Verastem, Inc.
Form 10-K
March 13, 2018
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UNITED STATES

SECURITIES AND EXCHANGE COMMISSION

WASHINGTON, D.C. 20549

FORM 10-K

(Mark One)

ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934

For the fiscal year ended December 31, 2017

or

TRANSITION REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934

For the transition period from to

Commission file number 001-35403

Verastem, Inc.

(Exact name of registrant as specified in its charter)

Delaware	27-3269467
(State or other jurisdiction of incorporation or organization)	(I.R.S. Employer Identification No.)
117 Kendrick Street, Suite 500 Needham, Massachusetts	02494
(Address of principal executive offices)	(Zip Code)

Registrant’s telephone number, including area code: (781) 292-4200

Securities registered pursuant to Section 12(b) of the Act:

Title of each class	Name of each exchange on which registered
Common Stock, $0.0001 par value	Nasdaq Global Market

Securities registered pursuant to Section 12(g) of the Act: None

Indicate by check mark if the registrant is a well-known seasoned issuer, as defined in Rule 405 of the Securities Act. Yes No

Indicate by check mark if the registrant is not required to file reports pursuant to Section 13 or Section 15(d) of the Act. Yes No

Indicate by check mark whether the registrant (1) has filed all reports required to be filed by Section 13 or 15(d) of the Securities Exchange Act of 1934 during the preceding 12 months (or for such shorter period that the registrant was required to file such reports), and (2) has been subject to such filing requirements for the past 90 days. Yes No

Indicate by check mark whether the registrant has submitted electronically and posted on its corporate Website, if any, every Interactive Data File required to be submitted and posted pursuant to Rule 405 of Regulation S-T (§232.405 of this chapter) during the preceding 12 months (or for such shorter period that the registrant was required to submit and post such files). Yes No

Indicate by check mark if disclosure of delinquent filers pursuant to Item 405 of Regulation S-K is not contained herein, and will not be contained, to the best of registrant's knowledge, in definitive proxy or information statements incorporated by reference in Part III of this Form 10-K or any amendment to this Form 10-K.

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

Large accelerated filer	Accelerated filer	Non accelerated filer (Do not check if a smaller reporting company)	Smaller reporting company	Emerging growth company

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act.

Indicate by check mark whether the registrant is a shell company (as defined in Rule 12b-2 of the Exchange Act). Yes No

Aggregate market value of the voting and non-voting common equity held by non-affiliates of the registrant as of June 30, 2017 was $79,779,254.

The number of shares outstanding of the registrant's common stock as of March 7, 2018 was 50,800,908.

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FORWARD LOOKING STATEMENTS

This Annual Report on Form 10-K contains forward-looking statements that involve substantial risks and uncertainties. All statements, other than statements related to present facts or current conditions or historical facts, contained in this Annual Report on Form 10-K, 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 and defactinib, and our PI3K and FAK 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 and commercialization activities and fund operations for a specified period. The words “anticipate,” “believe,” “estimate,” “expect,” “intend,” “may,” “predict,” “project,” “target,” “potential,” “will,” “would,” “could,” “should,” “continue” and similar expressions are intended t 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. Applicable risks and uncertainties include the risks that the full data from the Phase 3 DUO™ 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 and the product may not prove to be safe and effective; 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; acceptance or approval of our New Drug Application for duvelisib will not occur on the expected timeframe or at all and that our product candidates will not receive regulatory approval, become commercially successful products, or result in new treatment options being offered to patients. Other risks and uncertainties include those identified under the heading "Risk Factors" in this Annual Report on Form 10-K for the year ended December 31, 2017 and in any subsequent filings with the Securities and Exchange Commission (SEC).

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

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PART I

Item 1. Business

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 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) 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 (CLL/SLL) and indolent non-Hodgkin lymphoma (iNHL), which includes follicular lymphoma (FL), and other subtypes of lymphoma, including peripheral T-cell lymphoma (PTCL). Duvelisib has U.S. Food and Drug Administration (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.

Duvelisib was evaluated in late- and mid-stage clinical trials, including DUO™, a randomized, Phase 3 monotherapy study in patients with relapsed or refractory CLL/SLL, and DYNAMO™, a single-arm, Phase 2 monotherapy study in patients with double-refractory iNHL, including FL, SLL, and marginal zone lymphoma (MZL). Both DUO and DYNAMO achieved their primary endpoints upon top-line analysis of efficacy data. We submitted a New Drug Application (NDA) to the FDA 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 in February 2018.

Defactinib is a targeted inhibitor of the Focal Adhesion Kinase (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.

Defactinib is currently being evaluated in a Phase 1b study in combination with Merck & Co.'s PD-1 inhibitor pembrolizumab and gemcitabine in patients with advanced pancreatic cancer, a Phase 1/2 clinical collaboration with Pfizer Inc. (Pfizer) and Merck KGaA to evaluate defactinib in combination with avelumab, an anti-PD-L1 antibody, in patients with ovarian cancer, and a Phase 1/2 study in collaboration with Cancer Research UK and Merck & Co. for the combination of defactinib with pembrolizumab in patients with non-small cell lung cancer (NSCLC),

mesothelioma or pancreatic cancer.

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THE PROBLEM

Cancer is a group of diseases characterized by uncontrolled growth and spread of abnormal cells. The American Cancer Society estimates 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. The following table sets forth the U.S. annual incidence of certain cancers, based on 2017 estimates from the National Cancer Institute's Surveillance, Epidemiology, and End Results Program (NCI; SEER).

Cancer type	U.S. annual incidence
Lymphoma	
Non-Hodgkin lymphoma	72,240
Chronic lymphocytic leukemia/small lymphocytic leukemia	20,110
Follicular lymphoma	14,448
Solid tumor	
Lung and bronchus cancer	222,500
Pancreatic cancer	53,670
Ovarian cancer	22,440

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 STRATEGY

Our product candidates seek to utilize a multi-faceted approach to treat cancer by directly targeting the cancer cells, enhancing anti-tumor immunity, and modulating the local tumor microenvironment. Our goal is to build a leading biopharmaceutical company focused on the development and commercialization of novel drugs that use a multi-faceted approach to improving outcomes for patients with cancer.

Key elements of our strategy to achieve this goal are:

- Selectively build a commercial infrastructure in the U.S. for the potential launch of duvelisib in hematologic malignancies as an oral monotherapy for patients needing additional lines of therapy following previous treatment.
- Advance our product candidates through clinical development. We have ongoing clinical trials of duvelisib and defactinib both as single agents and in combination with other agents in several hematologic and solid tumor indications.
- Expand the indications in which our product candidates may be used. In parallel to CLL/SLL, iNHL, PTCL, NSCLC, ovarian cancer, pancreatic cancer and mesothelioma trials that we are currently conducting, we plan to pursue additional disease indications to expand the potential of our product candidates.

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- Collaborate selectively to augment and accelerate translational research, development and commercialization. We may seek third party collaborators for the development and eventual commercialization of our product candidates. In particular, we may enter into third party arrangements for target oncology indications in which our potential collaborator has particular expertise or for which we need access to additional research, development, or commercialization resources.
- Consider acquiring or in licensing rights to additional agents. We may pursue the acquisition or in license of rights to additional agents from third parties that may supplement our internal programs and allow us to initiate clinical development of a diverse pipeline of agents more quickly.
- Build and maintain scientific leadership in the areas of lymphoid malignancies, immuno-oncology, and the tumor microenvironment. We plan to continue to conduct research in the hematological and immuno-oncology fields to further our understanding of the underlying biology of enhancing the body's immune response to tumors as well as cancer progression and metastasis. We also plan to continue fostering relationships with top scientific advisors, researchers and physicians. We believe that exceptional advisors, employees and management are critical to leadership in the development of new therapies for the treatment of cancer.

OUR PRODUCT CANDIDATES

We are focused on the development and commercialization of small molecules for optimized efficacy and safety primarily as orally available drug candidates. We have several product candidates currently in clinical trials, including duvelisib and defactinib. We are running clinical trials in cancers where there are limited treatment options, including CLL/SLL, iNHL, T-cell lymphoma, lung cancer, ovarian cancer, pancreatic cancer, mesothelioma, and other advanced cancers.

Conventional chemotherapy works by stopping the function of cancer cells through a variety of mechanisms. Chemotherapies are usually not targeted at any specific differences between cancer cells and normal cells. Rather, they kill cancer cells because cancer cells generally grow more rapidly than normal cells and, as a result, are relatively more affected by the chemotherapy than normal cells. As a result, the treatments may succeed at initially decreasing tumor burden but ultimately fail to kill all of the cancer cells or effectively disrupt the tumor microenvironment, potentially resulting in disease progression.

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. Agents that can modulate the tumor microenvironment to increase cytotoxic T-cell access to the tumor cells and decrease immunosuppressive T-cells in tumors have been sought after to increase the proportion of responding cancer patients and the duration of response (DOR) to cancer treatment.

Chronic Lymphocytic Leukemia/Small Lymphocytic Leukemia, Non-Hodgkin Lymphoma

Hematologic malignancies are cancers of the blood or bone marrow such as CLL/SLL and non-Hodgkin lymphoma (NHL). In general, NHLs are a disease that occurs in patients over the age of 65.

The NCI estimates that there were 20,110 new cases of CLL/SLL in the U.S. in 2017 and that the five-year relative survival rate from 2007 to 2013 for patients with CLL/SLL was approximately 83%. As CLL/SLL is generally a slow-growing disease, the advent of new oral anti-cancer therapies since 2013 have been a significant advance as treatment options beyond chemotherapy or anti-B-lymphocyte antigen CD20 (CD20) immunotherapies, including ofatumumab. For example, the Bruton's Tyrosine Kinase (BTK) and B-cell lymphoma 2 (BCL-2) inhibitors have demonstrable activity in the treatment of CLL/SLL. However, evidence coming from studies on real-world use of these agents is revealing that a significant number of patients either relapse following treatment, become refractory to current agents, or are unable to tolerate treatment due to unmanageable side effects resulting from treatment, representing a significant medical need.

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The five year relative survival rate from 2007 to 2013 for patients with NHL was approximately 71%. The type and stage of the lymphoma can often provide useful information about a person's prognosis, but for some types of lymphomas the stage is less informative on its own. In these cases, other factors can give doctors a better idea about a person's prognosis. These factors are included in the International Prognostic Index and other metrics which take into account the patient's age, stage of disease, presence of metastases, performance status and blood levels of lactate dehydrogenase.

The potential of additional oral agents, particularly as a monotherapy that can be used in the general community physician's armamentarium, may hold significant value in the treatment of patients with CLL/SLL.

Follicular Lymphoma

FL comprises 20% of all NHL and as many as 70% of the indolent lymphomas reported in American and European clinical trials. Common symptoms of FL include enlargement of the lymph nodes in the neck, underarms, abdomen, or groin, as well as fatigue, shortness of breath, night sweats, and weight loss. Often, patients with FL have no obvious symptoms of the disease at diagnosis. Most patients with FL are age 50 years and older and present with widespread disease at diagnosis. Nodal involvement is most common and is often accompanied by splenic and bone marrow disease. Rearrangement of the BCL-2 gene is present in more than 90% of patients with FL; overexpression of the BCL-2 protein is associated with the inability to eradicate the lymphoma by inhibiting apoptosis.

