Verastem, Inc.
Form 424B2
December 18, 2017
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Filed Pursuant to Rule 424(b)(2)
Registration No. 333-217048

Prospectus Supplement

(To Prospectus dated April 24, 2017)

8,422,877 Shares

Common Stock

We are offering 8,422,877 shares of our common stock. Our common stock is listed on The Nasdaq Global Market under the symbol VSTM. On December 13, 2017, the last reported sale price of our common stock on The Nasdaq Global Market was $3.80 per share.

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

Investing in our common stock involves a high degree of risk. 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.

The underwriter has agreed to purchase shares of common stock from us at a price of $2.97 per share, which will result in approximately $25.0 million of proceeds to us before expenses. The underwriter proposes to offer the shares of common stock from time to time for sale in one or more transactions on Nasdaq, in the over-the-counter market, through negotiated transactions or otherwise, at market prices prevailing at the time of sale, at prices related to prevailing market prices or at negotiated prices, subject to receipt and acceptance by it and subject to its right to reject any order in whole or in part. We have agreed to reimburse the underwriter for certain expenses in connection with this offering. See Underwriting.

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.

Delivery of the shares of common stock is expected to be made on or about December 19, 2017.

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Prospectus Supplement dated December 14, 2017

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PROSPECTUS SUPPLEMENT

PROSPECTUS

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ABOUT THIS PROSPECTUS SUPPLEMENT

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

We have not authorized any dealer, agent or other person to give any information or to make any representation other than those contained or incorporated by reference in this prospectus supplement and the accompanying prospectus or in any related free writing prospectus filed by us with the SEC. Neither we nor the underwriter has 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.

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PROSPECTUS SUPPLEMENT SUMMARY

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

Company Overview

We are a biopharmaceutical company focused on discovering and developing drugs to improve outcomes for patients with cancer. Our most advanced product candidates, duvelisib and defactinib (VS-6063), 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, and defactinib targets the Focal Adhesion Kinase, or 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. Duvelisib has orphan drug designation for patients with chronic lymphocytic leukemia, or CLL, small lymphocytic lymphoma, or SLL, and follicular lymphoma, or FL, in the United States and European Union. 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 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 cancer.

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.

Recent Developments

The following is a summary of selected key developments affecting our business that have occurred since September 30, 2017.

Phase 3 DUO Results

In December 2017, we reported the results from our Phase 3 DUO study evaluating the efficacy and safety of duvelisib, a first in class oral dual inhibitor of PI3K-delta and PI3K-gamma, in patients with relapsed or refractory CLL/SLL. In the DUO study, 319 patients were randomized 1:1 to receive either duvelisib 25 mg orally twice daily or ofatumumab monotherapy, an approved standard of care treatment for use in CLL, per its label with an initial infusion of 300 mg followed by seven weekly infusions and four monthly infusions of 2,000 mg. In addition to the primary endpoint of Progression-Free Survival, or PFS, per the Independent Review Committee, or IRC, in the ITT population, additional analyses to evaluate the outcome in several patient subgroups, including those with 17p deletion CLL/SLL, a known poor prognostic subgroup, were also conducted. PFS and other efficacy endpoints were analyzed using response determinations per the IRC using the international workshop on CLL/National Cancer Institute Work-Group Criteria, or iwCLL/IWG criteria.

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DUO Efficacy Results

The DUO study met its primary endpoint with oral duvelisib monotherapy achieving a statistically significant improvement in PFS compared to ofatumumab in patients with relapsed or refractory CLL/ SLL per a blinded IRC using iwCLL/IWG Criteria (median PFS=13.3 months versus 9.9 months, respectively; HR=0.52, p<0.0001), representing a 48% reduction in the risk of progression or death. Similar efficacy of duvelisib was observed regardless of whether patients had 17p deletion, or del[17p]. The primary outcome of PFS via IRC review in the del[17p] subgroup significantly favored duvelisib over ofatumumab (median PFS=12.7 months versus 9.0 months, respectively; HR=0.41, p=0.0011), representing a 59% reduction in the risk of progression or death. Per investigator assessment, duvelisib demonstrated an mPFS of 17.6 months, compared to 9.7 months for ofatumumab (HR=0.40, p<0.0001). Duvelisib maintained a PFS advantage in all patient subgroups analyzed as a subset of pre-specified sensitivity analyses.

The secondary efficacy outcome of Overall Response Rate, or ORR, via IRC assessment according to iwCLL/IWG Criteria, significantly favored duvelisib over ofatumumab, 73.8% versus 45.3%, respectively (p<0.0001), and reduced lymph node burden >50% in most patients compared to ofatumumab, 85% versus 16%, respectively. In the del[17p] subpopulation of patients, ORR was also significantly higher for duvelisib compared to ofatumumab, 70.0% versus 43.0%, respectively (p=0.0182). The Overall Survival, or OS, in the ITT population was observed to be nearly identical to those randomized to duvelisib and to ofatumumab during the study (HR=0.99, p=0.4807). Patients who progressed in the DUO study were given the option to enroll in a crossover study to receive the opposite treatment. In the optional crossover study, 89 patients who were previously treated with ofatumumab in DUO and experienced disease progression were subsequently treated with duvelisib monotherapy. As in the parent DUO study, duvelisib demonstrated robust clinical activity in this crossover study with an ORR of 73%, a median duration of response of 12.7 months and an mPFS of 15 months by investigator assessments.

