INFINITY PHARMACEUTICALS, INC.
Form 10-K
March 14, 2017

UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
Washington, D.C. 20549

FORM 10-K

(Mark One)
ý ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934
For the fiscal year ended: December 31, 2016
¨ 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: 000-31141

INFINITY PHARMACEUTICALS, INC.
(Exact name of registrant as specified in its charter)

Delaware	33-0655706
(State or other jurisdiction of incorporation or organization)	(I.R.S. Employer Identification No.)

784 Memorial Drive, Cambridge, Massachusetts 02139
(Address of principal executive offices) (zip code)
Registrant's telephone number, including area code: (617) 453-1000
Securities registered pursuant to Section 12(b) of the Act:

Common Stock, $0.001 par value	NASDAQ Global Select Market
(Title of each class)	(Name of each exchange on which listed)

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 ý

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 ý

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 ý No ¨

Indicate by check mark whether the registrant has submitted electronically and posted on its corporate Web site, 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 ý 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. ý

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 ý	Non-accelerated filer ¨ (Do not check if a smaller reporting company)	Smaller reporting company ¨

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

The aggregate market value of voting Common Stock held by non-affiliates of the registrant as of June 30, 2016 was $64,584,042 based on the last reported sale price of the registrant's Common Stock on the NASDAQ Global Select Market on that date.

Number of shares outstanding of the registrant's Common Stock as of March 1, 2017: 50,426,205

Documents incorporated by reference:

Portions of our definitive proxy statement to be filed with the Securities and Exchange Commission no later than May 1, 2017 in connection with our 2017 annual meeting of stockholders are incorporated by reference into Part III of this Annual Report on Form 10-K.

TABLE OF CONTENTS

Forward-Looking Information

The following discussion of our financial condition and results of operations contained in this Annual Report on Form 10-K should be read in conjunction with our consolidated financial statements and related notes included elsewhere in this report. Some of the information contained in this discussion and analysis and set forth elsewhere in this report, including information with respect to our plans and strategy for our business, the possible achievement of development goals and milestones in 2017, our future development efforts, our collaborations, and our future operating results and financial position, includes forward-looking statements that involve risks and uncertainties. We often use words such as “anticipate,” “believe,” “estimate,” “expect,” “intend,” “may,” “plan,” “predict,” “project,” “target,” “p “would,” “could,” “should,” “continue,” and other words and terms of similar meaning to help identify forward-looking statements, although not all forward-looking statements contain these identifying words. You also can identify these forward-looking statements by the fact that they do not relate strictly to historical or current facts. There are a number

of important risks and uncertainties that could cause actual results or events to differ materially from those indicated by forward-looking statements made herein. These risks and uncertainties include those inherent in pharmaceutical research and development, such as adverse results in our drug development activities, decisions made by the U.S. Food and Drug Administration, or FDA, and other regulatory authorities

with respect to the development and commercialization of our product candidates, our ability to obtain, maintain and enforce intellectual property rights for our product candidates, our dependence on our alliance partners, competition, our ability to obtain any necessary financing to conduct our planned activities and other risk factors described herein. We have included important factors in the cautionary statements included in this Annual Report on Form 10-K, particularly in Part I, Item 1A, Risk Factors, that could cause actual results to differ materially from the results described in or implied by the forward-looking statements contained in the following discussion and analysis. Unless required by law, we do not undertake any obligation to update any forward-looking statements.

PART I

Item 1. Business

Overview

We are an innovative biopharmaceutical company dedicated to developing best-in-class medicines for patients with difficult-to-treat diseases. We combine proven scientific expertise with a passion for developing novel small molecule drugs that target disease pathways for potential applications in oncology.

IPI-549: Targeting Solid Tumors by Selective Inhibition of the PI3K-Gamma Isoform

We are focusing our efforts on our lead product candidate, IPI-549, an orally administered, clinical-stage, immuno-oncology product candidate that selectively inhibits the enzyme phosphoinositide-3-kinase-gamma, or PI3K-gamma.

Role of PI3K-gamma in Cancer Growth and Survival

The body’s immune system is responsible for fighting off infections and disease, including cancer, and helping the body to heal. The immune system functions by identifying and destroying foreign cells and substances within the body. When confronted by pathogens or disease, an early response of the body's immune system comes in the form of macrophages, a type of white blood cell that produces pro-inflammatory proteins called cytokines. These cytokines activate T cells, another type of immune cell, to attack the health threat. The macrophages then switch gears to produce other types of cytokines that dampen T cell activation, which, in turn, stimulates repair of the affected tissue. Cancer cells arise from normal cells that have changed in a way that allows them to grow out of control. Cancer cells are not always recognized by the immune system as foreign cells that should be destroyed. However, if cancer cells are recognized by the immune system, mechanisms exist to dampen this immune response and include upregulation of “checkpoint proteins” on T cells, such as programmed death receptor 1, or PD-1. Additionally, in cancer there exists a tumor microenvironment, or TME, which refers to the non-cancerous cells present in the tumor. Cells within the TME, including macrophages, can suppress the immune response and provide signals to cancer cells allowing the tumor to grow. The presence of the supportive TME is thought to be one reason why some cancer therapies, including checkpoint inhibitors, have not provided durable or effective results to date. Targeting cells that suppress the immune system represents an emerging approach within the field of cancer immunotherapy, and inhibition of PI3K-gamma by IPI-549 represents a novel approach to targeting this immune-suppressive microenvironment.

Anti-Tumor Activity of IPI-549 in Preclinical Models

Preclinical research found that macrophage PI3K-gamma signaling promotes a genetic program that results in a macrophage type that suppresses the activation of anti-tumor T cells. Preclinical data demonstrated that blockade of PI3K-gamma by treatment with IPI-549 leads to a shift in the type of macrophages present in the TME from macrophages associated with suppression of the immune response, known as the M2 phenotype, to macrophages that are supportive of a pro-inflammatory, anti-tumor immune response, known as the M1 phenotype. Treatment with IPI-549 increased the M1/M2 macrophage ratio, the number of T cells that attack the tumor, and the production of pro-inflammatory cytokines.

Preclinical studies to investigate the anti-tumor activity of IPI-549 have demonstrated dose-dependent, single-agent, anti-tumor activity in multiple solid tumor models, including models of lung cancer (see below), colon cancer and breast cancer.

4

Additionally, in preclinical models, treatment with IPI-549 in combination with a checkpoint inhibitor showed greater tumor growth inhibition and survival, including a greater number of complete tumor regressions, compared to treatment with either IPI-549 or the checkpoint inhibitor alone. The combination treatment results in long-lasting anti-tumor immune memory as evidenced by the lack of tumor growth when animals are re-challenged with tumor in the absence of any treatment.

These findings support the hypothesis that inhibition of PI3K-gamma by IPI-549 leads to an activated and more efficient anti-tumor immune response through its effects on the immune-suppressive TME.

Overcoming Resistance to Checkpoint Inhibition

In recent years, checkpoint inhibitors have shown promising results as a treatment for multiple types of cancer, but many patients eventually become resistant to checkpoint inhibitors and require treatment with an additional therapy. Preclinical studies in a number of tumor models showed that resistance to checkpoint inhibition is associated with increased numbers of tumor-associated macrophages and is directly mediated by the immune-suppressive activity of these macrophages on T cells. Furthermore, the data showed that inhibition of PI3K-gamma by IPI-549 switched the activation of macrophages from an immune-suppressive M2 state to a pro-inflammatory M1 state, leading to enhanced anti-tumor cytotoxic T cell activity, particularly when combined with checkpoint inhibitors. These data demonstrate that IPI-549 treatment is able to reverse the lack of response to checkpoint inhibitors in models that are initially insensitive to checkpoint inhibition as a single therapy (see below).

Phase 1 Clinical Study of IPI-549

Based on our preclinical data generated to date, we are conducting a Phase 1 study evaluating IPI-549 in approximately 175 patients with advanced solid tumors. The study includes a dose-escalation phase to evaluate the safety, tolerability, pharmacokinetics, and pharmacodynamics of IPI-549 as a monotherapy, as well as a dose-escalation phase evaluating IPI-549 in combination with nivolumab, also known as Opdivo. Nivolumab, a checkpoint inhibitor therapy being commercialized by Bristol-Myers Squibb, or BMS, targets PD-1. If supported by data from the initial portion of the study, a Phase 1b portion would investigate IPI-549 in a monotherapy expansion cohort as well as in expansion cohorts in combination with nivolumab in patients with selected solid tumors, including non-small cell lung cancer, or NSCLC, melanoma and squamous cell carcinoma of the head and neck, or SCCHN, whose tumors have shown initial resistance or subsequently have developed resistance to checkpoint inhibitor therapy. We expect to begin enrolling patients in both the monotherapy and combination expansion cohorts during the second half of 2017.

In connection with our Phase 1 study of IPI-549, we have entered into a clinical supply agreement with BMS under which BMS agreed to provide nivolumab at no cost to us for use in our Phase 1 study of IPI-549. Under the agreement with BMS, we would provide BMS with clinical data from the study.

In September 2016, we presented initial clinical data from our Phase 1 study of IPI-549 in a poster session at the Second CRI-CIMT-EATI-AACR International Cancer Immunotherapy Conference: Translating Science into Survival and in January 2017 at the Keystone Symposia Conference, "PI3K Pathways in Immunology, Growth Disorders and Cancer". Preliminary results from nine patients with advanced solid tumors showed that the safety, pharmacokinetics and pharmacodynamics of IPI-549 monotherapy treatment appeared favorable. As of the September 2016 data cutoff, no dose limiting toxicities and no serious adverse events were observed. Pharmacokinetic and pharmacodynamic data supported once daily dosing of IPI-549 based on the observed half-life and inhibition of the PI3K-gamma pathway. We expect to report additional Phase 1 study data from the monotherapy dose-escalation phase as well as the dose-escalation phase evaluating IPI-549 in combination with nivolumab in 2017.

The expansion cohorts of our Phase 1 clinical study represent patient populations for which there exists a significant unmet medical need, including patients with NSCLC, melanoma and SCCHN whom either relapse or do not respond to treatment with a checkpoint inhibitor such as Opdivo. The American Cancer Society estimates approximately 189,000 new

cases of NSCLC and approximately 87,000 new cases of melanoma in 2017. Additionally, the American Society of Clinical Oncology estimates approximately 62,000 new cases of SCCHN in 2017.

Strategic Alliances

Since our inception, corporate alliances have been integral to our strategy. These alliances have provided access to breakthrough science, significant research and development support and funding, and innovative drug development programs, all intended to help us realize the full potential of our product pipeline. All of our revenues since September 2006 have been generated under collaborative research agreements including our corporate alliances.