Despite the advanced stage, the median survival ranges from 8 to 15 years, leading to the designation of being indolent. Patients with advanced-stage FL are not cured with current therapeutic options. The rate of relapse is fairly consistent over time, even in patients who have achieved complete responses to treatment.

There are various treatment options for FL based on the severity of associated symptoms and the rate of cancer growth. If patients show no or very few symptoms, physicians may recommend not to treat the disease right away, an approach referred to as "active surveillance" (also known as "watchful waiting"). Active treatment is started if the patient begins to develop lymphoma-related symptoms or there are signs that the disease is progressing based on testing during follow-up visits.

FL is generally responsive to radiation and chemotherapy. Radiation alone can provide a long-lasting remission in some patients with limited disease. In more advanced stages, physicians may use one or more chemotherapy drugs or the monoclonal antibody rituximab (Rituxan), alone or in combination with other agents.

There have been only incremental advances in treatment options for FL beyond chemotherapy or immunotherapies like the antibodies against CD20, such as rituximab and obinutuzumab, and the overall clinical outlook for patients still remains poor. The potential of additional oral agents, particularly as a monotherapy that can be used in the general community physician's armamentarium, may hold significant value in the treatment of patients with FL.

Peripheral T-Cell Lymphoma

PTCL consists of a group of rare and usually aggressive (fast-growing) NHLs that develop from mature T-cells. Most T-cell lymphomas are PTCLs, which collectively account for about 10% to 15% of all NHL cases in the United States.

PTCLs are sub-classified into various subtypes, each of which are typically considered to be separate diseases based on their distinct clinical differences. Most of these subtypes are very rare; the three most common subtypes of PTCL, peripheral T-cell lymphoma not otherwise specified (PTCL-NOS), anaplastic large-cell lymphoma (ALCL), and angioimmunoblastic T-cell lymphoma (AITL), account for approximately 70% of all PTCLs in the United States.

For most subtypes of PTCL, the frontline treatment regimen is typically a combination chemotherapy, such as CHOP (cyclophosphamide, doxorubicin, vincristine, prednisone), EPOCH (etoposide, vincristine, doxorubicin,

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cyclophosphamide, prednisone), or other multi-drug regimens. Because most patients with PTCL will relapse, some oncologists recommend giving high-dose chemotherapy followed by an autologous stem cell transplant (in which patients receive their own stem cells) to some patients who had a good response to their initial chemotherapy. While promising, there is no firm clinical data to support that undergoing a transplant in this setting is better than not undergoing a transplant.

The potential of additional oral agents, particularly as a monotherapy that can be used in the general community physician's armamentarium, may hold significant value in the treatment of patients with PTCL.

Ovarian Cancer

Ovarian cancer forms in tissues of the ovary, one of a pair of female reproductive glands in which the ova, or eggs, are formed. Most ovarian cancers are either ovarian epithelial carcinoma, cancer that begins in the cells on the surface of the ovary, or malignant germ cell tumors that begin in egg cells. According to the NCI, epithelial carcinoma of the ovary is one of the most common gynecologic malignancies and the fifth most frequent cause of cancer death in women, with 50% of all cases occurring in women older than 65 years. The American Cancer Society estimates that in 2018 there will be approximately 22,200 new cases of ovarian cancer diagnosed and approximately 14,100 ovarian cancer related deaths.

Most patients are treated with a combination of surgery, chemotherapy, targeted therapy and radiation therapy. Surgery is often comprehensive to remove as much of the tumor as possible and may include removal of the ovaries or a total hysterectomy where the uterus is also removed. Unfortunately, available therapies are rarely curative in the treatment of ovarian cancer and many tumors become resistant to platinum based chemotherapy, which is the primary treatment regimen. Further therapy with conventional chemotherapy is generally palliative, not curative, as the tumor is able to metastasize and spread to other sites in the body.

Pancreatic Cancer

Pancreatic cancer is the tenth most common cancer diagnosed in the United States and the disease represents the third leading cause of cancer-related death in the country.

Pancreatic cancer often has a poor prognosis, even when diagnosed early. Pancreatic cancer typically spreads rapidly and is seldom detected in its early stages, which is a major reason why it is a leading cause of cancer death. Signs and symptoms may not appear until pancreatic cancer is so advanced that complete surgical removal is not possible. An estimated 54,000 Americans were diagnosed with pancreatic cancer in 2017 and over 43,000 were estimated to have died from the disease. Pancreatic cancer is one of the few cancers where survival has not improved significantly during the past 40 years. Pancreatic cancer has a very high mortality rate with approximately 92% of patients dying within five years of their initial diagnosis based on the five-year relative survival rate from 2007 to 2013. The median age for diagnosis is 70 with the disease affecting males slightly more than females.

Treatment options for pancreatic cancer are limited with surgical resection of the tumor possible in less than 20% of patients. Chemotherapy or chemotherapy plus radiation is offered to patients whose tumors are unable to be removed surgically. Immuno-oncology agents have not demonstrated a significant improvement in treatment outcome for patients with pancreatic cancer. The limited impact of chemotherapies and immunotherapies to improve the outcome may be due to the dense stroma that is prevalent in pancreatic tumors and the tumor microenvironment.

Non-Small Cell Lung Cancer

According to the NCI, the most common types of NSCLC are squamous cell carcinoma, large cell carcinoma, and adenocarcinoma. Although NSCLCs are associated with cigarette smoke, adenocarcinomas may be found in patients who have never smoked. As a class, NSCLCs are relatively insensitive to chemotherapy and radiation therapy compared with small cell lung cancer (SCLC). The NCI estimates that in 2017 there were 222,500 new cases of lung cancer (both NSCLC and SCLC) in the United States and more than 150,000 deaths. Lung cancer is the leading cause of cancer related mortality in the United States. The five year relative survival rate from 2007 to 2013 for patients with lung cancer was approximately 18%.

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Patients with resectable disease may be cured by surgery or surgery followed by chemotherapy. Local control can be achieved with radiation therapy in a large number of patients with unresectable disease, but cure is seen only in a small number of patients. Patients with locally advanced unresectable disease may achieve long term survival with radiation therapy combined with chemotherapy. Patients with advanced metastatic disease may achieve improved survival and palliation of symptoms with chemotherapy, targeted agents, and other supportive measures. The disease becomes resistant to therapy and returns in the vast majority of patients.

Mesothelioma

Mesothelioma is a form of cancer most often caused by asbestos, that affects the smooth lining of the chest, lungs, heart, and abdomen. The layer of tissue surrounding these organs is made up of mesothelial cells, hence the name mesothelioma. Mesothelioma most often forms in the pleural cavity of the chest or into the abdomen. Mesothelioma forms a solid tumor that begins as a result of insult to the tissues caused by asbestos particles, which penetrate into the pleural cavity of the chest.

Pleural mesothelioma accounts for approximately 2,500 - 3,000 cases a year in the United States. This disease affects the pleura, which is the thin balloon shaped lining of the lungs. In its early stages, mesothelioma is difficult to detect as it may start with a thickening of the pleural rind, or fluid, which can be associated with many other conditions. This rind is normally thin and smooth in the non-diseased state. In time it begins to demonstrate progression, forming a more pronounced irregular rind and nodules which coalesce into a crust that compresses and invades into adjacent structures compromising lung and cardiac function.

The symptoms of mesothelioma gradually become more noticeable, prompting the patient to seek a medical consultation. By this time the progression of the disease may already be too advanced, as the tumor may have spread to the lymph nodes and/or begun to metastasize to remote organs of the body like the brain, spleen, liver or kidneys.

PI3K Inhibition Program

PI3K refers to a family of enzymes involved in multiple cellular functions, including cell proliferation and survival, cell differentiation, cell migration, and immunity. PI3K-delta and PI3K-gamma are two proteins with distinct and mostly non-overlapping roles believed to support the growth and survival of malignant B-cells and T-cells. Specifically, preclinical data suggest that PI3K-delta signaling can lead to the proliferation of malignant B-cells, and that both PI3K-gamma and PI3K-delta play an important role in the formation and maintenance of the supportive tumor microenvironment.

Duvelisib

Our lead product candidate, duvelisib, is an oral, dual inhibitor of PI3K-delta and PI3K-gamma. Duvelisib is an investigational compound in clinical trials for hematologic malignancies, and its safety and efficacy have not yet been evaluated by the FDA or any other health authority for marketing authorization.

The clinical investigation program for duvelisib is supported by data from a Phase 1, open-label, dose-escalation study designed to evaluate the safety, pharmacokinetics and clinical activity of duvelisib in patients with advanced hematologic malignancies. The maximum tolerated dose of duvelisib was defined at 75 mg twice daily (BID) and the trial has been completed. A 25 mg BID dosing regimen was determined for further development based on efficacy, safety, pharmacokinetics and pharmacodynamics. Data from this study, presented in December 2014 at the Annual Meeting of the American Society for Hematology (ASH 2014), showed that duvelisib is clinically active in CLL/SLL, iNHL, and T-cell lymphoma, as well as other hematologic malignancies.

Chronic Lymphocytic Leukemia/Small Lymphocytic Leukemia, Non-Hodgkin Lymphoma

The FDA and European Medicines Agency (EMA) have granted orphan drug designation to duvelisib for the potential treatment of CLL/SLL, and the FDA has granted fast track designation to the investigation of duvelisib for the treatment of patients with CLL/SLL who have received at least one prior therapy. Duvelisib was evaluated for the treatment of CLL/SLL in the DUO™ study. The DUO study is a Phase 3, monotherapy, open-label, two- arm, randomized, superiority trial designed to evaluate the efficacy and safety of duvelisib at 25mg BID compared

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to ofatumumab, a monoclonal antibody treatment, administered to patients who have been diagnosed with CLL/SLL whose disease is relapsed or refractory. Patients in DUO that continue to derive benefit remain on treatment. DUO enrollment criteria included patients with CLL/SLL, whose disease had progressed during or relapsed after at least one previous CLL/SLL therapy. The primary endpoint of the study was Progression-Free Survival (PFS).

The investigation of duvelisib in DUO is supported by preliminary data from a Phase 1 study that demonstrated that duvelisib administered at 25 mg BID was clinically active in patients with relapsed or refractory CLL, with a 57% overall response rate (ORR) (17 of 30 evaluable patients), including one complete response, as per investigator assessment. At the time of the presentation of the study at ASH 2014, the median PFS in the 31 patients who received the 25 mg BID dose had not yet been reached with 66% of patients progression free at twelve months and 59% of patients progression free at 24 months.

CR: Complete Response; PR: Partial Response; PD: Progressive Disease; TP53mut/del(17p): high-risk cytogenetic markers

*O'Brien et al., ASH 2014

The majority of side effects were Grade 1 or 2 in severity, reversible and/or clinically manageable. Across all doses evaluated in the study (n=55), the most common Grade 3 side effects were pneumonia (24%), neutropenia (18%) and anemia (16%). Grade 4 side effects included pneumonia in one patient (2%), neutropenia in 13 patients (24%) and anemia in one patient (2%).

The results from the DUO study were presented at the 2017 Annual Meeting of the American Society for Hematology conference (ASH 2017). 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 Independent Review Committee (IRC) using modified international workshop on CLL (iwCLL) or revised International Working Group (IWG) Response 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.