DUO Safety Results

Duvelisib as a monotherapy showed a manageable safety profile, with results from this study consistent with the well-characterized safety profile of duvelisib monotherapy in patients with advanced hematologic malignancies in previous studies. For duvelisib-treated patients, the median time on treatment was 50.3 weeks (range, 0.9 - 160.0) compared to 23.1 weeks (range, 0.1 - 26.1) for ofatumumab. The most common Grade ≥3 treatment-emergent hematologic adverse events (occurring in >10% of patients) were neutropenia (30%) and anemia (13%). The most common Grade ≥3 non-hematologic treatment-emergent adverse events (occurring in >10% of patients) were diarrhea (15%), pneumonia (14%) and colitis (12%). The rate of severe opportunistic infections was 6%, including two patients (1%) with Pneumocystis jirovecii pneumonia, or PJP, neither of whom was on prophylaxis for PJP at the time of the event. Adverse events led to discontinuation of treatment in 35% of patients; approximately 40% of patients treated with duvelisib remained on treatment for over 18 months, with a median total follow-up of nearly two years. Adverse events of interest infrequently led to discontinuation of duvelisib treatment (*e.g.*, diarrhea (5.1%), colitis (5.1%), pneumonitis (1.9%), neutropenia (1.3%), pneumonia (1.3%), transaminase elevations (0.6%) and rash (0.6%)). Duvelisib treatment-related adverse events leading to death (n=4) include general physical health deterioration (n=1), pneumonia staphylococcal (n=2) and sepsis (n=1).

We plan to submit a new drug application, or NDA, to the U.S. Food and Drug Administration, or the FDA, requesting 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. We expect to submit the duvelisib NDA during the first quarter of 2018. Along with the clinical data from the DUO study, the duvelisib NDA submission will also contain the results from the Phase 2 DYNAMO study in patients with indolent non-Hodgkin s lymphoma that are double-refractory to both rituximab and chemotherapy or radioimmunotherapy.

At-the-Market Offering Program

On March 30, 2017, we entered into a Controlled Equity Offering℠ 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. Since September 30, 2017, we have sold 2,105,501 shares of our common stock pursuant to this program and have received proceeds of approximately $8.7 million, net of commissions paid. As of December 13, 2017, we had 42,114,390 shares of common stock outstanding.

Corporate Information

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

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THE OFFERING

Common stock offered by us	8,422,877 shares
Common stock to be outstanding after this offering	48,367,905 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 candidates, for the continued clinical development of our lead product candidates and to fund working capital, capital expenditure 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-32.
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 39,945,028 shares of our common stock outstanding as of September 30, 2017, and excludes:

- 8,431,355 shares of our common stock issuable upon the exercise of stock options outstanding under our equity incentive plans, as of September 30, 2017, at a weighted average price of $5.08 per share;

- 1,043,130 shares of our common stock available for future issuance as of September 30, 2017 under our 2012 equity incentive plan, plus up to a maximum of 78,591 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; and

- 2,105,501 shares of our common stock issued pursuant to our at-the-market equity offering program since September 30, 2017.

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

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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. 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.

Risks Related to the Discovery, Development and Commercialization of Our Product Candidates

Preclinical testing and clinical trials of our product candidates may not be successful. ***In the near term, we are dependent on the success of our PI3K inhibitor program. If we are unable to complete the clinical development of, obtain marketing approval for or successfully commercialize duvelisib, or any of our other product candidates or if we experience significant delays in doing so, our business may be materially harmed.***

We have invested a significant portion of our efforts and financial resources in the research and development of our product candidates, including duvelisib and defactinib, for which we are conducting clinical trials in multiple indications. Our ability to generate product revenues will depend heavily on the successful development and potential commercialization of our product candidates. The success of our product candidates will depend on several factors, including the following:

- initiation and successful enrollment and completion of our clinical trials;
- receipt of marketing approvals from the FDA and other regulatory authorities for our product candidates, including pricing approvals where required;
- establishing commercial manufacturing capabilities or making arrangements with third-party manufacturers;
- obtaining and maintaining patent and trade secret protection and regulatory exclusivity for our product candidates;

- establishing commercial capabilities, including hiring and training a sales force, and launching commercial sales of the products, if and when approved, whether alone or in collaboration with others;

- acceptance of the products, if and when approved, by patients, the medical community and third-party payors;

- effectively competing with other therapies; and

- a continued acceptable safety and efficacy profile of the products following approval.

Many of these factors are beyond our control, including clinical development, the regulatory submission process, potential threats to our intellectual property rights and the manufacturing, marketing and sales efforts of any collaborator. If we do not achieve one or more of these factors in a timely manner or at all, we could experience significant delays or an inability to successfully commercialize our product candidates, which would materially harm our business.

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

If any of our product candidates receive marketing approval, they may nonetheless fail to gain sufficient market acceptance by physicians, patients, healthcare payors and others in the medical community. If our product candidates do not achieve an adequate level of acceptance, or if we are unable to increase market acceptance of our products as compared to existing or competitive products, we may not generate significant product revenues and we may not become profitable. In addition, clinical studies of duvelisib showed side effects that may need to be managed to be profitable. The degree of market acceptance of our product candidates, if approved for commercial sale, will depend on a number of factors, including:

- efficacy and potential advantages compared to alternative treatments;

- the ability to offer our products for sale at competitive prices;

- convenience and ease of administration compared to alternative treatments;

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- the willingness of the target patient population to try new therapies and of physicians to prescribe these therapies;

- the line of therapy our products are designated under physician treatment guidelines;

- changes in the standard of care for the targeted indications for our products;

- limitations or warnings, including distribution or use restrictions, contained in the approved labeling for any of our products;

- the strength of marketing and distribution support;

- sufficient third-party coverage or reimbursement;

- the ability of the medical community to appropriately recognize and manage side effects;

- safety concerns with similar products marketed by others; and

- the prevalence and severity of any side effects as a result of treatment with our product candidates.