Verastem

On October 29, 2016, we and Verastem, Inc., or Verastem, entered into a license agreement, which we and Verastem amended and restated on November 1, 2016, effective as of October 29, 2016. We refer to the amended and restated license agreement as the Verastem Agreement. Under the Verastem Agreement, we granted to Verastem an exclusive worldwide license for the research, development, commercialization, and manufacture of duvelisib and products containing duvelisib, which we refer to as the Licensed Products, in each case in oncology indications. Duvelisib, also known as IPI-145, is a selective inhibitor of the PI3K delta and gamma isoforms. Upon entry into the Verastem Agreement, Verastem assumed financial responsibility for activities that were part of our ongoing duvelisib program, including a randomized, Phase 3 monotherapy clinical study in patients with relapsed/refractory chronic lymphocytic leukemia which we refer to as the DUO Study. Verastem is obligated to use diligent efforts, as defined in the Verastem Agreement, to develop and commercialize one Licensed Product. During the term of the Verastem Agreement, we have agreed not to research, develop, manufacture or commercialize duvelisib in any indication in humans or animals.

Under the Verastem Agreement, we have financial responsibility for up to $4.5 million of costs related to the shutdown of certain specified clinical studies. We expect to reach the $4.5 million maximum for clinical study shutdown costs during the first half of 2017. Following a short transition period, Verastem has assumed all financial and operational responsibility for the duvelisib program except for the clinical shutdown costs and certain clinical study close-out activities we agreed to retain and will reimburse us for costs incurred by us during the transition period, together with certain prepaid expenses associated with the clinical studies assumed by Verastem.

Pursuant to the terms of the Verastem Agreement, Verastem is required to make the following payments to us in cash or, at Verastem's election, in whole or in part, in shares of Verastem common stock: (i) $6.0 million upon the completion of the DUO Study if the results of the DUO Study meet certain pre-specified criteria and (ii) $22.0 million upon the approval for a Licensed Product of a new drug application, or NDA, in the United States or an application for marketing authorization with a regulatory authority outside of the United States. For any portion of any of the foregoing payments which Verastem elects to issue in shares of common stock in lieu of cash, the number of shares of Verastem common stock to be issued would 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 Verastem 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 would be issued as unregistered securities, and Verastem would have an obligation to promptly file a registration statement with the U.S. Securities and Exchange Commission, or SEC, to register such shares for resale. Any issuance of shares would be subject to the satisfaction of standard closing conditions, including that all material authorizations, consents and similar approvals necessary for such issuance shall have been obtained.

Verastem is also obligated to pay us royalties on worldwide net sales of Licensed Products ranging from the mid-single digits to the high single-digits. The royalty obligation will continue 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 Licensed Product in the applicable country, (ii) the last-to-expire patent right covering the manufacture of the applicable Licensed Product in the country of manufacture of such Licensed Product, (iii) the expiration of non-patent regulatory exclusivity for such Licensed Product in the applicable country and (iv) ten years following the first commercial sale of a Licensed Product in the applicable country, provided that, upon the expiration of the last-to-expire patent right covering the such Licensed Product in the United States, the applicable royalty on net sales for such Licensed 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 Verastem 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, Verastem is obligated to pay us a royalty of 4% on worldwide net sales of Licensed Products to cover the reimbursement of research and development costs owed by us to Mundipharma International Corporation Limited, or Mundipharma, and Purdue Pharmaceutical Products L.P., or Purdue. Once we have fully reimbursed Mundipharma and Purdue, Verastem's royalty obligations described in this paragraph will be reduced to 1% of net sales in the United States, which we refer to as the Trailing Mundipharma Royalties. The Trailing Mundipharma Royalties are payable on a product-by-

product basis until the latest to occur of (i) the last-to-expire patent right covering the applicable Licensed Product in the United States, (ii) the last-to-expire patent right covering the manufacture of the applicable Licensed Product in the country of manufacture of such Licensed Product, (iii) the expiration of non-patent regulatory exclusivity for such Licensed Product in the United States and (iv) ten years following the first commercial sale of such Licensed Product in the United States, provided that, upon the expiration of the last-to-expire patent right covering the a Licensed Product in the United States, the applicable royalty on net sales for such Licensed Product in the United States will be reduced by 50%. In addition, the Trailing Mundipharma 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 Verastem if litigation were to arise, with any such reductions capped at 50% of the amounts otherwise payable during the applicable royalty payment period.

The Verastem Agreement expires when each party no longer has any obligations to the other party under the Verastem Agreement. Verastem has the right to terminate the Verastem Agreement upon at least 180 days prior written notice to us at any time following the earlier of (i) Verastem's decision to discontinue the DUO Study under certain circumstances as specified in the Verastem Agreement and (ii) the determination of whether the DUO Study has met its pre-specified primary endpoint. Either party may terminate the Verastem Agreement if the other party materially breaches or defaults in the performance of its obligations. If we terminate the Verastem Agreement for Verastem's material breach, patent challenge, or insolvency, or if Verastem terminates for convenience, then, at our request and subject to our execution of a waiver of certain types of damages, Verastem will transition the duvelisib program back to us at Verastem's cost. If Verastem terminates for our breach or insolvency, Verastem will effect a more limited transition of the duvelisib program to us at our request and cost, subject to our execution of a waiver of certain types of damages, and we will thereafter pay to Verastem a low single-digit royalty on net sales of Licensed Products.

We and Verastem have made customary representations and warranties and have agreed to certain customary covenants, including confidentiality and indemnification.

AbbVie

The AbbVie Agreement

On September 2, 2014, we entered into a collaboration and license agreement between us and AbbVie Inc., which we refer to as the AbbVie Agreement. Under the AbbVie Agreement, we and AbbVie Inc., which we refer to as AbbVie, agreed to develop and commercialize products containing duvelisib in oncology indications. We refer to products containing duvelisib included under the AbbVie Agreement as Duvelisib Products. IPI-549, an orally administered, selective PI3K-gamma inhibitor, was excluded from the collaboration. On June 24, 2016, AbbVie delivered to us a written notice that AbbVie was exercising its right to terminate the AbbVie Agreement unilaterally upon 90 days' written notice, which we refer to as the AbbVie Opt-Out. The termination of the AbbVie agreement was effective on September 23, 2016.

Under the terms of the AbbVie Agreement, we and AbbVie agreed to share equally commercial profits or losses of Duvelisib Products in the United States, including sharing equally the existing royalty obligations to Mundipharma and Purdue for sales of Duvelisib Products in the United States, as well as sharing equally the existing U.S. milestone payment obligations to Takeda Pharmaceutical Company Limited, or Takeda, our PI3K program licensor. For more information about obligations to Takeda, refer to the section below titled "Takeda."

AbbVie had agreed to pay us tiered royalties on net sales of Duvelisib Products outside the United States ranging from 23.5% to 30.5%, depending on annual net sales of Duvelisib Products by AbbVie, its affiliates and its sublicensees. This tiered royalty could have been further reduced based on specified factors, including patent expiry, generic entry, and royalties paid to third parties.

We and AbbVie had shared oversight of development and had agreed to use diligent efforts, as defined in the AbbVie Agreement, to carry out our development activities under an agreed upon development plan. We had primary responsibility for the conduct of development of Duvelisib Products, unless otherwise agreed, and AbbVie had responsibility for the conduct of certain contemplated combination clinical studies, including those examining duvelisib and venetoclax, a selective first-in-class B-cell lymphoma 2 inhibitor, which we refer to as the AbbVie Studies. The development and manufacturing costs for the AbbVie Studies were shared equally.

We were responsible for the manufacture of Duvelisib Products until the transition of manufacturing responsibility to AbbVie, which we had expected to occur as promptly as practicable while ensuring continuity of supply. Excluding the AbbVie Studies, we were responsible for all costs to develop and manufacture Duvelisib Products up to a maximum amount of $667 million, after which costs were to be shared equally.

We and AbbVie shared operational responsibility and decision making authority for commercialization of Duvelisib Products in the United States. Prior to commercialization and regulatory approval, we recognized the cost of manufacturing as a component of research and development and the cost of commercialization as a component of general and administrative

expenses. During the years ended December 31, 2016, 2015 and 2014, we accounted for AbbVie's share of the costs as a reduction of the related expense.

Under the AbbVie Agreement, AbbVie paid us a non-refundable $275 million upfront payment in 2014 and a $130 million milestone payment in November 2015 associated with the completion of enrollment of DYNAMO™, our Phase 2 clinical study evaluating the efficacy and safety of duvelisib in patients with refractory indolent non-Hodgkin lymphoma, or iNHL. Of the total $405 million received from AbbVie, we allocated $234.3 million to the license which was recognized as revenue upon receipt of the upfront payment and achievement of the milestone payment. Revenue related to development services and committee services was recognized using the proportionate performance method. We initially estimated that services would be performed through 2019.

The AbbVie Agreement was intended to remain in effect until all development, manufacturing and commercialization of Duvelisib Products ceased, unless terminated earlier. AbbVie had the right to terminate the AbbVie Agreement for convenience after a specified notice period as described above.

AbbVie Opt-Out

Upon formal termination of the AbbVie Agreement on September 23, 2016, we received all rights to the regulatory filings related to duvelisib, our license to AbbVie terminated, and AbbVie granted us an exclusive, perpetual, irrevocable, royalty-free license, under certain patent rights and know-how controlled by AbbVie, to develop, manufacture and commercialize products containing duvelisib, excluding any compound which is covered by patent rights controlled by AbbVie or its affiliates, in oncology indications worldwide.

Neither party has any ongoing financial obligation to the other under the AbbVie Agreement. In connection with the AbbVie Opt-Out, AbbVie will not pay any royalties or any of the additional $400 million in milestone payments that we could have potentially earned under the AbbVie Agreement. During the third quarter of 2016, we and AbbVie finalized the wind-down plan to ensure a smooth transition of the responsibilities of the parties. We do not expect to receive any further proceeds from AbbVie for our wind-down activities, and we do not expect to incur any additional expenses for their clinical wind-down services.

Takeda

In July 2010, we entered into a development and license agreement with Intellikine, Inc., or Intellikine, under which we obtained rights to discover, develop and commercialize pharmaceutical products targeting the delta and/or gamma isoforms of PI3K, including duvelisib and IPI-549. In January 2012, Intellikine was acquired by Takeda, acting through its Millennium business unit. In December 2012, we amended and restated our development and license agreement with Takeda. We refer to our PI3K inhibitor program licensor as Takeda and to the amended and restated development and license agreement, as amended by the July 2014 and September 2016 amendments described in more detail below, as the Takeda Agreement.

Under the terms of the Takeda Agreement, we are obligated to pay Takeda an aggregate of up to $5 million in success-based milestone payments for the development of a product candidate other than duvelisib, which could include IPI-549. We are also obligated to pay Takeda up to an aggregate of $165 million in success-based milestone payments related to the approval and commercialization of one product, which could be a product containing IPI-549.