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Median PFS per IRC

*Flinn et al., ASH 2017

Similar efficacy of duvelisib was observed regardless of whether patients had 17p deletion (del[17p]). The primary outcome of median PFS via IRC review in the del[17p] subpopulation 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 a median PFS 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.

Median PFS per IRC for del[17p] Subpopulation

*Flinn et al., ASH 2017

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Median PFS per Investigator Assessment

*Flinn et al., ASH 2017

Median PFS by Subgroup

*Flinn et al., ASH 2017

The secondary efficacy outcome of ORR via IRC assessment according to modified iwCLL/IWG criteria, significantly favored duvelisib over ofatumumab, 74% versus 45%, respectively ($p<0.0001$), and reduced lymph node burden by more than 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% versus 43%, respectively ($p=0.0182$).

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*Flinn et al., ASH 2017

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 confirmed disease progression were subsequently treated with duvelisib as a monotherapy. As in the parent DUO study, duvelisib demonstrated robust clinical activity in this crossover study with an ORR of 73%, a median DOR of 12.7 months and a median PFS of 15 months by investigator assessments.

In the DUO study, the overall survival in the intent to treat (ITT) population was similar for those randomized to duvelisib and to ofatumumab during the study (HR=0.99, p=0.4807), as expected there was no detrimental effect on overall survival. Though the FDA has noted that overall survival is the most reliable and therefore the preferred endpoint for approval of drugs for oncology indications in general, the FDA has publicly stated that it understands the challenges of showing an overall survival improvement in CLL/SLL, given the long natural history of the disease and availability of multiple therapies. Therefore, while they may request drug companies to collect overall survival data to ensure there is no detrimental effect on overall survival and to observe any potential improvement, an improvement in overall survival is not necessary for approval in CLL. Rather, improvements in PFS together with a favorable benefit-risk profile may be acceptable to receive FDA approval.

Following prolonged exposure, duvelisib, as a monotherapy, demonstrated 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 more than 10% of patients) were neutropenia (30%) and anemia (13%). The most common Grade ≥3 non-hematologic treatment-emergent adverse events (occurring in more than 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 (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.

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Adverse events of special interest infrequently led to discontinuation of duvelisib treatment (e.g., diarrhea (5%), colitis (5%), pneumonitis (2%), neutropenia (1%), pneumonia (1%), transaminase elevations (1%), and rash (1%). 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)).

*Flinn et al., ASH 2017

Indolent Non-Hodgkin Lymphoma

The FDA and EMA have granted orphan drug designation to duvelisib for the potential treatment of FL, and the FDA has granted Fast Track Designation to the investigation of duvelisib for the treatment of patients with FL who have received at least two prior therapies. The DYNAMO study is a Phase 2, open-label, single-arm monotherapy study evaluating the safety and efficacy of duvelisib dosed at 25 mg BID in 129 patients with iNHL. Patients in DYNAMO that continue to derive a benefit remain on treatment. DYNAMO enrollment criteria included patients with FL, the most common subtype of iNHL, MZL and SLL, whose disease is double-refractory to rituximab, an anti-CD20 monoclonal antibody, and to either chemotherapy or radioimmunotherapy and who must have progressed within six months of receiving their final dose of a previous therapy. The primary endpoint of the study was an ORR as assessed by IRC and according to the revised IWG Criteria, which includes a change in target nodal lesions in combination with other measurements to determine response to treatment.

The results from the DYNAMO study were presented at the 2016 Annual Meeting of the American Society for Hematology conference (ASH 2016). DYNAMO achieved the primary endpoint in a heavily pre-treated, double-refractory patient population with an ORR of 46% (p=0.0001) in the ITT population, as assessed by an IRC with a median DOR of 10 months. The breakdown of ORR in the three subtypes of iNHL for the overall study population was 41% in FL (n=83), 68% in SLL (n=28) and 33% in MZL (n=18). 83% of patients had a reduction of target nodal lesions in lymph nodes.

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*Adapted from Flinn et al., ASH 2016

*Flinn et al., ASH 2016

Duvelisib demonstrated a consistent and manageable safety profile with appropriate risk mitigation. The majority of adverse events were Grade 1 or 2 in severity, reversible and/or clinically manageable. The most common (greater than 5%) Grade 3 adverse effects were an increase in diarrhea (14%), anemia (10%), and neutropenia (9%). Grade 3 or 4 adverse effects of special interest included neutropenia (28%), infection (18%), diarrhea (15%), thrombocytopenia (13%), anemia (12%), pneumonia (9%), hepatotoxicity (8%), rash (7%), colitis (5%), and pneumonitis (2%). Serious opportunistic infections were less than 5% with none being fatal. Four treatment-related adverse events had the outcome of death (one septic shock; one viral infection; one drug reaction/eosinophilia/systemic symptoms; and one toxic epidermal necrolysis/sepsis syndrome).

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T-cell Lymphoma, Aggressive NHL and Other Lymphomas

In the Phase 1 study, the ORR in patients with PTCL (n=16) was 50%, including three complete responses (CRs) and five partial responses (PRs). Responses were seen across the spectrum of PTCL subtypes, including CRs and PRs in patients with enteropathy-associated T-cell lymphoma (EATL), AITL, subcutaneous panniculitis-like T-cell lymphoma (SPTCL), and anaplastic large-cell lymphoma (ALCL), among others. DOR in the PTCL population ranged from 1.8 to 17.3 months with median PFS of 8.3 months and median overall survival of 8.4 months. In cutaneous T-cell lymphoma (CTCL) (n=19), the ORR was 32%, with six PRs. DOR ranged from 0.7 to 10.1 months and median PFS was 4.5 months. Median overall survival was not reached; however, the estimated probability of survival was determined to be of 90% at 6 months, 79% at 12 and 18 months, and 73% at 24 months. Duvelisib monotherapy demonstrated a manageable safety profile, with results from this study consistent with the well-characterized safety profile of duvelisib monotherapy in patients with hematologic malignancies in other studies. These clinical results were supported by preclinical findings showing that duvelisib exhibited cell-killing activity in vivo and promoted beneficial changes within the tumor microenvironment.

During 2017, the FDA granted Fast Track designation for the treatment of patients with PTCL, who have received at least one prior therapy. During the first quarter of 2018, we initiated an open-label, multicenter, Phase 2 clinical trial evaluating the efficacy and safety of duvelisib in patients with relapsed or refractory PTCL. We expect the study to be conducted in both the United States, the European Union, and Japan.

FAK Inhibition Program

Our product candidates that inhibit FAK utilize a multi-faceted approach to treat cancer by enhancing anti-tumor immunity and modulating the local tumor microenvironment. Our lead FAK inhibitor is known as defactinib. The effects of FAK inhibition on the tumor microenvironment make defactinib a good candidate for combination therapy with immuno-oncology agents and other anti-cancer compounds. FAK expression is greater in many tumor types compared to normal tissue, particularly in cancers that have a high invasive and metastatic capability. The contact between cancer cells and connective tissue stimulates FAK signaling.

In September 2015, researchers from the University of Edinburgh published a study in the journal Cell that highlights the potential of FAK inhibition to enable the body’s immune system to fight cancer. The paper discussed results from preclinical research showing that FAK enables cancer cells to evade attack by the immune system. This research showed that genetic knock down of FAK or oral dosing of mice with a FAK inhibitor decreases immunosuppressive cells called T-regulatory cells (Figure 1a) and increases cytotoxic T-cells (Figure 1b) in skin cancer tumors leading to a reduction in tumor burden (Figure 1c). This work has since been expanded into pancreatic cancer and colorectal cancer models in which FAK inhibition similarly extends survival of tumor-bearing mice through increasing cytotoxic T-cells in the tumor and decreasing T regulatory cells as published in Nature Medicine in August, 2016. Additionally, FAK inhibition was found to decrease other key immunosuppressive cell populations in tumors, known as myeloid-derived suppressor cells and M2 tumor-associated macrophages. Coincident with this immuno-modulation, FAK inhibition was shown to substantially increase survival of mice when combined with an anti-PD-1 immune checkpoint antibody. These results have indicated the potential promise of FAK inhibitors in combination with immune checkpoint inhibitors in the clinic.

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FIGURE 1

*Adapted from: Serrels et al. Nuclear FAK controls chemokine transcription, Tregs, and evasion of anti-tumor immunity. Cell. 2015.

In the 2016 Nature Medicine paper, preclinical data were presented (Jiang, et al) demonstrating that FAK inhibition reduces stromal density and increases T-cell entry into tumors. In this study, it was discovered that treating mice bearing pancreatic cancer tumors with a FAK inhibitor reduces stromal density. This was measured as a decrease in the number (Figure 2a) and proliferation (Figure 2b) of tumor-associated fibroblasts, together with a decrease in collagen and other extracellular matrix proteins (Figure 2c) in the tumors. The paper's authors went on to show that this reduction in stromal density by FAK inhibition augments the effectiveness of the chemotherapeutic agent gemcitabine, and also allowed cytotoxic T-cells to enter the tumors (Figure 2d) to induce more durable survival of transgenic mice bearing pancreatic tumors (Figure 3). We believe these data provide strong rationale for the clinical evaluation of FAK inhibitors, including defactinib, in combination with a PD-1 or PD-L1 antibody in patients with pancreatic and other cancers. Based on this research, we have initiated clinical trials to assess the combination of defactinib with either avelumab (anti-PD-L1) or pembrolizumab (anti-PD-1) for the treatment of patients with ovarian cancer, pancreatic cancer, mesothelioma, or NSCLC.

FIGURE 2

*Adapted from: Jiang et al. Targeting focal adhesion kinase renders pancreatic cancers responsive to checkpoint immunotherapy. Nature Medicine. 2016.

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FIGURE 3

Vehicle: Placebo control; Immuno: Gem +/- anti-PD-1 +/- anti-CTLA-4

*Adapted from: Jiang et al. Targeting focal adhesion kinase renders pancreatic cancers responsive to checkpoint immunotherapy. Nature Medicine. 2016.

Defactinib

Defactinib is an orally available small molecule kinase inhibitor designed to inhibit FAK signaling. We are currently evaluating defactinib as a potential therapy for ovarian cancer, pancreatic cancer, mesothelioma, NSCLC, and other solid tumors. 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.

The clinical evaluation of defactinib is supported by a growing body of preclinical research suggesting that FAK inhibition, when combined with PD-1 inhibitors, increases the anti-tumor activity of these immunotherapeutic agents. As published in the journals Cell and Nature Medicine, FAK inhibition has been shown to increase cytotoxic (CD8+) T-cells in tumors, decrease T-cell exhaustion, decrease immunosuppressive cell populations, enhance T-cell killing of tumor cells, and create a generally more favorable tumor microenvironment, which may allow for enhanced efficacy of immuno-oncology therapeutics.

Pancreatic cancer, along with other tumors such as ovarian cancer and prostate cancer, are tumor types in which immunotherapeutics have achieved limited clinical benefit, possibly due to the dense desmoplastic stroma and the abundance of immunosuppressive cells. Preclinical research has demonstrated that high stromal density prevents anti-cancer agents and T-cells from entering pancreatic tumors thereby limiting efficacy. In preclinical research conducted by us and others, FAK inhibition was shown to reduce stromal density and allow cytotoxic T-cells to better penetrate the tumor and kill the cancer cells. Collectively, these data provide strong rationale for combining our FAK inhibitors with checkpoint inhibitors in the clinic for pancreatic and other solid tumors.