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

Before obtaining marketing approval from regulatory authorities for the sale of our product candidates, we must complete extensive clinical trials to demonstrate the safety and efficacy of our product candidates in humans. Clinical testing is expensive, difficult to design and implement, can take many years to complete and is uncertain as to outcome. A failure of one or more clinical trials can occur at any stage of testing. The outcome of preclinical testing and early clinical trials may not be predictive of the success of later clinical trials, and interim results of a clinical trial do not necessarily predict final results. For example, a further review and analysis of this data may change the conclusions drawn from this unaudited data indicating less promising results than we currently anticipate.

In some instances, there can be significant variability in safety and/or efficacy results between different trials of the same product candidate due to numerous factors, including changes in trial protocols, differences in size and type of the patient populations, adherence to the dosing regimen and other trial protocols and the rate of dropout among clinical trial participants. There also may be significant variability in the safety results obtained through the long-term follow-up of patients from ongoing studies. We do not know whether any clinical trial we may conduct or follow-up data we collect will demonstrate consistent or adequate efficacy and/or safety sufficient to obtain regulatory approval to market our product candidates.

In addition, the design of a clinical trial may determine whether its results will support approval of a product and flaws in the design of a clinical trial may not become apparent until the clinical trial is well advanced. Moreover, preclinical and clinical data are often susceptible to varying interpretations and analyses, and many companies that have believed their product candidates performed satisfactorily in preclinical studies and clinical trials have nonetheless failed to obtain marketing approval of their products. Although we view the results from our Phase 3 DUO, Phase 2 DYNAMO and other studies as promising, the FDA or other regulatory authorities may require additional testing to substantiate our claims, which could delay or prevent marketing approval for duvelisib.

A failure of one or more clinical trials could indicate a higher likelihood that subsequent clinical trials of the same product candidate in the same or other indications or subsequent clinical trials of other related product candidates will be unsuccessful for the same reasons as the unsuccessful clinical trials.

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

- regulators or institutional review boards may not authorize us or our investigators to commence a clinical trial or conduct a clinical trial at a prospective trial site;

- we may have delays in reaching or fail to reach agreement on clinical trial contracts or clinical trial protocols with prospective trial sites;

- clinical trials of our product candidates may produce negative or inconclusive results, and we may decide, or regulators may require us, to conduct additional clinical trials or abandon product development programs;

- the number of patients required for clinical trials of our product candidates may be larger than we anticipate, enrollment in these clinical trials may be slower than we anticipate or participants may drop out of these

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clinical trials at a higher rate than we anticipate;

- our third-party contractors may fail to comply with regulatory requirements or meet their contractual obligations to us in a timely manner, or at all;

- regulators or institutional review boards may require that we or our investigators suspend or terminate clinical trials for various reasons, including noncompliance with regulatory requirements or a finding that the participants are being exposed to unacceptable health risks;

- the cost of clinical trials of our product candidates may be greater than we anticipate;

- the supply or quality of our product candidates or other materials necessary to conduct clinical trials of our product candidates may be insufficient or inadequate; and

- our product candidates may have undesirable side effects or other unexpected characteristics, causing us or our investigators, regulators or institutional review boards to suspend or terminate the trials.

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

- be delayed in obtaining marketing approval for our product candidates;

- not obtain marketing approval at all;

- obtain approval for indications or patient populations that are not as broad as intended or desired;

- obtain approval with labeling that includes significant use or distribution restrictions including imposition of a Risk Evaluation and Mitigation Strategy, or REMS, or safety warnings, including boxed warnings;

- be subject to additional post marketing testing requirements; or

- have the product removed from the market after obtaining marketing approval.

The FDA and foreign regulatory authorities may determine that the results from our ongoing and future trials do not support regulatory approval and may require us to conduct an additional clinical trial or trials. If these agencies take such a position, the costs of development of our product candidates could increase materially and their potential market introduction could be delayed. The regulatory agencies could also require that we conduct additional clinical, nonclinical or manufacturing validation studies and submit that data before it will consider an NDA. Our product development costs will also increase if we experience delays in clinical testing or marketing approvals. We do not know whether any clinical trials will begin as planned, will need to be restructured or will be completed on schedule, or at all. Significant clinical trial delays also could shorten any periods during which we may have the exclusive right to commercialize our product candidates or allow our competitors to bring products to market before we do and impair our ability to successfully commercialize our product candidates and may harm our business and results of operations.

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

We may not be able to initiate or continue clinical trials for our product candidates if we are unable to locate and enroll a sufficient number of eligible patients to participate in these trials as required by the FDA or similar regulatory authorities outside the United States. In addition, there are a number of ongoing clinical trials being conducted by other companies for product candidates treating cancer. Patients who would otherwise be eligible for our clinical trials may instead enroll in clinical trials of our competitors product candidates, particularly if they view such treatments to be more conventional and established.

Patient enrollment is affected by other factors including:

- the size and nature of the patient population;

- severity of the disease under investigation;

- eligibility criteria for the study in question;

- perceived risks and benefits of the product candidate under study in relation to other available treatments including any new treatments that may be approved for the indications we are investigating;

- efforts to facilitate timely enrollment in clinical trials;

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- patient referral practices of physicians;

- the ability to monitor patients adequately during and after treatment; and

- proximity and availability of clinical trial sites for prospective patients.

Furthermore, enrolled patients may drop out of a clinical trial, which could impair the validity or statistical significance of the clinical trial. A number of factors can influence the patient discontinuation rate, including, but not limited to:

- the inclusion of a placebo arm in a trial;

- possible inactivity or low activity of the product candidate being tested at one or more of the dose levels being tested;

- the occurrence of adverse side effects, whether or not related to the product candidate; and

- the availability of numerous alternative treatment options, including clinical trials evaluating competing product candidates, that may induce patients to discontinue their participation in the trial.