Except for duvelisib in oncology indications, we are obligated to pay Takeda tiered royalties ranging from 7% to 11% on worldwide net sales of products described in the agreement, which could include IPI-549 if successfully developed and commercialized. Such royalties are payable until the later to occur of the expiration of specified patent rights and the expiration of non-patent regulatory exclusivities in a country, subject to reduction of the royalties and, in certain

circumstances, limits on the number of products subject to a royalty obligation.

The Takeda Agreement expires on the later of the expiration of certain patents and the expiration of the royalty payment terms for the products, unless earlier terminated in accordance with its terms. Either party may terminate the Takeda Agreement on 75 days' prior written notice if the other party materially breaches the agreement and fails to cure such breach within the applicable notice period, provided that the notice period is reduced to 30 days where the alleged breach is non-payment. Takeda may also terminate the Takeda Agreement if we are not diligent in developing or commercializing the licensed products and do not, within three months after notice from Takeda, demonstrate to Takeda's reasonable satisfaction that we have not failed to be diligent. The foregoing periods are subject to extension in certain circumstances. Additionally, Takeda may terminate the Takeda Agreement upon 30 days' prior written notice if we or a related party bring an action challenging the validity of any of the licensed patents, provided that we have not withdrawn such action before the end of the

30-day notice period. We may terminate the agreement at any time upon 180 days' prior written notice. The Takeda Agreement also provides for customary reciprocal indemnification obligations of the parties.

July 2014 Amendment
On March 31, 2015, we paid a $52.5 million fee to exercise an option that we purchased from Takeda in July 2014 for a one-time upfront payment of $5.0 million. As a result of our exercise of this option, we are no longer obligated under the Takeda Agreement to pay to Takeda tiered royalties with respect to worldwide net sales in oncology indications of products containing or comprised of duvelisib.

September 2016 Amendment
In September 2016, we entered into a second amendment with Takeda. Under the second amendment, effective as of our execution of (i) a license or sublicense of rights under certain intellectual property to use, develop, or commercialize duvelisib or (ii) a sale, in an asset sale, of any of our rights necessary to practice duvelisib, each of which ((i) and (ii)) we refer to as a qualifying transaction, we are no longer obligated to pay Takeda any remaining milestone payments under the Takeda Agreement for the development, approval or commercialization of duvelisib. Additionally, upon execution of a qualifying transaction, our obligation to use diligent efforts to develop products under the Takeda Agreement is reduced from two products to one product. In return, we are obligated to pay Takeda 50% of all revenue arising from each qualifying transaction for duvelisib, subject to certain exceptions. We believe the Verastem Agreement constitutes a qualifying transaction.

Intellectual Property
Our intellectual property consists of patents, trademarks, trade secrets and know-how. Our ability to compete effectively depends in large part on our ability to obtain patents and trademarks for our technologies and products, maintain trade secrets, operate without infringing the rights of others and prevent others from infringing our proprietary rights. We will be able to protect our proprietary technologies from unauthorized use by third parties only to the extent that they are covered by valid and enforceable patents, or are effectively maintained as trade secrets. As a result, patents or other proprietary rights are an essential element of our business.

We have three issued or allowed U.S. patents related to our IPI-549 program, which expire on various dates between 2033 and 2034, excluding any patent term extension. In addition, we have approximately 70 patents and patent applications pending worldwide related to our PI3K-gamma program. Any patents that may issue from our pending patent applications would expire between 2033 and 2036, excluding any patent term extension. These patents and patent applications disclose compositions of matter, pharmaceutical compositions, methods of use and synthetic methods.

The term of individual patents depends upon the legal term for patents in the countries in which they are obtained. In most countries, including the United States, the patent term is 20 years from the earliest filing date of a non-provisional patent application. In the United States, a patent's term may be lengthened by patent term adjustment, which compensates a patentee for administrative delays by the United States Patent and Trademark Office, or USPTO, in examining and granting a patent, or may be shortened if a patent is terminally disclaimed over an earlier filed patent. The term of a patent that covers a drug or biological product may also be eligible for patent term extension when FDA approval is granted, provided statutory and regulatory requirements are met. In the future, if and when our product candidates receive approval by the FDA or foreign regulatory authorities, we expect to apply for patent term extensions on issued patents covering those drugs, depending upon the length of the clinical trials for each drug and other factors. There can be no assurance that any of our pending patent applications will issue or that we will benefit from any patent term extension or favorable adjustment to the term of any of our patents.

As with other biotechnology and pharmaceutical companies, our ability to maintain and solidify our proprietary and intellectual property position for our product candidates and technologies will depend on our success in obtaining effective patent claims and enforcing those claims, if granted. However, our pending patent applications, and any patent applications that we may in the future file or license from third parties may not result in the issuance of patents. We also cannot predict the breadth of claims that may be allowed or enforced in our patents. Any issued patents that we may receive in the future may be challenged, invalidated or circumvented. For example, we cannot be certain of the priority of inventions covered by pending third-party patent applications. If third parties prepare and file patent applications in the United States that also claim technology or therapeutics to which we have rights, we may have to participate in interference proceedings in the USPTO to determine priority of invention, which could result in substantial costs to us, even if the eventual outcome is favorable to us, which is highly unpredictable. In addition, because of the extensive time required for clinical development and regulatory

review of a product candidate we may develop, it is possible that, before any of our product candidates can be commercialized, any related patent may expire or remain in force for only a short period following commercialization, thereby limiting protection such patent would afford the respective product and any competitive advantage such patent may provide.

Our policy is to obtain and enforce the patents and proprietary technology rights that are commercially important to our business, and we intend to continue to file patent applications to protect such technology and compounds in countries where we believe it is commercially reasonable and advantageous to do so. We also rely on trade secrets to protect our technology where patent protection is deemed inappropriate or unobtainable. We seek to protect our proprietary information, in part, by executing confidentiality agreements with our collaborators and scientific advisors, and non-competition, non-solicitation, confidentiality, and invention assignment agreements with our employees and consultants. We have also executed agreements requiring assignment of inventions with selected scientific advisors and collaborators. The confidentiality agreements we enter into are designed to protect our proprietary information and the agreements or clauses requiring assignment of inventions to us are designed to grant us ownership of technologies that are developed through our relationship with the respective counterparty. We cannot guarantee, however, that these agreements will afford us adequate protection of our intellectual property and proprietary information rights.

Competition

The pharmaceutical and biotechnology industries are intensely competitive. Many companies, including biotechnology, chemical and pharmaceutical companies, are actively engaged in the research and development of drugs for the treatment of the same diseases and conditions as our current and potential future product candidates. Many of these companies have substantially greater financial and other resources, larger research and development staffs and more extensive marketing and manufacturing organizations than we do. In addition, some of them have considerably more experience than us in preclinical testing, clinical trials and other regulatory approval procedures. There are also academic institutions, governmental agencies and other research organizations that are conducting research in areas in which we are working. They may also develop products that may be competitive with our product candidates, either on their own or through collaborative efforts.

We expect to encounter significant competition for any drugs we develop. Companies that complete clinical trials, obtain required regulatory approvals and commence commercial sales of their products before their competitors may achieve a significant competitive advantage. We are aware that many other companies or institutions are pursuing the development of drugs in the areas in which we are currently seeking to develop our own product candidates, and there may be other companies working on competitive projects of which we are not aware.

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.

We believe that IPI-549 is the only PI3K-gamma selective inhibitor in clinical development. However, there are many competitors developing or commercializing therapies targeting macrophage biology, including the following competitors which we believe to be conducting clinical studies of product candidates targeting one or more aspects of macrophage biology: Incyte Corporation (through its collaboration with Calithera Inc.), Five Prime Therapeutics, Inc., Plexxikon Inc., Eli Lilly and Company, Amgen Inc., F. Hoffmann-La Roche Ltd, Forty Seven Inc., Celgene Corporation, Trillium Therapeutics Inc., Pfizer, XBiotech, Inc., AbbVie Inc., Takeda Pharmaceuticals, International,

Inc., Novartis AG, Efranat Ltd., Seattle Genetics, Inc., Apexigen Inc., X4 Pharmaceuticals, Inc. and Alligator Bioscience AB.

Research and Development

As of March 1, 2017, our research and development group consisted of 8 employees, of whom 7 hold Ph.D. or M.D. degrees and the remaining employee holds a masters degree. Our research and development group is focused on preclinical research, translational medicine, clinical trials and manufacturing technologies. Our research and development expense for the years ended December 31, 2016, 2015 and 2014 was approximately $119.6 million, $199.1 million, and $143.6 million, respectively.

Manufacturing and Supply

We rely primarily on third parties, and in some instances we rely on only one third party, to manufacture critical raw materials, drug substance and final drug product for our research, preclinical development and clinical trial activities. Commercial quantities of any drugs we seek to develop will have to be manufactured in facilities and by processes that comply with the United States Food and Drug Administration, or FDA, and other regulations, and we plan to rely on third parties to manufacture commercial quantities of any products we successfully develop.

Sales and Marketing

We currently have no marketing, commercial sales, or distribution capabilities. We do, however, currently have worldwide commercialization rights for our PI3K-gamma inhibitor program, including IPI-549. In order to commercialize IPI-549, if and when it is approved for sale, we will need to, and we intend to, develop the necessary marketing, sales and distribution capabilities.

Government Regulation and Product Approvals

Government authorities in the United States, at the federal, state and local level, and in other countries and jurisdictions, including the European Union, extensively regulate, among other things, the research, development, testing, manufacture, quality control, approval, packaging, storage, recordkeeping, labeling, advertising, promotion, distribution, marketing, post-approval monitoring and reporting, and import and export of pharmaceutical products. The processes for obtaining marketing approvals in the United States and in foreign countries and jurisdictions, along with subsequent compliance with applicable statutes and regulations and other regulatory authorities, require the expenditure of substantial time and financial resources.

Review and Approval of Drugs in the United States

In the United States, the FDA approves and regulates drugs under the Federal Food, Drug, and Cosmetic Act, or FDCA, and implementing regulations. The failure to comply with requirements under the FDCA and other applicable laws at any time during the product development process, approval process or after approval may subject an applicant and/or sponsor to a variety of administrative or judicial sanctions, including refusal by the FDA to approve pending applications, withdrawal of an approval, imposition of a clinical hold, issuance of warning letters and other types of 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 investigations and penalties brought by the FDA and the Department of Justice or other governmental entities.