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Phase 1/2 study with Pfizer and Merck KGaA in combination with immunotherapy in ovarian cancer. In March 2016, we announced a new clinical collaboration with Pfizer and Merck KGaA to evaluate defactinib in combination with avelumab in patients with ovarian cancer. Avelumab is a human programmed death ligand 1 (PD-L1), blocking antibody that binds to the PD-L1 ligand expressed on tumor cells.

Phase 1/2 study with Cancer Research United Kingdom (CRUK) in combination with pembrolizumab. In September 2016, we announced a new clinical collaboration with CRUK and Merck & Co. to evaluate defactinib in combination with pembrolizumab, a PD-1 inhibitor, in patients with NSCLC, mesothelioma, or pancreatic cancer.

Phase 1/1b study in combination with immunotherapy in pancreatic cancer. Defactinib is in a dose escalation study in combination with Merck & Co.'s PD-1 inhibitor pembrolizumab and gemcitabine in patients with advanced pancreatic cancer. This Phase 1 clinical trial is anticipated to enroll approximately 50 patients and is being conducted at the Washington University School of Medicine's Division of Oncology under the direction of Andrea Wang-Gillam, M.D., Ph.D., Clinical Director of the Gastrointestinal Oncology Program. This trial is primarily designed to evaluate the safety of the combination regimen and may also provide a greater understanding of how FAK inhibition in combination with immunotherapies could improve outcomes for patients with pancreatic cancer.

OUR MANAGEMENT TEAM AND SCIENTIFIC CO FOUNDERS AND ADVISORS

Our experienced management team includes our President and Chief Executive Officer, Robert Forrester, Chief Strategy Officer, Steven Bloom, Chief Financial Officer, Julie Feder, Chief Medical Officer, Diep Le, M.D., Ph.D., Chief Commercial Officer, Joseph Lobacki, and Chief Operating Officer, Daniel Paterson.

Mr. Forrester has been the Chief Executive Officer, Chief Operating Officer and Chief Financial Officer of both private and public life science companies, including Forma Therapeutics, Inc., CombinatoRx, Inc. and Coley Pharmaceutical Group, Inc., which was acquired by Pfizer Inc. in 2007.

Mr. Bloom joined Verastem in March 2014 and recently took on the role of Chief Strategy Officer, focusing on Corporate and Business Development, Medical Affairs, Patient Advocacy and Corporate Communications. Prior to joining the company, Mr. Bloom was Senior Vice President at Ziopharm Oncology where for 6 years he led business development and the commercial planning initiatives for a late stage oncology asset. Before joining Ziopharm, Mr. Bloom was Vice President for the health informatics company Pharmetrics and spent the first 19 years of his career at Eli Lilly and Company in leadership roles in marketing, sales and corporate affairs.

Ms. Feder joined Verastem in July 2017 as our Chief Financial Officer. Ms. Feder served as the Chief Financial Officer for the Clinton Health Access Initiative, Inc. (CHAI) for the previous six years. Prior to joining CHAI, Ms. Feder spent three years at Genzyme Corporation, first as Vice President of Internal Audit and also as Finance Integration Leader. In these roles, she managed the day-to-day operations of Genzyme's global internal audit function, while leading the Genzyme Global Finance integration into Sanofi's organization following Sanofi's acquisition of Genzyme.

Dr. Le joined us in October 2017 as our Chief Medical Officer, is a trained medical oncologist, board certified in internal medicine and has 15 years of drug development experience across all phases in both solid and hematologic malignancies as well as IND and NDA submissions. Dr. Le joins Verastem from MedImmune (a subsidiary of AstraZeneca) where she served as Vice President, Immuno-Oncology Innovative Medicines and led the product development teams for multiple high-priority immuno-oncology assets. Prior to joining MedImmune, Dr. Le held roles of increasing responsibility at Novartis and at GlaxoSmithKline where she led the MEK inhibitor, trametinib (Mekinist™), from the first-in-human studies to FDA approval.

Mr. Lobacki joined Verastem in January 2018 as our Chief Commercial Officer. He most recently served as the Chief Operating Officer of Finch Therapeutics Group and previously as the Chief Commercial Officer and Executive Council Member of Medivation, where he was responsible for the strategy and execution of commercial operations including Xtandi, a treatment for advanced prostate cancer. Previously, Mr. Lobacki was Senior Vice President and Chief Commercial Officer of Micromet Inc., where he oversaw commercial activities including

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medical affairs and strategic marketing. Prior to joining Micromet, Mr. Lobacki was Senior Vice President and General Manager at Genzyme Corporation, where he managed the launch of Mozobil and Clolar/Evoltra in the US and EU.

Mr. Paterson has over 25 years of experience in management roles at healthcare and biotechnology companies, including as chief executive officer, Chief Operating Officer and Chief Business Officer, and specific expertise in oncology drug and diagnostic product development, business development, and launch planning. Mr. Paterson was Head of Global Strategy for Specialty Market and Patient Level Data at IMS Health after playing a key role in the acquisition of PharMetrics by IMS Health as Vice President of Marketing and Corporate Development.

Our scientific co founders are recognized leaders in the field of cancer biology. Robert Weinberg, Ph.D., Founding Member of the Whitehead Institute and Professor of Biology at MIT, has played a key role in identifying the genetic basis of cancer. Dr. Weinberg discovered the first tumor oncogene, the first tumor suppressor gene, the role of a protein related to the cell surface receptor HER2 in preclinical studies and the mechanisms underlying the formation of cancer stem cells. Eric Lander, Ph.D., Founding Director of the Broad Institute, Professor of Biology at MIT and Professor of Systems Biology at Harvard Medical School, played a central role in the Human Genome Project.

INTELLECTUAL PROPERTY

We strive to protect the proprietary technology that we believe is important to our business, including seeking and maintaining patents intended to cover our product candidates and compositions, their methods of use and processes for their manufacture, and any other aspects of inventions that are commercially important to the development of our business. We also rely on trade secrets to protect aspects of our business that are not amenable to, or that we do not consider appropriate for, patent protection.

We plan to continue to expand our intellectual property estate by filing patent applications directed to compositions, methods of treatment and patient selection created or identified from our ongoing development of our product candidates. Our success will depend on our ability to obtain and maintain patent and other proprietary protection for commercially important technology, inventions and know how related to our business, defend and enforce our patents, preserve the confidentiality of our trade secrets and operate without infringing the valid and enforceable patents and proprietary rights of third parties. We also rely on know how, continuing technological innovation and in licensing opportunities to develop and maintain our proprietary position. We seek to obtain domestic and international patent protection, and endeavor to promptly file patent applications for new commercially valuable inventions.

The patent positions of biopharmaceutical companies like us are generally uncertain and involve complex legal, scientific and factual questions. In addition, the coverage claimed in a patent application can be significantly reduced before the patent is issued, and patent scope can be reinterpreted by the courts after issuance. Moreover, many jurisdictions permit third parties to challenge issued patents in administrative proceedings, which may result in further narrowing or even cancellation of patent claims. We cannot predict whether the patent applications we are currently pursuing will issue as patents in any particular jurisdiction or whether the claims of any issued patents will provide sufficient protection from competitors.

Because patent applications in the United States and certain other jurisdictions are maintained in secrecy for 18 months or potentially even longer, and since publication of discoveries in the scientific or patent literature often lags behind actual discoveries, we cannot be certain of the priority of inventions covered by pending patent applications. Moreover, we may have to participate in interference proceedings or derivation proceedings declared by the U.S. Patent and Trademark Office to determine priority of invention.

Patents

Our patent portfolio includes issued and pending applications worldwide. These patent applications fall into three categories: (1) PI3K inhibition program; (2) FAK inhibition program; and (3) other programs.

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PI3K inhibition program

We are currently developing the PI3K inhibitor duvelisib.

We have exclusively licensed a portfolio of patent applications owned by Intellikine LLC and Infinity Pharmaceuticals, Inc. (Infinity), which are directed to PI3K inhibitor compounds and methods of their use, for example, in cancer. Certain patent families are related to duvelisib. These patent families include issued patents having claims covering duvelisib generically and specifically. Also included are issued patents covering certain polymorphs of duvelisib. Exemplary patents covering duvelisib, pharmaceutical compositions comprising duvelisib, methods of use, polymorphs, and methods of manufacture include US 8,193,182; US 8,785,456, and US 9,216,982. These U.S. patents have issued and will expire between 2029 and 2032. Related issued and pending worldwide patents and applications with claims to duvelisib, pharmaceutical compounds, methods of use, polymorphs, and methods of manufacture are pending in about 40 countries. Additional patent applications related to certain methods of use and combination therapies, as issued, would expire between 2029 and 2036.

FAK inhibition program

We are currently developing the FAK inhibitor defactinib.

We have exclusively licensed a portfolio of patent applications owned by Pfizer, which are directed to FAK inhibitor compounds and methods of their use, for example in cancer. One patent family is related generally to defactinib. This patent family includes issued patents having claims covering defactinib generically and specifically. For example, US 7,928,109 covers the composition of matter of defactinib specifically and US 8,247,411 covers the composition of matter of defactinib generically. Also included are issued and pending patent applications having claims directed to methods of treatment and methods of making defactinib. For example, US 8,440,822 covers methods of making defactinib. Any U.S. patents that have issued or will issue in this family will have a statutory expiration date in April of 2028. Related cases are pending worldwide, including for example in Europe, Brazil, Thailand, Hong Kong, and India, and granted in Australia, Mexico, Canada, China, Korea, Israel, New Zealand, South Africa, Singapore, Taiwan, and Japan.

In addition to the issued and pending patent applications exclusively licensed from Pfizer, we own three patent families covering defactinib. One family is directed to compositions (e.g., oral dosage forms) of defactinib and certain methods of use. Any U.S. patents that will issue in this family will have a statutory expiration date in January of 2035. The other two families are directed to methods of using a FAK inhibitor in combination with another agent, such as defactinib in combination with a mitogen-activated protein kinase kinase enzymes (MEK) inhibitor for treating a patient or defactinib in combination with an immunotherapeutic agent. Any U.S. patents that will issue in these families will have a statutory expiration date in February of 2035 and June of 2036.

Our licensed portfolio of patent applications from Pfizer also includes four families of patent applications directed to VS 6062 and related methods of use. The patent families include issued and pending patent applications having claims directed to VS 6062, methods of manufacture, and pharmaceutical salts. Patents have issued in these families in the U.S. that will expire in December of 2023, April of 2025, and November of 2028, respectively. Related cases have been granted worldwide, including for example in Australia, Canada, China, Japan, and Europe.

Patent Term

The base term of a U.S. patent is 20 years from the filing date of the earliest filed non provisional patent application from which the patent claims priority. The term of a U.S. patent can be lengthened by patent term adjustment, which compensates the owner of the patent for administrative delays at the U.S. Patent and Trademark Office. In some cases,

the term of a U.S. patent is shortened by terminal disclaimer that reduces its term to that of an earlier expiring patent.