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

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

All of our product candidates are in various stages of clinical development and their risk of failure is high. It is impossible to predict when or if any of our product candidates will prove effective or safe in humans or will receive marketing approval. If our product candidates are associated with undesirable side effects or have characteristics that are unexpected, we may need to abandon their development or limit development to certain uses or subpopulations in which the undesirable side effects or other characteristics are less prevalent, less severe or more acceptable

from a risk benefit perspective. Patients in our clinical trials have experienced serious adverse events, or SAEs, deemed by us and the clinical investigator to be related to our product candidates. SAEs generally refer to adverse events, or AEs, that result in death, are life threatening, require hospitalization or prolonging of hospitalization, or cause a significant and permanent disruption of normal life functions, congenital anomalies or birth defects, or require intervention to prevent such outcomes.

Defactinib is in our Phase 1 and Phase 2 clinical trials and the development program continues to progress. The toxicities reported thus far are consistent with other drugs in this class.

As a result of adverse events observed to date, or further safety or toxicity issues that we may experience in our clinical trials in the future, we may not receive approval to market any product candidates, which could prevent us from ever generating revenue from the sale of products or achieving profitability. Results of our trials could reveal an unacceptably high severity and prevalence of side effects. In such an event, our trials could be suspended or terminated and the FDA or comparable foreign regulatory authorities could order us to cease further development of or deny approval of our products candidates for any or all targeted indications.

Many compounds that initially showed promise in early stage testing for treating cancer have later been found to cause side effects that prevented further development of the compound. In addition, while we and our clinical trial investigators currently determine if serious adverse or unacceptable side effects are drug related, the FDA or other non-U.S. regulatory authorities may disagree with our or our clinical trial investigators interpretation of data from clinical trials and the conclusion that a serious adverse effect or unacceptable side effect was not drug related.

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Preclinical studies and preliminary and interim data from clinical trials of our product candidates are not necessarily predictive of the results or success of ongoing or later clinical trials of our product candidates. If we cannot replicate the results from our preclinical studies and clinical trials of our product candidates, we may be unable to successfully develop, obtain regulatory approval for and commercialize our product candidates.

Preclinical studies and any positive preliminary and interim data from our clinical trials of our product candidates may not necessarily be predictive of the results of ongoing or later clinical trials. Even if we are able to complete our planned clinical trials of our product candidates according to our current development timeline, the positive results from clinical trials of our product candidates may not be replicated in subsequent clinical trial results. Also, our later stage clinical trials could differ in significant ways from earlier stage clinical trials, which could cause the outcome of the later stage trials to differ from our earlier stage clinical trials. For example, these differences may include changes to inclusion and exclusion criteria, efficacy endpoints and statistical design. Many companies in the pharmaceutical and biotechnology industries, including us, have suffered significant setbacks in late stage clinical trials after achieving positive results in an earlier stage of development. If we fail to produce positive results in our planned clinical trials of any of our product candidates, the development timeline and regulatory approval and commercialization prospects for our product candidates, and, correspondingly, our business and financial prospects, would be materially adversely affected.

Our approach to the treatment of cancer through the killing of cancer cells and disruption of the tumor micro-environment is unproven, and we do not know whether we will be able to develop any products of commercial value.

We are discovering and developing product candidates to treat cancer by using targeted agents to kill cancer cells or disrupt the tumor microenvironment and thereby thwart their growth and proliferation of cancer cells. Research on the use of small molecules to inhibit PI3K and FAK signaling pathways and disrupt the tumor microenvironment is an emerging field and, consequently, there is uncertainty about whether duvelisib and defactinib are effective in improving outcomes for patients with cancer. With respect to our FAK inhibition program, there is some debate in the scientific community regarding cancer stem cells, or CSCs, the existence of these cells, the defining characteristics of these cells, as well as whether targeting such cells is an effective approach to treating cancer. Some believe that targeting CSCs as part of our multi-faceted approach should be sufficient for a positive clinical outcome, while others believe that, at times or always, the use of FAK inhibitors that reduce CSCs should be coupled with conventional chemotherapies for a positive clinical outcome.

Any products that we develop may not effectively target cancer cells, enhance anti-tumor immunity, or modulate the local tumor microenvironment. While we are currently conducting clinical trials for product candidates that we believe will attack cancer cells through the inhibition of the PI3K or FAK signaling pathways and potentially disrupt the tumor microenvironment, we may not ultimately be successful in demonstrating their efficacy, alone or in combination with other treatments.

The approval of our product candidates as part of a combination therapy for the treatment of certain cancers may be more costly than our prior clinical trials, may take longer to achieve regulatory approval, may be associated with new, more severe or serious and unanticipated adverse events, and may have a smaller market opportunity.

Part of our current business model involves conducting clinical trials to study the effects of combining our product candidates with other approved and investigational targeted therapies, chemotherapies, and immunotherapies to treat patients with cancer. Regulatory approval for a combination treatment generally requires clinical trials to evaluate the activity of each component of the combination treatment. As a result, it may be more difficult and costly to obtain regulatory approval of our product candidate for use as part of a combination treatment than obtaining regulatory approval of our product candidates alone. In addition, we also risk losing the supply of any approved or investigational product being

combined with our product candidate in these clinical trials. Furthermore, the potential market opportunity for our product candidates is difficult to estimate precisely. For instance, if one of our product candidates receives regulatory approval from a combination study, it may be approved solely for use in combination with the approved or investigational product in a particular indication and the market opportunity our product candidate would be dependent upon the continued use and availability of the approved or investigational product. In addition, because physicians, patients and third-party payors may be sensitive to the addition of the cost of our product candidates to the cost of treatment with the other products, we may experience downward pressure on the price that we can charge for our product candidates if they receive regulatory approval. Further, we cannot be sure that physicians will view our product candidates, if approved as part of a combination treatment, as sufficiently superior to a treatment regimen consisting of only the approved or investigational product. Additionally, the adverse side effects of our product candidates may be enhanced when combined with other products. If such adverse side effects are experienced, we could be required to conduct additional pre-clinical and clinical studies and if such adverse side effects are severe, we may not be able to continue the clinical trials of the combination therapy because the risks may outweigh the therapeutic benefit of the combination.

