.

22

Table of Contents

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, 2016 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.

23

Table of Contents

7,166,666 shares



Common Stock
PROSPECTUS SUPPLEMENT