The term of a United States patent may be eligible for patent term extension under the Drug Price Competition and Patent Term Restoration Act of 1984, referred to as the Hatch Waxman Act, to account for at least some of the time the drug is under development and regulatory review after the patent is granted. With regard to a

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drug for which FDA approval is the first permitted marketing of the active ingredient, the Hatch Waxman Act allows for extension of the term of one United States patent that includes at least one claim covering the composition of matter of an FDA approved drug, an FDA approved method of treatment using the drug, and/or a method of manufacturing the FDA approved drug. The extended patent term cannot exceed the shorter of five years beyond the non extended expiration of the patent or 14 years from the date of the FDA approval of the drug. Some foreign jurisdictions, including Europe and Japan, have analogous patent term extension provisions, which allow for extension of the term of a patent that covers a drug approved by the applicable foreign regulatory agency. In the future, if and when our pharmaceutical products receive FDA approval, we expect to apply for patent term extension on patents covering those products, their methods of use, and/or methods of manufacture.

LICENSES

Infinity Pharmaceuticals, Inc.

In November 2016, we entered into an amended and restated license agreement with Infinity, under which we acquired an exclusive worldwide license for the research, development, commercialization, and manufacture of products in oncology indications containing duvelisib. In connection with the license agreement, we assumed operational and financial responsibility for certain activities that were part of Infinity's duvelisib program, including the DUO study for patients with relapsed/refractory CLL/SLL, and Infinity assumed financial responsibility for the shutdown of certain other clinical studies up to a maximum of $4.5 million. We are obligated to use diligent efforts to develop and commercialize a product in an oncology indication containing duvelisib. During the term of the license agreement, Infinity has agreed not to research, develop, manufacture or commercialize duvelisib in any other indication in humans or animals.

Pursuant to the terms of the license agreement, we are required to make the following payments to Infinity in cash or, at our election, in whole or in part, in shares of our common stock: (i) $6.0 million upon the completion of the DUO study if the results of the study meet certain pre-specified criteria, which was paid in cash by us to Infinity in October 2017, and (ii) $22.0 million upon the approval of an NDA in the United States or an application for marketing authorization with a regulatory authority outside of the United States for a product in an oncology indication containing duvelisib. For any portion of any of the foregoing payments that we elect to issue in shares of our common stock in lieu of cash, the number of shares of common stock to be issued will be determined by multiplying (1) 1.025 by (2) the number of shares of common stock equal to (a) the amount of the payment to be paid in shares of common stock divided by (b) the average closing price of a share of common stock as quoted on Nasdaq for a twenty-day period following the public announcement of the applicable milestone event. The shares of common stock will be issued as unregistered securities, and we will have an obligation to promptly file a registration statement with the SEC to register such shares for resale. Any issuance of shares will be subject to the satisfaction of closing conditions, including that all material authorizations, consents, approvals and the like necessary for such issuance shall have been obtained.

We are also obligated to pay Infinity royalties on worldwide net sales of any products in an oncology indication containing duvelisib ranging from the mid-single digits to the high single digits. The royalties will expire on a product-by-product and country-by-country basis until the latest to occur of (i) the last-to-expire patent right covering the applicable product in the applicable country, (ii) the last-to-expire patent right covering the manufacture of the

applicable product in the country of manufacture of such product, (iii) the expiration of non-patent regulatory exclusivity in such country and (iv) ten years following the first commercial sale of a product in a country, provided that if royalties on net sales for a product in the United States are payable solely on the basis of non-patent regulatory exclusivity, the applicable royalty on net sales for such product in the United States will be reduced by 50%. The royalties are also subject to reduction by 50% of certain third-party royalty payments or patent litigation damages or settlements which might be required to be paid by us if litigation were to arise, with any such reductions capped at 50% of the amounts otherwise payable during the applicable royalty payment period.

In addition to the foregoing, we are obligated to pay Infinity an additional royalty of 4% on worldwide net sales of any products in an oncology indication containing duvelisib to cover the reimbursement of research and development costs owed by Infinity to Mundipharma International Corporation Limited (MICL) and Purdue Pharmaceutical Products L.P. (Purdue). Once Infinity has fully reimbursed MICL and Purdue, the royalty obligations will be reduced to 1% of net sales in the United States. These trailing MICL royalties are payable until

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the later to occur of the last-to-expire of specified patent rights and the expiration of non-patent regulatory exclusivities in a country. Each of the above royalty rates is reduced by 50% on a product-by-product and country-by-country basis if the applicable royalty is payable solely on the basis of non-patent regulatory exclusivity. In addition, the trailing MICL royalties are subject to reduction by 50% of certain third-party royalty payments or patent litigation damages or settlements which might be required to be paid by us if litigation were to arise, with any such reductions capped at 50% of the amounts otherwise payable during the applicable royalty payment period.

Pfizer Inc.

On July 11, 2012, we entered into a license agreement with Pfizer under which Pfizer granted us worldwide, exclusive rights to research, develop, manufacture and commercialize products containing certain of Pfizer's inhibitors of FAK, including defactinib, for all therapeutic, diagnostic and prophylactic uses in humans. We have the right to grant sublicenses under the foregoing licensed rights, subject to certain restrictions. We are solely responsible, at our own expense, for the clinical development of these products, which is to be conducted in accordance with an agreed upon development plan. We are also responsible for all manufacturing and commercialization activities at our own expense. Pfizer provided us with an initial quantity of clinical supplies of one of the products for an agreed upon price.

Upon entering into the license agreement, we made a one time cash payment to Pfizer in the amount of $1.5 million and issued 192,012 shares of our common stock. Pfizer is also eligible to receive up to $2.0 million in developmental milestones and up to an additional $125.0 million based on the successful attainment of regulatory and commercial sales milestones. Pfizer is also eligible to receive high single to mid-double digit royalties on future net sales of the products. Our royalty obligations with respect to each product in each country begin on the date of first commercial sale of the product in that country, and end on the later of 10 years after the date of first commercial sale of the product in that country or the date of expiration or abandonment of the last claim contained in any issued patent or patent application licensed by Pfizer to us that covers the product in that country.

The license agreement will remain in effect until the expiration of all of our royalty obligations to Pfizer, determined on a product by product and country by country basis. So long as we are not in breach of the license agreement, we have the right to terminate the license agreement at will on a product by product and country by country basis, or in its entirety, upon 90 days written notice to Pfizer. Either party has the right to terminate the license agreement in connection with an insolvency event involving the other party or a material breach of the license agreement by the other party that remains uncured for a specified period of time. If the license agreement is terminated by either party for any reason, worldwide rights to the research, development, manufacture and commercialization of the products revert back to Pfizer.

COMPETITION

The biotechnology and pharmaceutical industries are characterized by rapidly advancing technologies, intense competition and a strong emphasis on proprietary products. While we believe that our technology, development experience and scientific knowledge provide us with competitive advantages, we face potential competition from many different sources, including major pharmaceutical, specialty pharmaceutical and biotechnology companies, academic institutions and governmental agencies and public and private research institutions. Any product candidates that we successfully develop and commercialize will compete with existing therapies and new therapies that may become available in the future.

Many of our competitors may 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, biotechnology and diagnostic industries may result in even more resources being concentrated among a smaller number of our competitors. These competitors also compete with us in recruiting and retaining qualified scientific and management personnel and establishing clinical trial sites and patient registration for clinical trials, as well as in acquiring technologies complementary to, or necessary for, our programs. Smaller or early stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies.

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The key competitive factors affecting the success of all of our product candidates, if approved, are likely to be their efficacy, safety, convenience, price, the level of generic competition and the availability of reimbursement from government and other third party payors.

Our commercial opportunity could be reduced or eliminated if our competitors develop and commercialize products that are safer, more effective, have fewer or less severe side effects, are more convenient or are less expensive than any products that we may develop. Our competitors also may obtain FDA or other regulatory approval for their products more rapidly than we may obtain approval for ours, which could result in our competitors establishing a strong market position before we are able to enter the market. In addition, our ability to compete may be affected in many cases by insurers or other third party payors seeking to encourage the use of generic products. There are many generic products currently on the market for the indications that we are pursuing, and additional products are expected to become available on a generic basis over the coming years. If our therapeutic product candidates are approved, we expect that they will be priced at a significant premium over competitive generic products.

The most common methods of treating patients with cancer are surgery, radiation and drug therapy, including chemotherapy, hormone therapy and targeted drug therapy. There are a variety of available drug therapies marketed for cancer. In many cases, these drugs are administered in combination to enhance efficacy. While our product candidates may compete with many existing drug and other therapies, to the extent they are ultimately used in combination with or as an adjunct to these therapies, our product candidates will not be competitive with them. Some of the currently approved drug therapies 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. In general, although there has been considerable progress over the past few decades in the treatment of cancer and the currently marketed therapies provide benefits to many patients, these therapies all are limited to some extent in their efficacy and frequency of adverse events, and none of them are successful in treating all patients. As a result, the level of morbidity and mortality from cancer remains high.

In addition to currently marketed therapies, there are also a number of products in late stage clinical development to treat cancer. These products in development may provide efficacy, safety, convenience and other benefits that are not provided by currently marketed therapies. As a result, they may provide significant competition for any of our product candidates for which we obtain market approval.

Our competitors may commence and complete clinical testing of their product candidates, obtain regulatory approvals and begin commercialization of their products sooner than we may for our own product candidates. These competitive products may have superior safety or efficacy, or be manufactured less expensively, than our product candidates. If we are unable to compete effectively against these companies on the basis of safety, efficacy or cost, then we may not be able to commercialize our product candidates or achieve a competitive position in the market. This would adversely affect our business.

PI3K inhibition program

We believe that the following companies, among others, have developed or are in the clinical stage of development of compounds targeting PI3K:

- Gilead Sciences, Inc. has received approval from the FDA of idelalisib for the treatment of patients with CLL, SLL, or FL, and which we believe is conducting a Phase 1b clinical trial of acalisib (GS-9820);
- Bayer AG has received approval from the FDA of copanlisib for the treatment of patients with relapsed FL;
- Novartis, which we believe is conducting a Phase 2 clinical trial of buparlisib;
- AstraZeneca, which we believe is conducting Phase 2 clinical trials of ACP 319;
- TG Therapeutics, Inc., which we believe is conducting multiple clinical trials of TGR-1202; and

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- Incyte Corporation, which we believe is conducting a Phase 2 clinical trial of INCB-050465, and which we also believe is conducting a Phase 2 clinical trial of INCB-040093.