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

Part of our strategy involves identifying or discovering product candidates. Our research programs may initially show promise in identifying potential product candidates, yet fail to yield product candidates for clinical development for a number of reasons, including:

- the research methodology used may not be successful in identifying potential product candidates;

- potential product candidates may, on further study, be shown to have harmful side effects or other characteristics that indicate that they are unlikely to be products that will receive marketing approval and achieve market acceptance; or

- potential product candidates may not be effective in treating their targeted diseases.

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

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

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

We may seek to acquire new compounds and product candidates from other pharmaceutical and biotechnology companies, academic scientists and other researchers, such as our recent exclusive in-license from Infinity Pharmaceuticals, Inc., or Infinity, to research, develop, commercialize, and manufacture products in oncology indications containing duvelisib. The success of this strategy depends partly upon our ability to identify, select, discover and acquire promising pharmaceutical product candidates and products. The process of proposing, negotiating and implementing a license or acquisition of a product candidate or approved product is lengthy and complex. Other companies, including some with substantially greater financial, marketing and sales resources, may compete with us for the license or acquisition of product candidates and approved products. In addition, companies that perceive us to be a competitor may be unwilling to assign or license rights to us. We have limited resources to identify and execute the acquisition or in-licensing of third-party products, businesses and technologies and integrate them into our current infrastructure. Moreover, we may devote resources to potential acquisitions or in-licensing opportunities that are never completed, or we may fail to realize the anticipated benefits of such efforts. We also may be unable to license or acquire the relevant compound or product candidate on terms that would allow us to make an appropriate return on our investment. Any product candidate that we acquire may require additional development efforts prior to commercial sale, including manufacturing, pre-clinical testing, extensive clinical testing and approval by the FDA and applicable foreign regulatory authorities. All product candidates are prone to risks of failure typical of pharmaceutical product development.

In addition, future product or business acquisitions may entail numerous operational and financial risks, including:

- exposure to unknown liabilities;
- disruption of our business and diversion of our management s time and attention to develop acquired products, product candidates or technologies;
- higher than expected acquisition and integration costs;
- increased amortization expenses; and
- incurrence of substantial debt, dilutive issuances of securities or depletion of cash to pay for acquisitions.
- Future business acquisitions may also entail certain additional risks, such as:
- difficulty in combining the operations and personnel of any acquired businesses with our operations and personnel;
- impairment of relationships with key suppliers or customers of any acquired businesses due to changes in management and ownership; and
- inability to motivate key employees of any acquired businesses.

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If we fail to obtain regulatory approval in jurisdictions outside the United States, we will not be able to market our products in those jurisdictions.

We intend to seek regulatory approval for our product candidates in a number of countries outside of the United States and expect that these countries will be important markets for our products, if approved. Marketing our products in these countries will require separate regulatory approvals in each market and compliance with numerous and varying regulatory requirements. The regulations that apply to the conduct of clinical trials and approval procedures vary from country to country and may require additional testing. Moreover, the time required to obtain approval may differ from that required to obtain FDA approval. In addition, in many countries outside the United States, a drug must be approved for reimbursement before it can be approved for sale in that country. Approval by the FDA does not ensure approval by regulatory authorities in other countries or jurisdictions, and approval by one foreign regulatory authority does not ensure approval by regulatory authorities in other foreign countries or by the FDA. Failure to obtain regulatory approval in one country may have a negative effect on the regulatory approval process in others. The foreign regulatory approval process may include all of the risks associated with obtaining FDA approval. We may not obtain foreign regulatory approvals on a timely basis, if at all. We may not be able to file for regulatory approvals and may not receive necessary approvals to commercialize our products in any foreign market.

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

Because we have limited financial and managerial resources, we focus on research programs and product candidates that we identify for specific indications. As a result, we may forego or delay pursuit of opportunities with other product candidates or for other indications that later prove to have greater commercial potential. Our resource allocation decisions may cause us to fail to capitalize on viable commercial products or profitable market opportunities. Our spending on current and future research and development programs and product candidates for specific indications may not yield any commercially viable products.

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

We do not have a sales or marketing infrastructure and have limited experience in the sale, marketing or distribution of pharmaceutical products. To achieve commercial success for any approved product, we must either develop a sales and marketing organization or outsource these functions to third parties. In the future, we may choose to build a focused sales and marketing infrastructure to market or co-promote some of our product candidates if and when they are approved.

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

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

- our inability to recruit and retain adequate numbers of effective sales and marketing personnel;

- the inability of sales personnel to obtain access to physicians or persuade adequate numbers of physicians to prescribe any future products;

- the lack of complementary products to be offered by sales personnel, which may put us at a competitive disadvantage relative to companies with more extensive product lines; and

- unforeseen costs and expenses associated with creating an independent sales and marketing organization.

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

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

The development and commercialization of new drug products is highly competitive. We face competition with respect to our current product candidates and will face competition with respect to any product candidates that we may seek to develop or commercialize in the future, from major pharmaceutical companies, specialty pharmaceutical companies and biotechnology companies worldwide. There are a number of large pharmaceutical and biotechnology companies that currently market and sell products or are pursuing the development of products for the treatment of the disease indications for which we are developing our product candidates, including Gilead Sciences, Inc., Abbvie, Pharmacyclics LLC, Roche, Celgene Corporation, AstraZeneca, Incyte Corporation, TG Therapeutics, Inc., Novartis and others. Some of these competitive products and therapies are based on scientific approaches that are the same as or similar to our approach, and others are based on entirely different approaches. Potential competitors also include academic institutions, government agencies and other public and private research organizations that conduct research, seek patent protection and establish collaborative arrangements for research, development, manufacturing and commercialization.