A product candidate must be approved by the FDA through the new drug application, or NDA. An applicant seeking approval to market and distribute a new drug product in the United States must typically undertake the following:

- completion of preclinical laboratory tests, animal studies and formulation studies in compliance with the FDA's good laboratory practice, or GLP, regulations;
- submission to the FDA of an investigational new drug, or IND, application, which must take effect before human clinical trials may begin;
- approval by an independent institutional review board, or IRB, representing each clinical site before each clinical trial may be initiated;
- performance of adequate and well-controlled human clinical trials in accordance with good clinical practices, or GCP, to establish the safety and efficacy of the proposed drug product for each indication;
- preparation and submission to the FDA of an NDA, requesting marketing for one or more proposed indications;
- review by an FDA advisory committee, where appropriate or if applicable;
- satisfactory completion of one or more FDA inspections of the manufacturing facility or facilities at which the product, or components thereof, are produced to assess compliance with current Good Manufacturing Practices, or cGMP, requirements and to assure that the facilities, methods and controls are adequate to preserve the product's identity, strength, quality and purity;
- satisfactory completion of FDA audits of clinical trial sites to assure compliance with GCPs and the integrity of the clinical data;

- payment of user fees and securing FDA approval of the NDA; and
- compliance with any post-approval requirements, including the potential requirement to implement a Risk Evaluation and Mitigation Strategy, or REMS, and the potential requirement to conduct post-approval studies.

Preclinical Studies

Before an applicant begins testing a compound with potential therapeutic value in humans, the drug candidate enters the preclinical testing stage. Preclinical studies include laboratory evaluation of product chemistry, toxicity and formulation, and the purity and stability of the drug substance, as well as in vitro and animal studies to assess the potential safety and

activity of the drug for initial testing in humans and to establish a rationale for therapeutic use. The conduct of preclinical studies is subject to federal regulations and requirements, including GLP regulations. Applicants usually must complete some long-term nonclinical testing, such as animal tests of reproductive adverse events and carcinogenicity, and must also develop additional information about the chemistry and physical characteristics of the drug and finalize a process for manufacturing the drug in commercial quantities in accordance with cGMP requirements. The manufacturing process must be capable of consistently producing quality batches of the drug candidate and, among other things, the manufacturer must develop methods for testing the identity, strength, quality and purity of the final drug product. Additionally, appropriate packaging must be selected and tested and stability studies must be conducted to demonstrate that the drug candidate does not undergo unacceptable deterioration over its shelf life. Preclinical tests and studies can take several years to complete.

The IND Process

An IND is an exemption from the FDCA that allows an unapproved drug to be shipped in interstate commerce for use in an investigational clinical trial and a request for FDA authorization to administer an investigational drug to humans. Such authorization must be secured prior to interstate shipment and administration of any new drug that is not the subject of an approved NDA. In support of a request for an IND, applicants must submit a protocol for each clinical trial and any subsequent protocol amendments must be submitted to the FDA as part of the IND. In addition, the results of the preclinical tests, together with manufacturing information, analytical data, any available clinical data or literature and plans for clinical trials, among other things, are submitted to the FDA as part of an IND. The FDA requires a 30-day waiting period after the filing of each IND before clinical trials may begin. This waiting period is designed to allow the FDA to review the IND to determine whether human research subjects will be exposed to unreasonable health risks. At any time during this 30-day period, the FDA may raise concerns or questions about the conduct of the trials as outlined in the IND and impose a clinical hold. In this case, the IND sponsor and the FDA must resolve any outstanding concerns before clinical trials can begin.

Following commencement of a clinical trial under an IND, the FDA may also place a clinical hold or partial clinical hold on that trial. A clinical hold is an order issued by the FDA to the sponsor to delay a proposed clinical investigation or to suspend an ongoing investigation. A partial clinical hold is a delay or suspension of only part of the clinical work requested under the IND. For example, a specific protocol or part of a protocol is not allowed to proceed, while other protocols may do so. No more than 30 days after imposition of a clinical hold or partial clinical hold, the FDA will provide the sponsor a written explanation of the basis for the hold. Following issuance of a clinical hold or partial clinical hold, an investigation may only resume after the FDA has notified the sponsor that the investigation may proceed. The FDA will base that determination on information provided by the sponsor correcting the deficiencies previously cited or otherwise satisfying the FDA that the investigation can proceed.

A sponsor may choose, but is not required, to conduct a foreign clinical study under an IND. When a foreign clinical study is conducted under an IND, all FDA IND requirements must be met unless waived. When the foreign clinical study is not conducted under an IND, the sponsor must ensure that the study complies with FDA certain regulatory requirements in order to use the study as support for an IND or application for marketing approval. Specifically, on April 28, 2008, the FDA amended its regulations governing the acceptance of foreign clinical studies not conducted under an investigational new drug application as support for an IND or a new drug application. The final rule provides that such studies must be conducted in accordance with good clinical practice, or GCP, including review and approval by an independent ethics committee, or IEC, and informed consent from subjects. The GCP requirements in the final rule encompass both ethical and data integrity standards for clinical studies. The FDA’s regulations are intended to help ensure the protection of human subjects enrolled in non-IND foreign clinical studies, as well as the quality and integrity of the resulting data. They further help ensure that non-IND foreign studies are conducted in a manner comparable to that required for IND studies.

In addition to the foregoing IND requirements, an IRB representing 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 and reapprove the study at least annually. 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. An IRB can suspend or terminate approval of a clinical trial at its institution, or an institution it represents, if the clinical trial is not being conducted in accordance with the IRB's requirements or if the product candidate has been associated with unexpected serious harm to patients.

Additionally, some trials are overseen by an independent group of qualified experts organized by the trial sponsor, known as a data safety monitoring board or committee. This group provides authorization for whether or not a trial may move forward at designated check points based on access that only the group maintains to available data from the study. Suspension or termination of development during any phase of clinical trials can occur if it is determined that the participants or patients

are being exposed to an unacceptable health risk. Other reasons for suspension or termination may be made by us based on evolving business objectives and/or competitive climate.

Information about certain clinical trials must be submitted within specific timeframes to the National Institutes of Health, or NIH, for public dissemination on its ClinicalTrials.gov website.

Human Clinical Trials in Support of an NDA

Clinical trials involve the administration of the investigational product 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 inclusion and exclusion criteria, the objectives of the study, the parameters to be used in monitoring safety and the effectiveness criteria to be evaluated.

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

- Phase 1. The drug is initially introduced into a small number of healthy human subjects or, in certain indications such as cancer, patients with the target disease or condition (e.g., cancer) and tested for safety, dosage tolerance, absorption, metabolism, distribution, excretion and, if possible, to gain an early indication of its effectiveness and to determine optimal dosage.
- 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. These clinical trials are commonly referred to as “pivotal” studies, which denotes a study that presents the data that the FDA or other relevant regulatory agency will use to determine whether or not to approve a drug. The drug is administered to an expanded patient population, generally at geographically dispersed clinical trial sites, in well-controlled clinical trials to generate enough data to statistically evaluate the efficacy and safety of the product for approval, identify adverse effects, establish the overall risk-benefit profile of the product and to provide adequate information for the labeling of the product.
- Phase 4. Post-approval studies may be conducted after initial marketing approval. These studies are used to gain additional experience from the treatment of patients in the intended therapeutic indication.

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. In addition, IND safety reports must be submitted to the FDA for any of the following: serious and unexpected suspected adverse reactions; findings from other studies or animal or in vitro testing that suggest a significant risk in humans exposed to the drug; and any clinically important increase in the case of a serious suspected adverse reaction over that listed in the protocol or investigator brochure. The FDA or the sponsor or the data monitoring committee 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, or an institution it represents, 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. The FDA will typically inspect one or more clinical sites to assure compliance with GCP and the integrity of the clinical data submitted.

Concurrent with clinical trials, companies often complete additional animal studies and must also develop additional information about the chemistry and physical characteristics of the drug as well as finalize a process for manufacturing the product in commercial quantities in accordance with cGMP requirements. The manufacturing process must be capable of consistently producing quality batches of the drug candidate and, among other things, must develop methods for testing the identity, strength, quality, purity, and potency of the final drug. Additionally, appropriate packaging must be selected and tested and stability studies must be conducted to demonstrate that the drug

candidate does not undergo unacceptable deterioration over its shelf life.

Review of an NDA by the FDA

If clinical trials are successful, the next step in the drug development process is the preparation and submission to the FDA of a NDA. The NDA is the vehicle through which drug applicants formally propose that the FDA approve a new drug for marketing and sale in the United States for one or more indications. The NDA must contain a description of the manufacturing process and quality control methods, as well as results of preclinical tests, toxicology studies, clinical trials and proposed labeling, among other things. Every new drug must be the subject of an approved NDA before it may be commercialized in the United States. Under federal law, the submission of most NDAs is subject to an application user fee, which for federal fiscal year 2017 is $2,038,100. The sponsor of an approved NDA is also subject to annual product and establishment user fees, which for fiscal year 2017 are $97,750 per product and $512,000 per establishment. Certain exceptions and waivers are available for

some of these fees, such as an exception from the application fee for drugs with orphan designation and a waiver for certain small businesses, an exception from the establishment fee when the establishment does not engage in manufacturing the drug during a particular fiscal year, and an exception from the product fee for a drug that is the same as another drug approved under an abbreviated pathway.

Following submission of an NDA, the FDA conducts a preliminary review of an NDA generally within 60 calendar days of its receipt and strives to inform the sponsor by the 74th day after the FDA's receipt of the submission to determine whether the application is 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 certain performance goals in the review process of NDAs. Under that agreement, 90% of applications seeking approval of New Molecular Entities, or NMEs, are meant to be reviewed within ten months from the date on which FDA accepts the NDA for filing, and 90% of applications for NMEs that have been designated for "priority review" are meant to be reviewed within six months of the filing date. For applications seeking approval of drugs that are not NMEs, the ten-month and six-month review periods run from the date that FDA receives the application. The review process and the Prescription Drug User Fee Act goal date may be extended by the FDA for three additional months to consider new information or clarification provided by the applicant to address an outstanding deficiency identified by the FDA following the original submission.

Before approving an NDA, the FDA typically will inspect the facility or facilities where the product is or will be manufactured. These pre-approval inspections may cover all facilities associated with an NDA submission, including drug component manufacturing (e.g., active pharmaceutical ingredients), finished drug product manufacturing, and control testing laboratories. 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. Additionally, before approving an NDA, the FDA will typically inspect one or more clinical sites to assure compliance with GCP.

In addition, as a condition of approval, the FDA may require an applicant to develop a REMS. REMS use risk minimization strategies beyond the professional labeling to ensure that the benefits of the product outweigh the potential risks. To determine whether a REMS is needed, the FDA will consider the size of the population likely to use the product, seriousness of the disease, expected benefit of the product, expected duration of treatment, seriousness of known or potential adverse events, and whether the product is a new molecular entity. REMS can include medication guides, physician communication plans for healthcare professionals, and elements to assure safe use, or ETASU. ETASU may include, but are not limited to, special training or certification for prescribing or dispensing, dispensing only under certain circumstances, special monitoring, and the use of patient registries. The FDA may require a REMS before approval or post-approval if it becomes aware of a serious risk associated with use of the product. The requirement for a REMS can materially affect the potential market and profitability of a product.

The FDA may refer an application for a novel drug to an advisory committee or explain why such referral was not made. Typically, an advisory committee is a panel of independent experts, including clinicians and other scientific experts, that reviews, evaluates and provides a recommendation as to whether the application should be approved and under what conditions. The FDA is not bound by the recommendations of an advisory committee, but it considers such recommendations carefully when making decisions.