In addition, many companies are developing product candidates directed to disease targets such as Bruton's Tyrosine Kinase (BTK), B-cell lymphoma 2 (BCL-2), Janus Kinase (JAK), B-lymphocyte antigen CD-19, and programmed death 1/ligand 1 (PD-1/PD-L1), Cluster of Differentiation 79B antibody-drug conjugate (CD79B ADC), and pleiotropic pathways in the fields of hematology-oncology, including in the specific diseases for which we are currently developing duvelisib, or for which we may develop duvelisib or other PI3K inhibitors in the future. Such companies include:

- Pharmacyclics LLC, a wholly-owned subsidiary of AbbVie, through its collaboration with Janssen Biotech, which has received approval from the FDA of ibrutinib, a BTK inhibitor, for the treatment of patients with mantle cell lymphoma (MCL), CLL, MZL, SLL, or Waldenström's macroglobulinemia, and is conducting multiple late stage clinical studies of ibrutinib in additional hematologic malignancies;
- AbbVie, through its collaboration with Roche, which has received approval from the FDA of venetoclax, a BCL-2 inhibitor, for the treatment of patients with CLL, and is conducting multiple late stage clinical studies of venetoclax in additional hematologic malignancies;
- Celgene Corporation, which has received FDA approval of lenalidomide, an immunomodulator, for the treatment of patients with multiple myeloma, MCL, and myelodyplastic syndromes, and is conducting late stage clinical studies of lenalidomide in additional hematologic malignancies; we also believe that Celgene is conducting a Phase 1 clinical trial of CC-292, a BTK inhibitor, in patients with CLL;
- AstraZeneca, which we believe is conducting a Phase 3 clinical trial of ACP-196, a BTK inhibitor, in patients with CLL; and
- Incyte Corporation, which has received FDA approval of ruxolitinib, a JAK inhibitor, in patients with intermediate or high-risk myelofibrosis, and which we believe is conducting Phase 2 clinical trials in CLL.

FAK inhibition program

There are other companies working to develop therapies to treat cancer including some who also target the tumor microenvironment. These companies include divisions of large pharmaceutical companies including Astellas Pharma Inc., Celgene, Inc., Sanofi Aventis U.S. LLC, GlaxoSmithKline plc, Boehringer Ingelheim GmbH, Pfizer Inc. and others.

MANUFACTURING

We do not own or operate, and currently have no plans to establish, any manufacturing facilities. We currently rely, and expect to continue to rely, on third parties for the manufacture of our product candidates and any products that we may develop, other than small amounts of compounds that we may synthesize ourselves for preclinical testing. To date, we have obtained starting materials for our supply of the bulk drug substance and drug product for our product candidates from third party manufacturers. We obtain our supplies from these manufacturers on a purchase order basis and do not have long term supply arrangements in place. We do not currently have arrangements in place for redundant supply or a second source for bulk drug substance and drug product. If our current third party manufacturers should become unavailable to us for any reason, we believe that there are several potential replacements, although we might incur some delay in identifying and qualifying such replacements.

All of our drug candidates are organic compounds of low molecular weight, generally called small molecules. We select compounds not only on the basis of their potential efficacy and safety, but also for their ease of synthesis and reasonable cost of their starting materials. We expect to continue to develop drug candidates that can be produced cost effectively at third party manufacturing facilities.

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GOVERNMENT REGULATION

Government authorities in the United States, at the federal, state and local level, and in other countries extensively regulate, among other things, the research, development, testing, manufacture, including any manufacturing changes, packaging, storage, recordkeeping, labeling, advertising, promotion, distribution, marketing, post approval monitoring and reporting, import and export of pharmaceutical products, such as those we are developing.

United States drug approval process

In the United States, the FDA regulates drugs under the Federal Food, Drug, and Cosmetic Act (FDCA) and implementing regulations. The process of obtaining regulatory approvals and the subsequent compliance with appropriate federal, state, local and foreign statutes and regulations requires the expenditure of substantial time and financial resources. Failure to comply with the applicable United States requirements at any time during the product development process, approval process or after approval, may subject an applicant to a variety of administrative or judicial sanctions, such as the FDA's refusal to approve pending applications, withdrawal of an approval, imposition of a clinical hold, issuance of warning letters, product recalls, product seizures, total or partial suspension of production or distribution injunctions, fines, refusals of government contracts, restitution, disgorgement of profits or civil or criminal penalties.

The process required by the FDA before a drug may be marketed in the United States generally involves the following:

- completion of preclinical laboratory tests, animal studies and formulation studies in compliance with the FDA's good laboratory practice (GLP) regulations;
- submission to the FDA of an investigational new drug (IND) application, which must become effective before human clinical trials may begin;
- approval by an independent institutional review board (IRB) at each clinical site before each trial may be initiated;
- performance of adequate and well controlled human clinical trials in accordance with good clinical practices (GCP) to establish the safety and efficacy of the proposed drug for each indication;
- submission to the FDA of an NDA;
- satisfactory completion of an FDA advisory committee review, if applicable;
- satisfactory completion of an FDA inspection of the manufacturing facility or facilities at which the product is produced to assess compliance with current good manufacturing practices (cGMP) requirements and to assure that the facilities, methods and controls are adequate to preserve the drug's identity, strength, quality and purity; and
- FDA review and approval of the NDA.

Preclinical studies

Preclinical studies include laboratory evaluation of product chemistry and formulation, as well as in vitro and animal studies to assess the potential for adverse events and in some cases to establish a rationale for therapeutic use. The conduct of preclinical studies is subject to federal regulations and requirements, including GLP regulations. An IND sponsor must submit the results of the preclinical tests, together with manufacturing information, analytical data, any available clinical data or literature and plans for clinical studies, among other things, to the FDA as part of an IND. Some long term preclinical testing, such as animal tests of reproductive adverse events and carcinogenicity,

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may continue after the IND is submitted. An IND automatically becomes effective 30 days after receipt by the FDA, unless before that time the FDA raises concerns or questions related to one or more proposed clinical trials and places the trial on clinical hold. In such a case, the IND sponsor and the FDA must resolve any outstanding concerns before the clinical trial can begin. As a result, submission of an IND may not result in the FDA allowing clinical trials to commence.

Clinical trials

Clinical trials involve the administration of the investigational new drug to human subjects under the supervision of qualified investigators in accordance with GCP requirements, which include, among other things, the requirement that all research subjects provide their informed consent in writing before their participation in any clinical trial. Clinical trials are conducted under written study protocols detailing, among other things, the objectives of the study, the parameters to be used in monitoring safety and the effectiveness criteria to be evaluated. A protocol for each clinical trial and any subsequent protocol amendments must be submitted to the FDA as part of the IND. In addition, an IRB at each institution participating in the clinical trial must review and approve the plan for any clinical trial before it commences at that institution, and the IRB must conduct continuing review. The IRB must review and approve, among other things, the study protocol and informed consent information to be provided to study subjects. An IRB must operate in compliance with FDA regulations. Information about certain clinical trials must be submitted within specific timeframes to the National Institutes of Health for public dissemination on their ClinicalTrials.gov website.

Human clinical trials are typically conducted in three sequential phases, which may overlap or be combined:

- Phase 1: The drug is initially introduced into healthy human subjects or patients with the target disease or condition and tested for safety, dosage tolerance, absorption, metabolism, distribution, excretion and, if possible, to gain an early indication of its effectiveness.
- Phase 2: The drug is administered to a limited patient population to identify possible adverse effects and safety risks, to preliminarily evaluate the efficacy of the product for specific targeted diseases and to determine dosage tolerance and optimal dosage.
- Phase 3: The drug is administered to an expanded patient population in adequate and well controlled clinical trials to generate sufficient data to statistically confirm the efficacy and safety of the product for approval, to establish the overall risk benefit profile of the product and to provide adequate information for the labeling of the product.

Progress reports detailing the results of the clinical trials must be submitted at least annually to the FDA and more frequently if serious adverse events occur. Phase 1, Phase 2 and Phase 3 clinical trials may not be completed successfully within any specified period, or at all. Furthermore, the FDA or the sponsor may suspend or terminate a clinical trial at any time on various grounds, including a finding that the research subjects are being exposed to an unacceptable health risk. Similarly, an IRB can suspend or terminate approval of a clinical trial at its institution if the clinical trial is not being conducted in accordance with the IRB's requirements or if the drug has been associated with unexpected serious harm to patients.

Marketing approval

Assuming successful completion of the required clinical testing, the results of the preclinical and clinical studies, together with detailed information relating to the product's chemistry, manufacture, controls and proposed labeling, among other things, are submitted to the FDA as part of an NDA requesting approval to market the product for one or more indications. Under federal law, the submission of most NDAs is additionally subject to a substantial application user fee, currently scheduled to exceed $2.4 million, and the sponsor of an approved NDA is also subject to annual program fees, based on the number of approved products. These fees are typically adjusted annually. User fee statutory authority expires every five years. The Prescription Drug User Fee Act, was re-authorized for an additional five years in 2017 until 2022. Fee waivers are available in certain circumstances, including a waiver of

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the application fee for an orphan drug application.

The FDA conducts a preliminary review of all NDAs within the first 60 days after submission before accepting them for filing to determine whether they are sufficiently complete to permit substantive review. The FDA may request additional information rather than accept an NDA for filing. In this event, the application must be resubmitted with the additional information. The resubmitted application is also subject to review before the FDA accepts it for filing. Once the submission is accepted for filing, the FDA begins an in depth substantive review. The FDA has agreed to specified performance goals in the review of NDAs. Under these goals, the FDA has committed to review most such applications for non priority products within 10 months after accepting the application for filing, and most applications for priority review products, that is, drugs that the FDA determines represent a significant improvement over existing therapy, within six months after accepting the application for filing. The review process may be extended by the FDA for three additional months to consider certain information or clarification regarding information already provided in the submission. The FDA may also refer applications for novel drugs or products that present difficult questions of safety or efficacy to an advisory committee, typically a panel that includes clinicians and other experts, for review, evaluation and a recommendation as to whether the application should be approved. The FDA is not bound by the recommendations of an advisory committee, but it considers such recommendations carefully when making decisions.

Before approving an NDA, the FDA typically will inspect the facility or facilities where the product is manufactured. The FDA will not approve an application unless it determines that the manufacturing processes and facilities are in compliance with cGMP requirements and adequate to assure consistent production of the product within required specifications. In addition, before approving an NDA, the FDA will typically inspect one or more clinical sites to assure compliance with GCP and integrity of the clinical data submitted.

The testing and approval process requires substantial time, effort and financial resources, and each may take many years to complete. Data obtained from clinical activities are not always conclusive and may be susceptible to varying interpretations, which could delay, limit or prevent regulatory approval. The FDA may not grant approval on a timely basis, or at all. We may encounter difficulties or unanticipated costs in our efforts to develop our product candidates and secure necessary governmental approvals, which could delay or preclude us from marketing our products.

After the FDA's evaluation of the NDA and inspection of the manufacturing facilities, the FDA may issue an approval letter or a complete response letter. An approval letter authorizes commercial marketing of the drug with specific prescribing information for specific indications. A complete response letter generally outlines the deficiencies in the submission and may require substantial additional testing or information in order for the FDA to reconsider the application. If and when those deficiencies have been addressed to the FDA's satisfaction in a resubmission of the NDA, the FDA will issue an approval letter. The FDA has committed to reviewing such resubmissions in two or six months depending on the type of information included. Even with submission of this additional information, the FDA ultimately may decide that the application does not satisfy the regulatory criteria for approval and refuse to approve the NDA.

Even if the FDA approves a product, it may limit the approved indications for use for the product, require that contraindications, warnings or precautions be included in the product labeling, require that post approval studies, including Phase 4 clinical trials, be conducted to further assess a drug's safety after approval, require testing and surveillance programs to monitor the product after commercialization, or impose other conditions, including distribution restrictions or other risk management mechanisms, which can materially affect the potential market and profitability of the product. The FDA may prevent or limit further marketing of a product based on the results of post market studies or surveillance programs. After approval, some types of changes to the approved product, such as adding new indications, manufacturing changes and additional labeling claims, are subject to further testing requirements and FDA review and approval.