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

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

In addition, to the extent that product or product candidates of our competitors demonstrate serious adverse side effects or are determined to be ineffective in clinical trials, the development of our product candidates could be negatively impacted.

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

The regulations that govern marketing approvals, pricing and reimbursement for new drug products vary widely from country to country. In the United States, recently passed legislation may significantly change the purchase of pharmaceutical products, resulting in lower prices and a reduction in product demand. Some countries require approval of the sale price of a drug before it can be marketed. In many countries, the pricing review period begins after marketing or product licensing approval is granted. In some foreign markets, prescription pharmaceutical pricing remains subject to continuing governmental control even after initial approval is granted.

As a result, we might obtain marketing approval for a product in a particular country, but then be subject to price regulations that delay our commercial launch of the product, possibly for lengthy time periods, and negatively impact the revenues we are able to generate from the sale of the product in that country. Adverse pricing limitations may hinder our ability to recoup our investment in one or more product candidates, even if our product candidates obtain marketing approval.

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

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not available or reimbursement is available only to limited levels, we may not be able to successfully commercialize any product candidate for which we obtain marketing approval.

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

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

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

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

- loss of revenue; and

- the inability to commercialize any products that we may develop.

We currently hold $10.0 million in product liability insurance coverage in the aggregate, with a per incident limit of $10.0 million, which may not be adequate to cover all liabilities that we may incur. We may need to increase our insurance coverage as we initiate additional clinical trials in the United States and around the world or upon the commercialization of our product candidates, if ever. Insurance coverage is increasingly expensive. We may not be able to maintain insurance coverage at a reasonable cost or in an amount adequate to satisfy any liability that may arise.

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

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

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

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

Risks Related to Our License Agreement with Infinity

If we do not realize the anticipated benefits of our license agreement with Infinity for the duvelisib program, our business could be adversely affected.

Our license agreement with Infinity for the duvelisib program may fail to further our business strategy as anticipated or to achieve anticipated benefits and success. We may make or have made assumptions relating to the impact of the acquisition of the duvelisib program on our financial results relating to numerous matters, including:

- transaction and integration costs;
- the cost of development and commercialization of duvelisib products; and
- other financial and strategic risks related to the license agreement with Infinity.

Further, we may incur higher than expected operating, transaction and integration costs, and we may encounter general economic and business conditions that adversely affect us relating to our license agreement with Infinity. If one or more of these assumptions are incorrect, it could have an adverse effect on our business and operating results, and the benefits from our license agreement with Infinity for the duvelisib program may not be realized or be of the magnitude expected. For instance, if the results of the DUO study fail to meet certain pre-specified criteria we may not be able to receive regulatory approval of duvelisib.

Risks Related to Our Financial Position and Need for Additional Capital

We require additional financing to execute our operating plan and continue to operate as a going concern.

Our unaudited condensed consolidated financial statements for the quarter ended September 30, 2017 have been prepared assuming we will continue to operate as a going concern, but we believe that our continuing operating losses raise substantial doubt about our ability to continue as

such. Because we continue to experience net operating losses, our ability to continue as a going concern is subject to our ability to obtain necessary capital from outside sources, including obtaining additional capital from the sale of our securities or assets, obtaining loans from financial institutions or entering into partnership arrangements. Our continued net operating losses increase the difficulty in obtaining such capital, and there can be no assurances that we will be able to obtain such capital on favorable terms or at all. If we are unable to obtain sufficient capital from the sale of our securities or from alternative sources, we may be required to reduce, defer, or discontinue certain or all of our research and development activities, including discontinuing development of duvelisib and defactinib, or we may not be able to continue as a going concern.

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

Since inception, we have incurred significant operating losses. As of September 30, 2017, we had an accumulated deficit of $284.9 million. To date, we have not generated any revenues and have financed our operations through private placements of our preferred stock, public offerings of our common stock, and sales of our common stock pursuant to our at-the-market equity offering programs. The proceeds of our term loan facility with Hercules, which we entered into in March 2017, will be used for our ongoing research and development programs and for general corporate purposes. We have devoted substantially all of our efforts to research and development. We expect to continue to incur significant expenses and increasing operating losses for the foreseeable future. The net losses we incur may fluctuate significantly from quarter to quarter. We anticipate that our expenses will increase substantially if and as we:

- prepare our NDA filing for duvelisib and for the anticipated commercialization of duvelisib;

- continue our ongoing clinical trials with our product candidates, including with our most advanced product candidates duvelisib and defactinib;

- initiate additional clinical trials for our product candidates;

- maintain, expand and protect our intellectual property portfolio;

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- acquire or in-license other products and technologies;

- hire additional clinical, development and scientific personnel;

- add operational, financial and management information systems and personnel, including personnel to support our product development and planned future commercialization efforts; and

- establish a sales, marketing and distribution infrastructure to commercialize any products for which we may obtain marketing approval.

To become and remain profitable, we must develop and eventually commercialize a product or products with significant market potential. This will require us to be successful in a range of challenging activities, including completing preclinical testing and clinical trials of our product candidates, obtaining marketing approval for these product candidates and manufacturing, marketing and selling those products for which we may obtain marketing approval. We may never succeed in these activities and, even if we do, may never generate revenues that are significant or large enough to achieve profitability. If we do achieve profitability, we may not be able to sustain or increase profitability on a quarterly or annual basis. Our failure to become and remain profitable would decrease the value of the company and could impair our ability to raise capital, maintain our research and development efforts, expand our business or continue our operations. A decline in the value of our company could also cause you to lose all or part of your investment.