The FDA's Decision on an NDA

On the basis of the FDA's evaluation of the NDA and accompanying information, including the results of the 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 product 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.

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 the 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, including REMS, 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, many 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, Breakthrough Therapy, Priority Review and Regenerative Advanced Therapy Designations
The FDA is authorized to designate certain products for expedited review if they are intended to address an unmet medical need in the treatment of a serious or life-threatening disease or condition. These programs are referred to as fast track designation, breakthrough therapy designation, priority review designation and regenerative advanced therapy designation.

Specifically, the FDA may designate a product for Fast Track review if it is intended, whether alone or in combination with one or more other products, for the treatment of a serious or life-threatening disease or condition, and it demonstrates the potential to address unmet medical needs for such a disease or condition. For Fast Track products, sponsors may have greater interactions with the FDA and the FDA may initiate review of sections of a Fast Track product's application before the application is complete. This rolling review may be available if the FDA determines, after preliminary evaluation of clinical data submitted by the sponsor, that a Fast Track product may be effective. The sponsor must also provide, and the FDA must approve, a schedule for the submission of the remaining information and the sponsor must pay 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 application 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.

Second, a product may be designated as a Breakthrough Therapy if it is intended, either alone or in combination with one or more other products, to treat a serious or life-threatening disease or condition and preliminary clinical evidence indicates that the product may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development. The FDA may take certain actions with respect to Breakthrough Therapies, including holding meetings with the sponsor throughout the development process; providing timely advice to the product sponsor regarding development and approval; involving more senior staff in the review process; assigning a cross-disciplinary project lead for the review team; and taking other steps to design the clinical trials in an efficient manner.

Third, the FDA may designate a product for priority review if it is a product that treats a serious condition and, if approved, would provide a significant improvement in safety or effectiveness. The FDA determines, on a case-by-case basis, whether the proposed product represents a significant improvement when compared with other available therapies. Significant improvement may be illustrated by evidence of increased effectiveness in the treatment of a condition, elimination or substantial reduction of a treatment-limiting product reaction, documented enhancement of patient compliance that may lead to improvement in serious outcomes, and evidence of safety and effectiveness in a new subpopulation. A priority designation is intended to direct overall attention and resources to the evaluation of such applications, and to shorten the FDA's goal for taking action on a marketing application from ten months to six months.

Finally, with passage of the 21st Century Cures Act, or the Cures Act, in December 2016, Congress authorized the FDA to accelerate review and approval of products designated as regenerative advanced therapies. A product is eligible for this designation if it is a regenerative medicine therapy that is intended to treat, modify, reverse or cure a serious or life-threatening disease or condition and preliminary clinical evidence indicates that the drug has the potential to address unmet medical needs for such disease or condition. The benefits of a regenerative advanced therapy designation include early interactions with FDA to expedite development and review, benefits available to

breakthrough therapies, potential eligibility for priority review and accelerated approval based on surrogate or intermediate endpoints.

Accelerated Approval Pathway

The FDA may grant accelerated approval to a product for a serious or life-threatening condition that provides meaningful therapeutic advantage to patients over existing treatments based upon a determination that the product has an effect on a surrogate endpoint that is reasonably likely to predict clinical benefit. The FDA may also grant accelerated approval for such a condition when the product has an effect on an intermediate clinical endpoint that can be measured earlier than an effect on irreversible morbidity or mortality, or IMM, and that is reasonably likely to predict an effect on irreversible morbidity or mortality or other clinical benefit, taking into account the severity, rarity, or prevalence of the condition and the availability or lack of alternative treatments. Products granted accelerated approval must meet the same statutory standards for safety and effectiveness as those granted regular approval.

For the purposes of accelerated approval, a surrogate endpoint is a marker, such as a laboratory measurement, radiographic image, physical sign, or other measure that is thought to predict clinical benefit, but is not itself a measure of clinical benefit. Surrogate endpoints can often be measured more easily or more rapidly than clinical endpoints. An intermediate clinical endpoint is a measurement of a therapeutic effect that is considered reasonably likely to predict the clinical benefit of a product, such as an effect on IMM. The FDA has limited experience with accelerated approvals based on intermediate clinical endpoints, but has indicated that such endpoints generally may support accelerated approval where the therapeutic effect measured by the endpoint is not itself a clinical benefit and basis for regular approval, if there is a basis for concluding that the therapeutic effect is reasonably likely to predict the ultimate clinical benefit of a product.

The accelerated approval pathway is most often used in settings in which the course of a disease is long and an extended period of time is required to measure the intended clinical benefit of a product, even if the effect on the surrogate or intermediate clinical endpoint occurs rapidly. Thus, accelerated approval has been used extensively in the development and approval of products for treatment of a variety of cancers in which the goal of therapy is generally to improve survival or decrease morbidity and the duration of the typical disease course requires lengthy and sometimes large trials to demonstrate a clinical or survival benefit.

The accelerated approval pathway is usually contingent on a sponsor's agreement to conduct, in a diligent manner, additional post-approval confirmatory studies to verify and describe the product's clinical benefit. As a result, 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 product from the market on an expedited basis. All promotional materials for product candidates approved under accelerated regulations are subject to prior review by the FDA.

Post-Approval Requirements

Drugs manufactured or distributed pursuant to FDA approvals are 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. There also are continuing, annual user fee requirements for any marketed products and the establishments at which such products are manufactured, as well as new application fees for supplemental applications with clinical data.

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 the sponsor and any third-party manufacturers that the sponsor may decide to use. Accordingly, manufacturers must continue to expend time, money, and effort in the area of production and quality control to maintain cGMP compliance.

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 REMS program. Other potential consequences include, among other things:

- restrictions on the marketing or manufacturing of the product, suspension of the approval, or 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 NDAs or supplements to approved NDAs, or suspension or revocation of product license approvals;
- product seizure or detention, or refusal to permit the import or export of products; or
- 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.

In addition, the distribution of prescription pharmaceutical products is subject to the Prescription Drug Marketing Act, or PDMA, and its implementing regulations, as well as the Drug Supply Chain Security Act, or DSCA, which regulate the distribution and tracing of prescription drugs and prescription drug samples at the federal level, and set minimum standards for the regulation of drug distributors by the states. The PDMA, its implementing regulations and state laws limit the distribution of prescription pharmaceutical product samples, and the DSCA imposes requirements to ensure accountability in distribution and to identify and remove counterfeit and other illegitimate products from the market.

Abbreviated New Drug Applications for Generic Drugs

In 1984, with passage of the Hatch-Waxman Amendments to the FDCA, Congress established an abbreviated regulatory scheme authorizing the FDA to approve generic drugs that are shown to contain the same active ingredients as, and to be bioequivalent to, drugs previously approved by the FDA pursuant to NDAs. To obtain approval of a generic drug, an applicant must submit an abbreviated new drug application, or ANDA, to the agency. An ANDA is a comprehensive submission that contains, among other things, data and information pertaining to the active pharmaceutical ingredient, bioequivalence, drug product formulation, specifications and stability of the generic drug, as well as analytical methods, manufacturing process validation data and quality control procedures. ANDAs are "abbreviated" because they generally do not include preclinical and clinical data to demonstrate safety and effectiveness. Instead, in support of such applications, a generic manufacturer may rely on the preclinical and clinical testing previously conducted for a drug product previously approved under an NDA, known as the reference-listed drug, or RLD.

Specifically, in order for an ANDA to be approved, the FDA must find that the generic version is identical to the RLD with respect to the active ingredients, the route of administration, the dosage form, the strength of the drug and the conditions of use of the drug. At the same time, the FDA must also determine that the generic drug is "bioequivalent" to the innovator drug. Under the statute, a generic drug is bioequivalent to a RLD if "the rate and extent of absorption of the drug do not show a significant difference from the rate and extent of absorption of the listed drug..."

Upon approval of an ANDA, the FDA indicates whether the generic product is "therapeutically equivalent" to the RLD in its publication "Approved Drug Products with Therapeutic Equivalence Evaluations," also referred to as the "Orange Book." Physicians and pharmacists consider a therapeutic equivalent generic drug to be fully substitutable for the RLD. In addition, by operation of certain state laws and numerous health insurance programs, the FDA's designation of therapeutic equivalence often results in substitution of the generic drug without the knowledge or consent of either the prescribing physician or patient.

Under the Hatch-Waxman Amendments, the FDA may not approve an ANDA until any applicable period of non-patent exclusivity for the RLD has expired. The FDCA provides a period of five years of non-patent data exclusivity for a new drug containing a new chemical entity. For the purposes of this provision, a new chemical entity, or NCE, is a drug that contains no active moiety that has previously been approved by the FDA in any other NDA. An active moiety is the molecule or ion responsible for the physiological or pharmacological action of the drug substance. In cases where such NCE exclusivity has been granted, an ANDA may not be filed with the FDA until the expiration of five years unless the submission is accompanied by a Paragraph IV certification (discussed below), in which case the applicant may submit its application four years following the original product approval.

The FDCA also provides for a period of three years of exclusivity if the NDA includes reports of one or more new clinical investigations, other than bioavailability or bioequivalence studies, that were conducted by or for the applicant and are essential to the approval of the application. 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.

Three-year exclusivity would be available for a drug product that contains a previously approved active moiety, provided the statutory requirement for a new clinical investigation is satisfied. Unlike five-year NCE exclusivity, an award of three-year exclusivity does not block the FDA from accepting ANDAs seeking approval for generic versions of the drug as of the date of approval of the original drug product. The FDA typically makes decisions about awards of data exclusivity shortly before a product is approved.

505(b)(2) NDAs

NDAs for most new drug products are based on two full clinical studies which must contain substantial evidence of the safety and efficacy of the proposed new product. These applications are submitted under Section 505(b)(1) of the FDCA. The FDA is, however, authorized to approve an alternative type of NDA under Section 505(b)(2) of the FDCA. This type of application allows the applicant to rely, in part, on the FDA's previous findings of safety and efficacy for a similar product or

published literature. Specifically, Section 505(b)(2) applies to NDAs for a drug for which the investigations made to show whether or not the drug is safe for use and effective in use and relied upon by the applicant for approval of the application "were not conducted by or for the applicant and for which the applicant has not obtained a right of reference or use from the person by or for whom the investigations were conducted."

Thus, Section 505(b)(2) authorizes the FDA to approve an NDA based on safety and effectiveness data that were not developed by the applicant. NDAs filed under Section 505(b)(2) may provide an alternate and potentially more expeditious pathway to FDA approval for new or improved formulations or new uses of previously approved products. If the 505(b)(2) applicant can establish that reliance on the FDA's previous approval is scientifically appropriate, the applicant may eliminate the need to conduct certain preclinical or clinical studies of the new product. The FDA may also require companies to perform additional studies or measurements to support the change from the approved product. The FDA may then approve the new drug candidate for all or some of the label indications for which the referenced product has been approved, as well as for any new indication sought by the Section 505(b)(2) applicant.