Fast track designation

The FDA is required to facilitate the development and expedite the review of drugs that are intended for the treatment of a serious or life threatening condition for which there is no effective treatment and which demonstrate the potential to address unmet medical needs for the condition. Under the fast track program, the sponsor of a new

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drug candidate may request the FDA to designate the product for a specific indication as a fast track product concurrent with or after the filing of the IND for the product candidate. The FDA must determine if the product candidate qualifies for fast track designation within 60 days after receipt of the sponsor's request.

In addition to other benefits, such as the ability to use surrogate endpoints and have greater interactions with the FDA, the FDA may initiate review of sections of a fast track product's NDA before the application is complete. This rolling review is available if the applicant provides and the FDA approves a schedule for the submission of the remaining information and the applicant pays applicable user fees. However, the FDA's time period goal for reviewing a fast track application does not begin until the last section of the NDA is submitted. In addition, the fast track designation may be withdrawn by the FDA if the FDA believes that the designation is no longer supported by data emerging in the clinical trial process.

Priority review

Under FDA policies, a product candidate may be eligible for priority review, or review within a six month time frame from the time a complete application is accepted for filing. Products regulated by the FDA's Center for Drug Evaluation and Research (CDER) are eligible for priority review if they provide a significant improvement compared to marketed products in the treatment, diagnosis or prevention of a disease.

Accelerated approval

Under the FDA's accelerated approval regulations, the FDA may approve a drug for a serious or life threatening illness that provides meaningful therapeutic benefit to patients over existing treatments based upon a surrogate endpoint that is reasonably likely to predict clinical benefit. In clinical trials, a surrogate endpoint is a measurement of laboratory or clinical signs of a disease or condition that substitutes for a direct measurement of how a patient feels, functions or survives. Surrogate endpoints can often be measured more easily or more rapidly than clinical endpoints. A product candidate approved on this basis is subject to rigorous post marketing compliance requirements, including the completion of Phase 4 or post approval clinical trials to confirm the effect on the clinical endpoint. Failure to conduct required post approval studies, or confirm a clinical benefit during post marketing studies, would allow the FDA to withdraw the drug from the market on an expedited basis. All promotional materials for drug candidates approved under accelerated regulations are subject to prior review by the FDA.

Orphan drugs

Under the Orphan Drug Act, the FDA may grant orphan drug designation to drugs intended to treat a rare disease or condition, which is generally defined as a disease or condition that affects fewer than 200,000 individuals in the United States. Orphan drug designation must be requested before submitting an NDA. After the FDA grants orphan drug designation, the generic identity of the drug and its potential orphan use are disclosed publicly by the FDA. Orphan drug designation does not convey any advantage in, or shorten the duration of, the regulatory review and approval process. The first NDA applicant to receive FDA approval for a particular active ingredient to treat a particular disease with FDA orphan drug designation is entitled to a seven year exclusive marketing period in the United States for that product, for that indication. During the seven year exclusivity period, the FDA may not approve any other applications to market the same drug for the same orphan indication, except in limited circumstances, such as a showing of clinical superiority to the product with orphan drug exclusivity in that it is shown to be safer, more effective or makes a major contribution to patient care. Orphan drug exclusivity does not prevent the FDA from approving a different drug for the same disease or condition, or the same drug for a different disease or condition. Among the other benefits of orphan drug designation are tax credits for certain research and a waiver of the NDA application user fee.

Pediatric information

Under the Pediatric Research Equity Act of 2003, as amended and reauthorized by the Food and Drug Administration Amendments Act of 2007 (FDAAA), an NDA or supplement to an NDA must contain data that are adequate to assess the safety and effectiveness of the drug for the claimed indications in all relevant pediatric subpopulations, and to support dosing and administration for each pediatric subpopulation for which the product is

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safe and effective. The FDA may, on its own initiative or at the request of the applicant, grant deferrals for submission of some or all pediatric data until after approval of the product for use in adults, or full or partial waivers from the pediatric data requirements. Unless otherwise required by regulation, the pediatric data requirements do not apply to products with orphan drug designation.

The Hatch Waxman act

Abbreviated New Drug Applications

In seeking approval for a drug through an NDA, applicants are required to list with the FDA each patent with claims that cover the applicant's product or a method of using the product. Upon approval of a drug, each of the patents listed in the application for the drug is then published in the FDA's Approved Drug Products with Therapeutic Equivalence Evaluations, commonly known as the Orange Book. Drugs listed in the Orange Book can, in turn, be cited by potential competitors in support of approval of an abbreviated New Drug Application (ANDA). Generally, an ANDA provides for marketing of a drug product that has the same active ingredients in the same strengths, dosage form and route of administration as the listed drug and has been shown to be bioequivalent through in vitro or in vivo testing or otherwise to the listed drug. ANDA applicants are not required to conduct or submit results of preclinical or clinical tests to prove the safety or effectiveness of their drug product, other than the requirement for bioequivalence testing. Drugs approved in this way are commonly referred to as "generic equivalents" to the listed drug, and can often be substituted by pharmacists under prescriptions written for the original listed drug.

The ANDA applicant is required to certify to the FDA concerning any patents listed for the approved product in the FDA's Orange Book, except for patents covering methods of use for which the ANDA applicant is not seeking approval. Specifically, the applicant must certify with respect to each patent that:

- the required patent information has not been filed;
- the listed patent has expired;
- the listed patent has not expired, but will expire on a particular date and approval is sought after patent expiration; or
- the listed patent is invalid, unenforceable or will not be infringed by the new product.

A certification that the new product will not infringe the already approved product's listed patents or that such patents are invalid or unenforceable is called a Paragraph IV certification. If the applicant does not challenge the listed patents or indicate that it is not seeking approval of a patented method of use, the ANDA application will not be approved until all the listed patents claiming the referenced product have expired.

If the ANDA applicant has provided a Paragraph IV certification to the FDA, the applicant must also send notice of the Paragraph IV certification to the NDA and patent holders once the ANDA has been accepted for filing by the FDA. The NDA and patent holders may then initiate a patent infringement lawsuit in response to the notice of the Paragraph IV certification. The filing of a patent infringement lawsuit within 45 days after the receipt of a Paragraph IV certification automatically prevents the FDA from approving the ANDA until the earlier of 30 months after the NDA or patent holder's receipt of the Paragraph IV certification, expiration of the patent, settlement of the lawsuit or a decision in the infringement case that is favorable to the ANDA applicant.

The ANDA also will not be approved until any applicable non patent exclusivity period, such as exclusivity for obtaining approval of a new chemical entity, for the referenced product has expired. Federal law provides a period of five years following approval of a drug containing no previously approved active moiety during which ANDAs for generic versions of those drugs cannot be submitted unless the submission contains a Paragraph IV challenge to a listed patent, in which case the submission may be made four years following the original product approval. Federal law provides for a period of three years of exclusivity during which the FDA cannot grant effective approval of an

ANDA for the conditions of use covered by the exclusivity, but FDA requires

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as a condition of approval new clinical trials conducted by or for the sponsor. This three year exclusivity period often protects changes to a previously approved drug product, such as a new dosage form, route of administration, combination or indication. Under the Best Pharmaceuticals for Children Act, federal law also provides that periods of patent and non patent marketing exclusivity listed in the Orange Book for a drug may be extended by six months if the NDA sponsor conducts pediatric studies identified by the FDA in a written request. For written requests issued by the FDA after September 27, 2007, the date of enactment of the FDAAA, the FDA must grant pediatric exclusivity no later than nine months prior to the date of expiration of patent or non patent exclusivity in order for the six month pediatric extension to apply to that exclusivity period.

Combination products

The FDA regulates combinations of products that cross FDA centers, such as drug, biologic or medical device components that are physically, chemically or otherwise combined into a single entity, as a combination product. The FDA center with primary jurisdiction for the combination product will take the lead in the premarket review of the product, with the other center consulting or collaborating with the lead center.

The FDA's Office of Combination Products (OCP) determines which center will have primary jurisdiction for the combination product based on the combination product's "primary mode of action." A mode of action is the means by which a product achieves an intended therapeutic effect or action. The primary mode of action is the mode of action that provides the most important therapeutic action of the combination product, or the mode of action expected to make the greatest contribution to the overall intended therapeutic effects of the combination product.

Often it is difficult for the OCP to determine with reasonable certainty the most important therapeutic action of the combination product. In those difficult cases, the OCP will consider consistency with other combination products raising similar types of safety and effectiveness questions, or which center has the most expertise to evaluate the most significant safety and effectiveness questions raised by the combination product.

A sponsor may use a voluntary formal process, known as a Request for Designation, when the product classification is unclear or in dispute, to obtain a binding decision as to which center will regulate the combination product. If the sponsor objects to that decision, it may request that the agency reconsider that decision.

Other regulatory requirements

Any drug manufactured or distributed by us pursuant to FDA approvals would be subject to pervasive and continuing regulation by the FDA, including, among other things, requirements relating to recordkeeping, periodic reporting, product sampling and distribution, advertising and promotion and reporting of adverse experiences with the product. After approval, most changes to the approved product, such as adding new indications or other labeling claims are subject to prior FDA review and approval.

The FDA may impose a number of post approval requirements as a condition of approval of an NDA. For example, the FDA may require post marketing testing, including Phase 4 clinical trials, and surveillance to further assess and monitor the product's safety and effectiveness after commercialization. Regulatory approval of oncology products often requires that patients in clinical trials be followed for long periods to determine the overall survival benefit of the drug.

In addition, drug manufacturers and other entities involved in the manufacture and distribution of approved drugs are required to register their establishments with the FDA and state agencies, and are subject to periodic unannounced inspections by the FDA and these state agencies for compliance with cGMP requirements. Changes to the manufacturing process are strictly regulated and often require prior FDA approval before being implemented. FDA

regulations also require investigation and correction of any deviations from cGMP and impose reporting and documentation requirements upon us and any third party manufacturers that we may decide to use. Accordingly, manufacturers must continue to expend time, money and effort in the areas of production and quality control to maintain cGMP compliance.

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Once an approval is granted, the FDA may withdraw the approval if compliance with regulatory requirements and standards is not maintained or if problems occur after the product reaches the market. Later discovery of previously unknown problems with a product, including adverse events of unanticipated severity or frequency, or with manufacturing processes, or failure to comply with regulatory requirements, may result in revisions to the approved labeling to add new safety information, imposition of post market studies or clinical trials to assess new safety risks or imposition of distribution or other restrictions under a Risk Evaluation and Mitigation Strategy program. Other potential consequences include, among other things:

- restrictions on the marketing or manufacturing of the product, complete withdrawal of the product from the market or product recalls;
- fines, warning letters or holds on post approval clinical trials;
- refusal of the FDA to approve pending applications or supplements to approved applications, or suspension or revocation of product license approvals;
- product seizure or detention, or refusal to permit the import or export of products; or
- consent decrees, injunctions or the imposition of civil or criminal penalties.

The FDA strictly regulates marketing, labeling, advertising and promotion of products that are placed on the market. Drugs may be promoted only for the approved indications and in accordance with the provisions of the approved label. The FDA and other agencies actively enforce the laws and regulations prohibiting the promotion of off label uses, and a company that is found to have improperly promoted off label uses may be subject to significant liability.