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

We expect our expenses to increase in connection with our ongoing activities, particularly as we continue the clinical development of our product candidates. In addition, as we seek marketing approval for duvelisib on the basis of our clinical studies to date, we expect to incur significant commercialization expenses related to product sales, marketing, manufacturing and distribution. Accordingly, we will need to obtain substantial additional funding in connection with our continuing operations. If we are unable to raise capital when needed or on attractive terms, we would be forced to delay, reduce or eliminate our clinical development programs or commercialization efforts.

We expect that the net proceeds from this offering together with our existing cash, cash equivalents and investments will enable us to fund our current operating plan and capital expenditure requirements into the second half of 2018. Our future capital requirements will depend on many factors, including:

- the scope, progress and results of our ongoing and potential future clinical trials;

- the extent to which we acquire or in-license other product candidates and technologies;

- the costs, timing and outcome of regulatory review of our product candidates (including our efforts to seek approval and fund the preparation and filing of regulatory submissions);

- the costs and timing of future commercialization activities for such product candidates, for which we receive marketing approval;

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

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

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

Conducting clinical trials is a time consuming, expensive and uncertain process that takes years to complete, and we may never generate the necessary data or results required to obtain marketing approval and achieve product sales. In addition, our product candidates, if approved, may not achieve commercial success. Our commercial revenues, if any, will be derived from sales of products that may not be commercially available for several years, if at all. Accordingly, even if we receive regulatory approval of one of our product candidates, it will take several years to achieve peak sales and we will need to continue to rely on additional financing to further our clinical development objectives. Adequate additional financing may not be available to us on acceptable terms, or at all.

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Raising additional capital or entering into certain licensing arrangements may cause dilution to our stockholders, restrict our operations or require us to relinquish rights to our product candidates.

Until such time, if ever, as we can generate substantial product revenues, we expect to finance our cash needs through a combination of equity offerings, debt financings, collaborations, grants and government funding, strategic alliances and licensing arrangements. To the extent that we raise additional capital through the sale of equity or convertible debt, the ownership interest of our existing stockholders will be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect the rights of our existing stockholders. To the extent that we enter into certain licensing arrangements, the ownership interest of our existing stockholders may be diluted if we elect to make certain payments in shares of our common stock. For example, pursuant to the terms of our license agreement with Infinity, we may elect to make certain milestone payments in shares of common stock in lieu of cash, according to a formula set forth in the license agreement. Debt financing, if available, may involve agreements that include covenants limiting or restricting our ability to take specific actions, such as incurring additional debt, making capital expenditures or declaring dividends. For example, see our risk factors under the heading Risks Related to Our Indebtedness.

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

Risks Related to Our Indebtedness

Our level of indebtedness and debt service obligations could adversely affect our financial condition, and may make it more difficult for us to fund our operations.

In March 2017, we entered into a Loan and Security Agreement, or the Loan Agreement, with Hercules. Under the Loan Agreement, Hercules will provide access to term loans with an aggregate principal amount of up to $25.0 million, or the Term Loan. Concurrently with the closing of the Loan Agreement, we borrowed an initial tranche of $2.5 million, and in October 2017, we drew an additional $7.5 million under the Loan Agreement.

All obligations under the Loan Agreement are secured by substantially all of our existing property and assets, excluding our intellectual property. This indebtedness may create additional financing risk for us, particularly if our business or prevailing financial market conditions are not conducive to paying off or refinancing our outstanding debt obligations at maturity. This indebtedness could also have important negative consequences, including:

- we will need to repay our indebtedness by making payments of interest and principal, which will reduce the amount of money available to finance our operations, our research and development efforts and other general corporate activities; and

- our failure to comply with the restrictive covenants in the Loan Agreement could result in an event of default that, if not cured or waived, would accelerate our obligation to repay this indebtedness, and Hercules could seek to enforce our security interest in the assets securing such indebtedness.

To the extent additional debt is added to our current debt levels, the risks described above could increase.

We may not have cash available in an amount sufficient to enable it to make interest or principal payments on its indebtedness when due.

Failure to satisfy our current and future debt obligations under the Loan Agreement, or breaching any of its covenants under the Loan Agreement, subject to specified cure periods with respect to certain breaches, could result in an event of default and, as a result, Hercules could accelerate all of the amounts due. In the event of an acceleration of amounts due under the Loan Agreement as a result of an event of default, we may not have enough available cash or be able to raise additional funds through equity or debt financings to repay such indebtedness at the time of such acceleration. In that case, we may be required to delay, limit, reduce or terminate our product candidate development or commercialization efforts or grant to others rights to develop and market product candidates that we would otherwise prefer to develop and market internally. Hercules could also exercise its rights as collateral agent to take possession and dispose of the collateral securing the term loans for its benefit, which collateral includes substantially all of our property other than our intellectual property. Our business, financial condition and results of operations could be materially adversely affected as a result of any of these events. We are subject to certain restrictive covenants which, if breached, could have a material adverse effect on our business and prospects.

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The Loan Agreement imposes operating and other restrictions on us. Such restrictions will affect, and in many respects limit or prohibit, our ability and the ability of any future subsidiary to, among other things:

- dispose of certain assets;
- change our lines of business;
- engage in mergers, acquisitions or consolidations;
- incur additional indebtedness;
- create liens on assets;
- pay dividends and make distributions or repurchase our capital stock; and
- engage in certain transactions with affiliates.

Risks Related to Our Dependence on Third Parties

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

We rely on third parties, such as contract research organizations, or CROs, clinical data management organizations, medical institutions and clinical investigators, to conduct, provide monitors for and manage data from all of our clinical trials. We compete with many other companies for the resources of these third parties.

Any of these third parties may terminate their engagements with us at any time. If we need to enter into alternative arrangements, it would delay our product development activities and ultimately the commercialization of our product candidates.