Hatch-Waxman Patent Certification and the 30-Month Stay

Upon approval of an NDA or a supplement thereto, NDA sponsors are required to list with the FDA each patent with claims that cover the applicant's product or an approved method of using the product. Each of the patents listed by the NDA sponsor is published in the Orange Book. When an ANDA or 505(b)(2) applicant files its application with the FDA, the applicant is required to certify to the FDA concerning any patents listed for the reference product in the 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 indicates that it is not seeking approval of a patented method of use, the application will not be approved until all the listed patents claiming the referenced product have expired (other than method of use patents involving indications for which the applicant is not seeking approval).

If the ANDA or 505(b)(2) 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 or the 505(b)(2) application 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 or 505(b)(2) application until the earliest of 30 months after the receipt of the Paragraph IV notice, expiration of the patent, or a decision in the infringement case that is favorable to the applicant. The ANDA or 505(b)(2) application also will not be approved until any applicable non-patent exclusivity listed in the Orange Book for the branded reference drug has expired.

Pediatric Studies and Exclusivity

Under the Pediatric Research Equity Act, an NDA or supplement thereto must contain data that are adequate to assess the safety and effectiveness of the drug product for the claimed indications in all relevant pediatric subpopulations, and to support dosing and administration for each pediatric subpopulation for which the product is safe and effective. With enactment of the Food and Drug Administration Safety and Innovation Act, or the FDASIA, in 2012, sponsors must also submit pediatric study plans prior to the assessment data. Those plans must contain an outline of the

proposed pediatric study or studies the applicant plans to conduct, including study objectives and design, any deferral or waiver requests, and any other information required by regulation. The applicant, the FDA, and the FDA's internal review committee must then review the information submitted, consult with each other, and agree upon a final plan. The FDA or the applicant may request an amendment to the plan at any time.

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. Additional requirements and procedures relating to deferral requests and requests for extension of deferrals are contained in FDASIA. Unless and until FDA promulgates a regulation stating otherwise, the pediatric data requirements do not apply to products with orphan designation.

Pediatric exclusivity is another type of non-patent marketing exclusivity in the United States and, if granted, provides for the attachment of an additional six months of marketing protection to the term of any existing regulatory exclusivity, including the non-patent and orphan exclusivity. This six-month exclusivity may be granted if an NDA sponsor submits pediatric data that fairly respond to a written request from the FDA for such data. The data do not need to show the product to be effective in the pediatric population studied; rather, if the clinical trial is deemed to fairly respond to the FDA's request, the additional protection is granted. If reports of requested pediatric studies are submitted to and accepted by the FDA within the statutory time limits, whatever statutory or regulatory periods of exclusivity or patent protection cover the product are extended by six months. This is not a patent term extension, but it effectively extends the regulatory period during which the FDA cannot approve another application. With regard to patents, the six-month pediatric exclusivity period will not attach to any patents for which an ANDA or 505(b)(2) applicant submitted a paragraph IV patent certification, unless the NDA sponsor or patent owner first obtains a court determination that the patent if valid and infringed by the proposed product.

Orphan Drug Designation and Exclusivity

Under the Orphan Drug Act, the FDA may designate a drug product as an "orphan drug" if it is intended to treat a rare disease or condition, generally meaning that it affects fewer than 200,000 individuals in the United States, or more in cases in which there is no reasonable expectation that the cost of developing and making a drug product available in the United States for treatment of the disease or condition will be recovered from sales of the product. A company must request orphan drug designation before submitting an NDA for the drug and rare disease or condition. If the request is granted, the FDA will disclose the identity of the therapeutic agent and its potential use. Orphan drug designation does not shorten the Prescriptoin Drug User Fee Act, or PDUFA, goal dates for the regulatory review and approval process, although it does convey certain advantages such as tax benefits and exemption from the PDUFA application fee.

If a product with orphan designation receives the first FDA approval for the disease or condition for which it has such designation or for a select indication or use within the rare disease or condition for which it was designated, the product generally will receive orphan drug exclusivity. Orphan drug exclusivity means that the FDA may not approve another sponsor's marketing application for the same drug for the same indication for seven years, except in certain limited circumstances. Orphan exclusivity does not block the approval of a different drug for the same rare disease or condition, nor does it block the approval of the same drug for different indications. If a drug designated as an orphan drug ultimately receives marketing approval for an indication broader than what was designated in its orphan drug application, it may not be entitled to exclusivity. Orphan exclusivity will not bar approval of another product under certain circumstances, including if a subsequent product with the same drug for the same indication is shown to be clinically superior to the approved product on the basis of greater efficacy or safety, or providing a major contribution to patient care, or if the company with orphan drug exclusivity is not able to meet market demand.

Patent Term Restoration and Extension

A patent claiming a new drug product or its method of use may be eligible for a limited patent term extension, also known as patent term restoration, under the Hatch-Waxman Act, which permits a patent restoration of up to five years for patent term lost during product development and the FDA regulatory review. Patent term extension is generally available only for drug products whose active ingredient has not previously been approved by the FDA. The restoration period granted is typically one-half the time between the effective date of an IND and the submission date of an NDA, plus the time between the submission date of an NDA and the ultimate approval date. Patent term extension cannot be used to extend the remaining term of a patent past a total of 14 years from the product's approval date. Only one patent applicable to an approved drug product is eligible for the extension, and the application for the extension must be submitted prior to the expiration of the patent in question. A patent that covers multiple drugs for which approval is sought can only be extended in connection with one of the approvals. The USPTO reviews and approves the application for any patent term extension in consultation with the FDA.

The 21st Century Cures Act

On December 13, 2016, President Obama signed the Cures Act into law. The Cures Act is designed to modernize and personalize healthcare, spur innovation and research, and streamline the discovery and development of new therapies through increased federal funding of particular programs. It authorizes increased funding for the FDA to spend on innovation projects. The new law also amends the Public Health Service Act, or PHSA, to reauthorize and expand funding for the NIH. The Cures Act establishes the NIH Innovation Fund to pay for the cost of development and implementation of a strategic plan, early stage investigators and research. It also charges NIH with leading and coordinating expanded pediatric research. Further, the Cures Act directs the Centers for Disease Control and Prevention to expand surveillance of neurological diseases.

With amendments to the FDCA and the PHSA, Title III of the Cures Act seeks to accelerate the discovery, development, and delivery of new medicines and medical technologies. To that end, and among other provisions, the Cures Act reauthorizes the existing priority review voucher program for certain drugs intended to treat rare pediatric diseases until 2020; creates a new priority review voucher program for drug applications determined to be material national security threat medical countermeasure applications; revises the FDCA to streamline review of combination product applications; requires FDA to evaluate the potential use of "real world evidence" to help support approval of new indications for approved drugs; provides a new "limited population" approval pathway for antibiotic and antifungal drugs intended to treat serious or life-threatening infections; and authorizes FDA to designate a drug as a "regenerative advanced therapy," thereby making it eligible for certain expedited review and approval designations.

Review and Approval of Drugs in Europe and other Foreign Jurisdictions

In addition to regulations in the United States, a manufacturer is subject to a variety of regulations in foreign jurisdictions to the extent it chooses to sell any drug products in those foreign countries. Even if a manufacturer obtains FDA approval of a product, it must still obtain the requisite approvals from regulatory authorities in foreign countries prior to the commencement of clinical trials or marketing of the product in those countries. To obtain regulatory approval of an investigational drug in the European Union (EU), a manufacturer must submit a marketing authorization application, or MAA, to the European Medicines Agency, or EMA. For other countries outside of the European Union, such as countries in Eastern Europe, Latin America or Asia, the requirements governing the conduct of clinical trials, product licensing, pricing and reimbursement vary from country to country. In all cases, clinical trials are to be conducted in accordance with GCP and the applicable regulatory requirements and the ethical principles that have their origin in the Declaration of Helsinki.

Clinical Trial Approval in the EU

Pursuant to the currently applicable Clinical Trials Directive 2001/20/EC and the Directive 2005/28/EC on GCP, an applicant must obtain approval from the competent national authority of the EU Member State in which the clinical trial is to be conducted. If the clinical trial is conducted in different EU Member States, the competent authorities in each of these EU Member States must provide their approval for the conduct of the clinical trial. Furthermore, the applicant may only start a clinical trial at a specific study site after the competent ethics committee has issued a favorable opinion.

In April 2014, the EU adopted a new Clinical Trials Regulation (EU) No 536/2014, which is set to replace the current Clinical Trials Directive 2001/20/EC. The new Clinical Trials Regulation will be directly applicable to and binding in all 28 EU Member States without the need for any national implementing legislation. The new Clinical Trials Regulation (EU) No 536/2014 will become applicable no earlier than 28 May 2016. It will overhaul the current system of approvals for clinical trials in the EU. Specifically, the new legislation aims at simplifying and streamlining the approval of clinical trials in the EU. Under the new coordinated procedure for the approval of clinical trials, the sponsor of a clinical trial will be required to submit a single application for approval of a clinical trial to a reporting EU Member State (RMS) through an EU Portal. The submission procedure will be the same irrespective of whether the clinical trial is to be conducted in a single EU Member State or in more than one EU Member State. The Clinical Trials Regulation also aims to streamline and simplify the rules on safety reporting for clinical trials.

Marketing Authorization

In the EU, marketing authorizations for medicinal products may be obtained through several different procedures founded on the same basic regulatory process.

The centralized procedure provides for the grant of a single marketing authorization that is valid for all EU Member States. The centralized procedure is compulsory for medicinal products produced by certain biotechnological processes, products designated as orphan medicinal products, and products with a new active substance indicated for

the treatment of certain diseases. It is optional for those products that are highly innovative or for which a centralized process is in the interest of patients. Under the centralized procedure in the EU, the maximum timeframe for the evaluation of a MAA is 210 days, excluding clock stops, when additional written or oral information is to be provided by the applicant in response to questions asked by the Committee for Medicinal Products for Human use or CHMP. Accelerated evaluation may be granted by the CHMP in exceptional cases. These are defined as circumstances in which a medicinal product is expected to be of a "major public health interest." Three cumulative criteria must be fulfilled in such circumstances: the seriousness of the disease, such as severely disabling or life-threatening diseases, to be treated; the absence or insufficiency of an appropriate alternative therapeutic approach; and anticipation of high therapeutic benefit. In these circumstances, the EMA ensures that the opinion of the CHMP is given within 150 days.