Additional provisions

Anti kickback and false claims laws

Although we currently have no products approved for commercial sale, we may be subject to various federal and state laws pertaining to healthcare “fraud and abuse,” including anti-kickback laws and false claims laws, for activities related to future sales of any of our product candidates that may in the future receive regulatory and marketing approval. Anti-kickback laws generally prohibit a pharmaceutical manufacturer from soliciting, offering, receiving, or paying any remuneration to generate business, including the purchase, prescription or use of a particular drug. Although the specific provisions of these laws vary, their scope is generally broad and there may not be regulations, guidance or court decisions that apply the laws to particular industry practices. There is therefore a possibility that our practices might be challenged under such anti-kickback laws. False claims laws prohibit anyone from knowingly and willingly presenting, or causing to be presented, any claims for payment for reimbursed drugs or services to third party payors (including Medicare and Medicaid) that are false or fraudulent.

Laws and regulations have been enacted by the federal government and various states to regulate the sales and marketing practices of pharmaceutical manufacturers with marketed products. The laws and regulations generally limit financial interactions between manufacturers and healthcare providers and/or require disclosure to the government and public of such interactions. Many of these laws and regulations contain ambiguous requirements or require administrative guidance for implementation. Given the lack of clarity in laws and their implementation, any future activities (if we obtain approval and/or reimbursement from federal healthcare programs for our product candidates) could be subject to challenge.

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If our operations are found to be in violation of the fraud and abuse laws described above, or any other laws that apply to us, we may be subject to penalties, including, without limitation, civil, criminal, and administrative penalties, damages, monetary fines, disgorgement, possible exclusion from participation in Medicare, Medicaid and other federal healthcare programs, contractual damages, reputational harm, diminished profits and future earnings, and curtailment or restructuring of our operations.

Physician drug samples

As part of the sales and marketing process, pharmaceutical companies frequently provide samples of approved drugs to physicians. The Prescription Drug Marketing Act (PDMA) imposes requirements and limitations upon the provision of drug samples to physicians, as well as prohibits states from licensing distributors of prescription drugs unless the state licensing program meets certain federal guidelines that include minimum standards for storage, handling and record keeping. In addition, the PDMA sets forth civil and criminal penalties for violations.

Foreign regulation

In order to market any product outside of the United States, we would need to comply with numerous and varying regulatory requirements of other countries regarding safety and efficacy and governing, among other things, clinical trials, marketing authorization, commercial sales and distribution of our products. Whether or not we obtain FDA approval for a product, we would need to obtain the necessary approvals by the comparable regulatory authorities of foreign countries before we can commence clinical trials or marketing of the product in those countries. The approval process varies from country to country and can involve additional product testing and additional administrative review periods. The time required to obtain approval in other countries might differ from and be longer than that required to obtain FDA approval. Regulatory approval in one country does not ensure regulatory approval in another, but a failure or delay in obtaining regulatory approval in one country may negatively impact the regulatory process in others.

Pharmaceutical coverage, pricing and reimbursement

Significant uncertainty exists as to the coverage and reimbursement status of any drug products for which we obtain regulatory approval. Sales of any of our product candidates, if approved, will depend, in part, on the extent to which the costs of the products will be covered by third party payors, including government health programs such as Medicare and Medicaid, commercial health insurers and managed care organizations. The process for determining whether a payor will provide coverage for a drug product may be separate from the process for setting the price or reimbursement rate that the payor will pay for the drug product once coverage is approved. Third party payors may limit coverage to specific drug products on an approved list, or formulary, which might not include all of the approved drugs for a particular indication.

In order to secure coverage and reimbursement for any product that might be approved for sale, we may need to conduct expensive pharmacoeconomic studies in order to demonstrate the medical necessity and cost effectiveness of the product, in addition to the costs required to obtain FDA or other comparable regulatory approvals. We may also need to provide discounts to purchasers, private health plans or government healthcare programs. Our product candidates may not be considered medically necessary or cost effective. A payor's decision to provide coverage for a drug product does not imply that an adequate reimbursement rate will be approved. Third party reimbursement may not be sufficient to enable us to maintain price levels high enough to realize an appropriate return on our investment in product development.

The containment of healthcare costs has become a priority of federal, state and foreign governments, and the prices of drugs have been a focus in this effort. Third party payors are increasingly challenging the prices charged for medical products and services and examining the medical necessity and cost effectiveness of medical products and services, in

addition to their safety and efficacy. If these third party payors do not consider our products to be cost effective compared to other available therapies, they may not cover our products after approval as a benefit under their plans or, if they do, the level of payment may not be sufficient to allow us to sell our products at a profit. The U.S. government, state legislatures and foreign governments have shown significant interest in implementing cost containment programs to limit the growth of government paid healthcare costs, including price

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controls, restrictions on reimbursement and requirements for substitution of generic products for branded prescription drugs. Adoption of such controls and measures, and tightening of restrictive policies in jurisdictions with existing controls and measures, could limit payments for pharmaceuticals such as the drug candidates that we are developing and could adversely affect our net revenue and results.

Pricing and reimbursement schemes vary widely from country to country. Some countries provide that drug products may be marketed only after a reimbursement price has been agreed. Some countries may require the completion of additional studies that compare the cost effectiveness of a particular product candidate to currently available therapies. For example, the European Union provides options for its member states to restrict the range of drug products for which their national health insurance systems provide reimbursement and to control the prices of medicinal products for human use. European Union member states may approve a specific price for a drug product or may instead adopt a system of direct or indirect controls on the profitability of the company placing the drug product on the market. Other member states allow companies to fix their own prices for drug products, but monitor and control company profits. The downward pressure on healthcare costs in general, particularly prescription drugs, has become very intense. As a result, increasingly high barriers are being erected to the entry of new products. In addition, in some countries, cross border imports from low priced markets exert competitive pressure that may reduce pricing within a country. There can be no assurance that any country that has price controls or reimbursement limitations for drug products will allow favorable reimbursement and pricing arrangements for any of our products.

The marketability of any products for which we receive regulatory approval for commercial sale may suffer if the government and third party payors fail to provide adequate coverage and reimbursement. In addition, an increasing emphasis on managed care in the United States has increased and we expect will continue to increase the pressure on drug pricing. Coverage policies, third party reimbursement rates and drug pricing regulation may change at any time. Even if favorable coverage and reimbursement status is attained for one or more products for which we receive regulatory approval, less favorable coverage policies and reimbursement rates may be implemented in the future.

New legislation and regulations

From time to time, legislation is drafted, introduced and passed in the United States Congress that could significantly change the statutory provisions governing the testing, approval, manufacturing and marketing of pharmaceutical products. For example, in December 2016, Congress enacted and President Obama signed into law the 21st Century Cures Act, that amends a number of sections of the FDCA, including provisions related to medical device approval. In addition to new legislation, FDA regulations and policies are often revised or interpreted by the agency in ways that may significantly affect our business and our products. It is impossible to predict whether further legislative changes will be enacted or whether FDA regulations, guidance, policies or interpretations changed or what the effect of such changes, if any, may be.

In the United States, federal and state governments continue to propose and pass legislation designed to reform delivery of, or payment for, healthcare, which include initiatives to reduce the cost of healthcare. For example, in March 2010, the United States Congress enacted the Patient Protection and Affordable Care Act and the Health Care and Education Reconciliation Act, or the Health Care Reform Act, which expanded healthcare coverage through Medicaid expansion and the implementation of the individual mandate for health insurance coverage and which included changes to the coverage and reimbursement of drug products under government healthcare programs as well as the imposition of annual fees on manufacturers of branded pharmaceuticals. Under the Trump administration, there have been ongoing efforts to modify or repeal all or certain provisions of the Health Care Reform Act. The Trump administration may also take executive action in the absence of legislative action. For example, in October 2017, the President announced that his administration will withhold the cost-sharing subsidies paid to health insurance exchange plans serving low-income enrollees. Actions by the administration are widely expected to lead to fewer Americans having more comprehensive health insurance compliant with the Health Care Reform Act, even in the absence of a

legislative repeal. Tax reform legislation was also enacted at the end of 2017 that includes provisions that will affect healthcare insurance coverage and payment, such as the elimination of the tax penalty for individuals who do not maintain sufficient health insurance coverage beginning in 2019 (the so-called “individual mandate”). In a November 2017 report, the Congressional Budget Office estimates that the elimination will increase the number of uninsured by 4 million in 2019 and 13 million in 2027.

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There have also been efforts by government officials or legislators to implement measures to regulate prices or payment for pharmaceutical products, including legislation on drug importation. Recently, there has been considerable public and government scrutiny of pharmaceutical pricing and proposals to address the perceived high cost of pharmaceuticals. There have also been recent state legislative efforts to address drug costs, which generally have focused on increasing transparency around drug costs or limiting drug prices.

Adoption of new legislation at the federal or state level could affect demand for, or pricing of, our product candidates if approved for sale. We cannot predict the ultimate content, timing or effect of any changes to the Health Care Reform Act or other federal and state reform efforts. There is no assurance that federal or state healthcare reform will not adversely affect our future business and financial results.

EMPLOYEES

As of February 28, 2018, we had 69 full time equivalent employees, including a total of 12 employees with M.D. or Ph.D. degrees. Of these full time employees, 31 employees are engaged in research and development activities. None of our employees is represented by a labor union or covered by a collective bargaining agreement. We consider our relationship with our employees to be good.

BUSINESS—EXECUTIVE OFFICERS OF THE REGISTRANT

The following table sets forth the name, age and position of each of our executive officers as of February 28, 2018.

Name	Age	Position
Robert Forrester	54	President, Chief Executive Officer
Steven Bloom	57	Chief Strategy Officer
Julie B. Feder	47	Chief Financial Officer
Diep Le, M.D., Ph.D.	50	Chief Medical Officer
Joseph Lobacki	59	Chief Commercial Officer
Daniel Paterson	57	Chief Operating Officer

Robert Forrester has served has served as our Chief Executive Officer since July 2013, as our Chief Operating Officer from March 2011 until July 2013 and our President since January 2013. Mr. Forrester has previously held executive level positions at both private and public life sciences companies. Prior to joining us, Mr. Forrester served as Chief Operating Officer of Forma Therapeutics, Inc. from 2010 until 2011. Previously he served as Interim President and Chief Executive Officer of CombinatoRx, Inc. from 2009 until 2010 and as its Executive Vice President and Chief Financial Officer from 2004 to 2009. Mr. Forrester served as Senior Vice President, Finance and Corporate Development at Coley Pharmaceuticals Group, Inc. from 2000 to 2003. He earned his LL.B. from Bristol University in England.

Steven Bloom has served as our Chief Strategy Officer since December 2017, our Senior Vice President of Corporate Development from January 2017 to November 2017 and as our Vice President of Commercial Planning and External Affairs from January 2015 until January 2017. Prior to joining us in March 2014, Mr. Bloom served as Senior Vice President at Ziopharm Oncology from March 2008 to March 2014. Before joining Ziopharm, Mr. Bloom was Vice President for the health informatics company Pharmetrics and spent the first 19 years of his career at Eli Lilly and

Company in leadership roles in marketing, sales and corporate affairs.

Julie B. Feder