Our reliance on these third parties for research and development activities will reduce our control over these activities but will not relieve us of our responsibilities. For example, we will remain responsible for ensuring that each of our clinical trials is conducted in accordance with the general investigational plan and protocols for the trial. Moreover, the FDA and other regulatory agencies require us to comply with standards, commonly referred to as Good Clinical Practices, or GCP, for conducting, recording and reporting the results of clinical trials to assure that data and reported results are credible and accurate and that the rights, integrity and confidentiality of trial participants are protected. Regulatory authorities enforce these GCP requirements through periodic inspections of trial sponsors, principal investigators and trial sites. If we or any of our CROs fail to comply with applicable GCP requirements, the clinical data generated in our clinical trials may be deemed unreliable and the FDA or other regulatory authorities may require us to perform additional clinical trials before approving our marketing applications. We cannot assure you that upon inspection by a given regulatory authority, such regulatory authority will determine that any of our clinical trials comply with GCP requirements. We also are required to register ongoing clinical trials and post the results of completed clinical trials on government-sponsored databases, such as ClinicalTrials.gov, within certain timeframes. Failure to do so can result in fines, adverse publicity and civil and criminal sanctions.

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

We intend to rely on third parties to conduct investigator sponsored clinical trials of our product candidates. Any failure by a third party to meet its obligations with respect to the clinical development of our product candidates may delay or impair our ability to obtain regulatory approval for our product candidates.

We intend to rely on academic and private non-academic institutions to conduct and sponsor clinical trials relating to our product candidates. We will not control the design or conduct of the investigator sponsored trials, and it is possible that the FDA or non-U.S. regulatory authorities will not view these investigator-sponsored trials as providing adequate support for future clinical trials, whether controlled by us or third parties, for any one or more reasons, including elements of the design or execution of the trials or safety concerns or other trial results.

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Such arrangements will provide us certain information rights with respect to the investigator sponsored trials, including access to and the ability to use and reference the data, including for our own regulatory filings, resulting from the investigator sponsored trials. However, we do not have control over the timing and reporting of the data from investigator sponsored trials, nor do we own the data from the investigator sponsored trials. If we are unable to confirm or replicate the results from the investigator sponsored trials or if negative results are obtained, we would likely be further delayed or prevented from advancing further clinical development of our product candidates. Further, if investigators or institutions breach their obligations with respect to the clinical development of our product candidates, or if the data proves to be inadequate compared to the firsthand knowledge we might have gained had the investigator sponsored trials been sponsored and conducted by us, then our ability to design and conduct any future clinical trials ourselves may be adversely affected.

Additionally, the FDA or non-U.S. regulatory authorities may disagree with the sufficiency of our right of reference to the preclinical, manufacturing or clinical data generated by these investigator-sponsored trials, or our interpretation of preclinical, manufacturing or clinical data from these investigator-sponsored trials. If so, the FDA or other non-U.S. regulatory authorities may require us to obtain and submit additional preclinical, manufacturing, or clinical data before we may initiate our planned trials and/or may not accept such additional data as adequate to initiate our planned trials.

We contract with third parties for the manufacture of our product candidates and for compound formulation research, and these third parties may not perform satisfactorily.

We do not have any manufacturing facilities or personnel. We currently obtain all of our supply of our product candidates for clinical development from third-party manufacturers or third-party collaborators, and we expect to continue to rely on third parties for the manufacture of clinical and, if necessary, commercial quantities of our product candidates. In addition, we currently rely on third parties for the development of various formulations of our product candidates. We obtain our supplies from these manufacturers on a purchase order basis, and we do not have any long term supply agreements in place. This reliance on third parties increases the risk that we will not have sufficient quantities of our product candidates or such quantities at an acceptable cost or quality, which could delay, prevent or impair our development or commercialization efforts.

Any of these third parties may terminate their engagement with us at any time. We do not currently have arrangements in place for redundant supply or a second source for bulk drug substance. Even if we are able to establish agreements with third-party manufacturers, reliance on third-party manufacturers entails additional risks, including:

- reliance on the third party for regulatory compliance and quality assurance;

- the possible breach of the manufacturing agreement by the third party, including the misappropriation of our proprietary information, trade secrets and know how;

- the possible termination or nonrenewal of the agreement by the third party at a time that is costly or inconvenient for us; and

- disruptions to the operations of our manufacturers or suppliers caused by conditions unrelated to our business or operations, including the bankruptcy of the manufacturer or supplier or a catastrophic event affecting our manufacturers or suppliers.

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

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

If our current contract manufacturers cannot perform as agreed, we may be required to replace that manufacturer. Although we believe that there are several potential alternative manufacturers who could manufacture our product candidates, we may incur added costs and delays in identifying and qualifying any such replacement, as well as producing the drug product. In addition, we have to enter into technical transfer agreements and share our know how with the third-party manufacturers, which can be time consuming and may result in delays.

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

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

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

We face significant competition in seeking appropriate collaborators. Whether we reach a definitive agreement for a collaboration will depend, among other things, upon our assessment of the collaborator s resources and expertise, the terms and conditions of the proposed collaboration and the proposed collaborator s evaluation of a number of factors. Those factors may include the design or results of clinical trials, the likelihood of approval by the FDA or similar regulatory authorities outside the United States, the potential market for the subject product candidate, the costs and complexities of manufacturing and delivering such product candidate to patients, the potential of competing products, the existence of uncertainty with respect to our ownership of technology, which can exist if there is a challenge to such ownership without regard to the merits of the challenge and industry and market conditions generally. The collaborator may also consider alternative product candidates or technologies for similar indications that may be available to collaborate on and whether such a collaboration could be more attractive than the one with us for our product candidate. Collaborations are complex and time consuming to negotiate and document. In addition, there have been a significant number of recent business combinations among large pharmaceutical companies that have resulted in a reduced number of potential future collaborators.

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

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

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

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

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

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

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