The decentralized procedure provides for approval by one or more other concerned EU Member States of an assessment of an application for marketing authorization conducted by one EU Member State, known as the reference EU Member State. In accordance with this procedure, an applicant submits an application for marketing authorization to the reference EU Member State and the concerned EU Member States. This application is identical to the application that would be submitted to the EMA for authorization through the centralized procedure. The reference EU Member State prepares a draft assessment and drafts of the related materials within 120 days after receipt of a valid application. The resulting assessment report is submitted to the concerned EU Member States which, within 90 days of receipt, must decide whether to approve the assessment report and related materials. If a concerned EU Member State cannot approve the assessment report and related materials due to concerns relating to a potential serious risk to public health, disputed elements may be referred to the European Commission, whose decision is binding on all EU Member States. In accordance with the mutual recognition procedure, the sponsor applies for national marketing authorization in one EU Member State. Upon receipt of this authorization the sponsor can then seek the recognition of this authorization by other EU Member States. Authorization in accordance with either of these procedures will result in authorization of the medicinal product only in the reference EU Member State and in the other concerned EU Member States.

A marketing authorization may be granted only to an applicant established in the EU. Regulation No. 1901/2006 provides that, prior to obtaining a marketing authorization in the EU, an applicant must demonstrate compliance with all measures included in a Pediatric Investigation Plan, or PIP, approved by the Pediatric Committee of the EMA, covering all subsets of the pediatric population, unless the EMA has granted a product-specific waiver, class waiver, or a deferral for one or more of the measures included in the PIP.

Regulatory Data Exclusivity in the European Union

Innovative medicinal products authorized in the EU on the basis of a full MAA (as opposed to an application for marketing authorization that relies on data available in the marketing authorization dossier for another, previously approved, medicinal product) are entitled to eight years of data exclusivity. During this period, applicants for authorization of generic versions of these innovative products cannot rely on data contained in the marketing authorization dossier submitted for the innovative medicinal product. Innovative medicinal products are also entitled to ten years' of market exclusivity. During this ten-year period no generic version of the medicinal product can be placed on the EU market. The overall ten-year period will be extended to a maximum of eleven years if, during the first eight years of those ten years, the marketing authorization holder obtains an authorization for one or more new therapeutic indications which, during the scientific evaluation prior to authorization, is held to bring a significant clinical benefit in comparison with existing therapies. Even if a compound is considered to be a new chemical entity so that the innovator gains the prescribed period of data exclusivity, another company may market another version of the product if such company obtained marketing authorization based on an MAA with a complete independent data package of pharmaceutical tests, preclinical tests and clinical trials.

Periods of Authorization and Renewals in the EU

A marketing authorization is valid for five years, in principle, and it may be renewed after five years on the basis of a reevaluation of the risk-benefit balance by the EMA or by the competent authority of the relevant EU Member State. To that end, the marketing authorization holder must provide the EMA or the relevant competent authority of the EU Member State with a consolidated version of the file in respect of quality, safety and efficacy, including all variations introduced since the marketing authorization was granted, at least six months before the marketing authorization ceases to be valid. Once renewed, the marketing authorization is valid for an unlimited period, unless the European Commission or the relevant competent authority of the EU Member State decides, on justified grounds relating to pharmacovigilance, to proceed with one additional five-year renewal period. Any marketing authorization that is not followed by the marketing of the medicinal product on the EU market (in the case of the centralized procedure) or on the market of the EU Member State which delivered the marketing authorization within three years after authorization ceases to be valid.

Regulatory Requirements after Marketing Authorization

As in the United States, marketing authorization holders and manufacturers of medicinal products are subject to comprehensive regulatory oversight by the EMA and the competent authorities of the individual EU Member States both before and after grant of the manufacturing and marketing authorizations.

The holder of an EU marketing authorization for a medicinal product must also comply with EU pharmacovigilance legislation and its related regulations and guidelines, which detail requirements for conducting pharmacovigilance or the assessment and monitoring of the safety of medicinal products. These rules can impose on central marketing authorization holders for medicinal products the obligation to conduct a labor intensive collection of data regarding the risks and benefits of

marketed products and to engage in ongoing assessments of those risks and benefits, including the possible requirement to conduct additional clinical studies.

The manufacturing process for medicinal products in the EU is highly regulated and regulators may shut down manufacturing facilities that they believe do not comply with regulations. Manufacturing requires a manufacturing authorization, and the manufacturing authorization holder must comply with various requirements set out in the applicable EU laws, regulations and guidance, including Directive 2001/83/EC, Directive 2003/94/EC, Regulation (EC) No 726/2004 and the European Commission Guidelines for Good Manufacturing Practice. These requirements include compliance with EU cGMP standards when manufacturing medicinal products and active pharmaceutical ingredients, including the manufacture of active pharmaceutical ingredients outside of the EU with the intention to import the active pharmaceutical ingredients into the EU. Similarly, the distribution of medicinal products into and within the EU is subject to compliance with the applicable EU laws, regulations and guidelines, including the requirement to hold appropriate authorizations for distribution granted by the competent authorities of the EU Member States.

In the EU, the advertising and promotion of products are subject to EU Member States' laws governing promotion of medicinal products, interactions with physicians, misleading and comparative advertising and unfair commercial practices. In addition, other legislation adopted by individual EU Member States may apply to the advertising and promotion of medicinal products. These laws require that promotional materials and advertising in relation to medicinal products comply with the product's Summary of Product Characteristics, or SmPC, as approved by the competent authorities. Promotion of a medicinal product that does not comply with the SmPC is considered to constitute off-label promotion. The off-label promotion of medicinal products is prohibited in the EU. The applicable laws at EU level and in the individual EU Member States also prohibit the direct-to-consumer advertising of prescription-only medicinal products. These laws may further limit or restrict the advertising and promotion of products to the general public and may also impose limitations on promotional activities with health care professionals.

Orphan Drug Designation and Exclusivity in the EU

Regulation (EC) No 141/2000 and Regulation (EC) No. 847/2000 provide that a product can be designated as an orphan medicinal product by the European Commission if its sponsor can establish that the product is intended for the diagnosis, prevention or treatment of: (1) a life-threatening or chronically debilitating condition affecting not more than five in ten thousand persons in the EU when the application is made, or (2) a life-threatening, seriously debilitating or serious and chronic condition in the EU and that without incentives the medicinal product is unlikely to be developed. For either of these conditions, the applicant must demonstrate that there exists no satisfactory method of diagnosis, prevention or treatment of the condition in question that has been authorized in the EU or, if such method exists, the medicinal product will be of significant benefit to those affected by that condition.

Once authorized, orphan medicinal products are entitled to ten years of market exclusivity in all EU Member States and, in addition, a range of other benefits during the development and regulatory review process, including scientific assistance for study protocols, authorization through the centralized marketing authorization procedure covering all member countries and a reduction or elimination of registration and marketing authorization fees. However, marketing authorization may be granted to a similar medicinal product with the same orphan indication during the ten-year period with the consent of the marketing authorization holder for the original orphan medicinal product or if the manufacturer of the original orphan medicinal product is unable to supply sufficient quantities. Marketing authorization may also be granted to a similar medicinal product with the same orphan indication if the product is safer, more effective or otherwise clinically superior to the original orphan medicinal product. The period of market exclusivity may, in addition, be reduced to six years if it can be demonstrated on the basis of available evidence that the original orphan medicinal product is sufficiently profitable not to justify maintenance of market exclusivity.

Pharmaceutical Coverage, Pricing and Reimbursement

In the United States and markets in other countries, patients who are prescribed treatments for their conditions and providers performing the prescribed services generally rely on third-party payors to reimburse all or part of the associated healthcare costs. Significant uncertainty exists as to the coverage and reimbursement status of products approved by the FDA and other government authorities. Thus, even if a product candidate is approved, sales of the product will depend, in part, on the extent to which third-party payors, including government health programs in the United States such as Medicare and Medicaid, commercial health insurers and managed care organizations, provide coverage, and establish adequate reimbursement levels for, the product. The process for determining whether a payor will provide coverage for a product may be separate from the process for setting the price or reimbursement rate that the payor will pay for the product once coverage is approved. Third-party payors are increasingly challenging the prices charged, examining the medical necessity, and reviewing

the cost-effectiveness of medical products and services and imposing controls to manage costs. Third-party payors may limit coverage to specific products on an approved list, also known as a formulary, which might not include all of the approved products for a particular indication.

In order to secure coverage and reimbursement for any product that might be approved for sale, a company 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 marketing approvals. Nonetheless, product candidates may not be considered medically necessary or cost effective. A decision by a third-party payor not to cover a product candidate could reduce physician utilization once the product is approved and have a material adverse effect on sales, results of operations and financial condition.

Additionally, a payor's decision to provide coverage for a product does not imply that an adequate reimbursement rate will be approved. Further, one payor's determination to provide coverage for a drug product does not assure that other payors will also provide coverage and reimbursement for the product, and the level of coverage and reimbursement can differ significantly from payor to payor.

The containment of healthcare costs also has become a priority of federal, state and foreign governments and the prices of drugs have been a focus in this effort. Governments have shown significant interest in implementing cost-containment programs, including price controls, restrictions on reimbursement and requirements for substitution of generic products. Adoption of price controls and cost-containment measures, and adoption of more restrictive policies in jurisdictions with existing controls and measures, could further limit a company's revenue generated from the sale of any approved products. Coverage policies and third-party reimbursement rates may change at any time. Even if favorable coverage and reimbursement status is attained for one or more products for which a company or its collaborators receive marketing approval, less favorable coverage policies and reimbursement rates may be implemented in the future.

Outside the United States, ensuring adequate coverage and payment for a product also involves challenges. Pricing of prescription pharmaceuticals is subject to governmental control in many countries. Pricing negotiations with governmental authorities can extend well beyond the receipt of regulatory marketing approval for a product and may require a clinical trial that compares the cost effectiveness of a product to other available therapies. The conduct of such a clinical trial could be expensive and result in delays in commercialization.

In the European Union, pricing and reimbursement schemes vary widely from country to country. Some countries provide that 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 drug candidate to currently available therapies or so called health technology assessments, in order to obtain reimbursement or pricing approval. For example, the European Union provides options for its member states to restrict the range of 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 product or it may instead adopt a system of direct or indirect controls on the profitability of the company placing the product on the market. Other member states allow companies to fix their own prices for products, but monitor and control prescription volumes and issue guidance to physicians to limit prescriptions. Recently, many countries in the European Union have increased the amount of discounts required on pharmaceuticals and these efforts could continue as countries attempt to manage healthcare expenditures, especially in light of the severe fiscal and debt crises experienced by many countries in the European Union. The downward pressure on health care costs in general, particularly prescription drugs, has become intense. As a result, increasingly high barriers are being erected to the entry of new products. Political, economic and regulatory developments may further complicate pricing negotiations, and pricing negotiations may continue after reimbursement has been obtained. Reference pricing used by various European Union member states, and parallel trade, i.e., arbitrage between low-priced and high-priced member states, can further reduce prices. There can be no

assurance that any country that has price controls or reimbursement limitations for pharmaceutical products will allow favorable reimbursement and pricing arrangements for any products, if approved in those countries.

Healthcare Law and Regulation

Healthcare providers and third-party payors play a primary role in the recommendation and prescription of drug products that are granted marketing approval. Arrangements with providers, consultants, third-party payors and customers are subject to broadly applicable fraud and abuse, anti-kickback, false claims laws, reporting of payments to physicians and teaching physicians and patient privacy laws and regulations and other healthcare laws and regulations that may constrain business and/or financial arrangements. Restrictions under applicable federal and state healthcare laws and regulations, include the following:

- the federal Anti-Kickback Statute, which prohibits, among other things, persons and entities from knowingly and willfully soliciting, offering, paying, receiving or providing remuneration, directly or indirectly, in cash or in kind, to induce or reward either the referral of an individual for, or the purchase, order or recommendation of, any good or service, for which payment may be made, in whole or in part, under a federal healthcare program such as Medicare and Medicaid;
- the federal civil and criminal false claims laws, including the civil False Claims Act, and civil monetary penalties laws, which prohibit individuals or entities from, among other things, knowingly presenting, or causing to be presented, to the federal government, claims for payment that are false, fictitious or fraudulent or knowingly making, using or causing to made or used a false record or statement to avoid, decrease or conceal an obligation to pay money to the federal government.
- the federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, which created additional federal criminal laws that prohibit, among other things, knowingly and willfully executing, or attempting to execute, a scheme to defraud any healthcare benefit program or making false statements relating to healthcare matters;
- HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act, and their respective implementing regulations, including the Final Omnibus Rule published in January 2013, which impose obligations, including mandatory contractual terms, with respect to safeguarding the privacy, security and transmission of individually identifiable health information;
- the federal false statements statute, which prohibits knowingly and willfully falsifying, concealing or covering up a material fact or making any materially false statement in connection with the delivery of or payment for healthcare benefits, items or services;
- the federal transparency requirements known as the federal Physician Payments Sunshine Act, under the Patient Protection and Affordable Care Act, as amended by the Health Care Education Reconciliation Act, or the ACA, which requires certain manufacturers of drugs, devices, biologics and medical supplies to report annually to the Centers for Medicare & Medicaid Services, or CMS, within the United States Department of Health and Human Services, information related to payments and other transfers of value made by that entity to physicians and teaching hospitals, as well as ownership and investment interests held by physicians and their immediate family members; and
- analogous state and foreign laws and regulations, such as state anti-kickback and false claims laws, which may apply to healthcare items or services that are reimbursed by non-governmental third-party payors, including private insurers.

Some state laws require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government in addition to requiring drug manufacturers to report information related to payments to physicians and other health care providers or marketing expenditures. State and foreign laws also govern the privacy and security of health information in some circumstances, many of which differ from each other in significant ways and often are not preempted by HIPAA, thus complicating compliance efforts.

Healthcare Reform

A primary trend in the United States healthcare industry and elsewhere is cost containment. There have been a number of federal and state proposals during the last few years regarding the pricing of pharmaceutical and biopharmaceutical products, limiting coverage and reimbursement for drugs and other medical products, government control and other changes to the healthcare system in the United States.

In March 2010, the United States Congress enacted the ACA, which, among other things, includes changes to the coverage and payment for products under government health care programs. Among the provisions of the ACA of importance to potential drug candidates are:

- an annual, nondeductible fee on any entity that manufactures or imports specified branded prescription drugs and biologic agents, apportioned among these entities according to their market share in certain government healthcare programs, although this fee would not apply to sales of certain products approved exclusively for orphan indications;

- expansion of eligibility criteria for Medicaid programs by, among other things, allowing states to offer Medicaid coverage to certain individuals with income at or below 133% of the federal poverty level, thereby potentially increasing a manufacturer's Medicaid rebate liability;
- expanded manufacturers' rebate liability under the Medicaid Drug Rebate Program by increasing the minimum rebate for both branded and generic drugs and revising the definition of "average manufacturer price," or AMP, for calculating and reporting Medicaid drug rebates on outpatient prescription drug prices and extending rebate liability to prescriptions for individuals enrolled in Medicare Advantage plans;

- addressed a new methodology by which rebates owed by manufacturers under the Medicaid Drug Rebate Program are calculated for drugs that are inhaled, infused, instilled, implanted or injected;
- expanded the types of entities eligible for the 340B drug discount program;
- established the Medicare Part D coverage gap discount program by requiring manufacturers to provide a 50% point-of-sale-discount off the negotiated price of applicable brand drugs to eligible beneficiaries during their coverage gap period as a condition for the manufacturers' outpatient drugs to be covered under Medicare Part D;
- a new Patient-Centered Outcomes Research Institute to oversee, identify priorities in, and conduct comparative clinical effectiveness research, along with funding for such research;
- the Independent Payment Advisory Board, or IPAB, which has authority to recommend certain changes to the Medicare program to reduce expenditures by the program that could result in reduced payments for prescription drugs. However, the IPAB implementation has been not been clearly defined. ACA provided that under certain circumstances, IPAB recommendations will become law unless Congress enacts legislation that will achieve the same or greater Medicare cost savings; and
- established the Center for Medicare and Medicaid Innovation within CMS to test innovative payment and service delivery models to lower Medicare and Medicaid spending, potentially including prescription drug spending. Funding has been allocated to support the mission of the Center for Medicare and Medicaid Innovation from 2011 to 2019.

Other legislative changes have been proposed and adopted in the United States since the ACA was enacted. For example, in August 2011, the Budget Control Act of 2011, among other things, created measures for spending reductions by Congress. A Joint Select Committee on Deficit Reduction, tasked with recommending a targeted deficit reduction of at least $1.2 trillion for the years 2012 through 2021, was unable to reach required goals, thereby triggering the legislation's automatic reduction to several government programs. This includes aggregate reductions of Medicare payments to providers of up to 2% per fiscal year, which went into effect in April 2013 and will remain in effect through 2024 unless additional Congressional action is taken. In January 2013, President Obama signed into law the American Taxpayer Relief Act of 2012, which, among other things, further reduced Medicare payments to several providers, including hospitals, imaging centers and cancer treatment centers, and increased the statute of limitations period for the government to recover overpayments to providers from three to five years.

With the new Administration and Congress, there will likely be additional legislative changes, including repeal and replacement of certain provisions of the ACA. In January 2017, Congress voted to adopt a budget resolution for fiscal year 2017, or the Budget Resolution, that authorizes the implementation of legislation that would repeal portions of the ACA. The Budget Resolution is not a law; however, it is widely viewed as the first step toward the passage of legislation that would repeal certain aspects of the ACA. Further, on January 20, 2017, President Trump signed an Executive Order directing federal agencies with authorities and responsibilities under the ACA to waive, defer, grant exemptions from, or delay the implementation of any provision of the ACA that would impose a fiscal or regulatory burden on states, individuals, healthcare providers, health insurers, or manufacturers of pharmaceuticals or medical devices.

The President and congressional leaders have expressed interest in repealing certain ACA provisions and replacing them with alternatives that may be less costly and provide state Medicaid programs and private health plans more flexibility. It is possible that these repeal and replacement initiatives, if enacted into law, could ultimately result in fewer individuals having health insurance coverage or in individuals having insurance coverage with less generous benefits. The scope of potential future legislation to repeal and replace ACA provisions is highly uncertain in many respects, and it is possible that some of the ACA provisions that generally are not favorable for the research-based pharmaceutical industry could also be repealed along with ACA coverage expansion provisions. However, at this time the coverage expansion provisions of the ACA appear most likely to be repealed and replaced.

Employees

As of March 1, 2017, we had 23 full-time employees, 8 of whom were engaged in research and development and 15 of whom were engaged in general business management, administration and finance. Approximately 78% of our employees hold advanced degrees. Our success depends, in part, on our ability to recruit and retain talented and trained scientific and business personnel and senior leadership. We believe that we have been successful to date in obtaining and retaining these individuals, but we do not know whether we will be successful in doing so in the future. None of our employees are represented by a labor union or covered by a collective bargaining agreement, nor have we experienced work stoppages. We believe that relations with our employees are good.

Corporate Information

We were incorporated in California on March 22, 1995 under the name IRORI and, in 1998, we changed our name to Discovery Partners International, Inc., or DPI. In July 2000, we reincorporated in Delaware. On September 12, 2006, DPI completed a merger with Infinity Pharmaceuticals, Inc., or IPI, pursuant to which a wholly-owned subsidiary of DPI merged with and into IPI. IPI, the surviving corporation in the merger, changed its name to Infinity Discovery, Inc., or IDI, and became a wholly-owned subsidiary of DPI. In addition, we changed our corporate name from Discovery Partners International, Inc. to Infinity Pharmaceuticals, Inc., and our ticker symbol on the NASDAQ Global Market to "INFI." Our common stock currently trades on the NASDAQ Global Select Market.

Our principal executive offices are located at 784 Memorial Drive, Cambridge, Massachusetts 02139, and our telephone number at that address is (617) 453-1000.

The Infinity logo and all other Infinity product names are trademarks of Infinity Pharmaceuticals, Inc. or its subsidiaries in the United States and in other select countries. We may indicate U.S. trademark registrations and U.S. trademarks with the symbols ®" and "™", respectively. Other third-party logos and product/trade names are registered trademarks or trade names of their respective owners.

Executive Officers

The following table lists the positions, names and ages of our executive officers as of March 1, 2017:

Name	Age	Position
Adelene Q. Perkins	57	Chief Executive Officer
Lawrence E. Bloch, M.D., J.D.	51	President and Treasurer
Jeffery L. Kutok, M.D., Ph.D.	50	Senior Vice President, Chief Scientific Officer
Seth A. Tasker, J.D.	38	Vice President, General Counsel and Secretary

Adelene Q. Perkins has served as our Chief Executive Officer since January 2010, our President between October 2008 and January 2017, our Chief Business Officer from October 2008 through December 2009 and our Executive Vice President and Chief Business Officer between September 2006 and October 2008. Ms. Perkins served as Executive Vice President of IPI from February 2006 until its merger with DPI in September 2006 and Chief Business Officer of IPI from June 2002 until the DPI merger. Prior to joining IPI, Ms. Perkins served as Vice President of Business and Corporate Development of TransForm Pharmaceuticals, Inc., a private pharmaceutical company, from 2000 to 2002. From 1992 to 1999, Ms. Perkins held various positions at Genetics Institute, most recently serving as Vice President of Emerging Business and General Manager of the DiscoverEase® business unit. Ms. Perkins has served as a director of the Biotechnology Industry Organization since 2012, a director of Project Hope, a not-for-profit social services company since 2013, a director of the Massachusetts Life Sciences Center, a quasi-public agency of the Commonwealth of Massachusetts, since 2014, a director of the Massachusetts Biotechnology Council, a not-for-profit organization, since 2014, and a director of Padlock Therapeutics, a privately held biopharmaceutical company since 2015. From 1985 to 1992, Ms. Perkins held a variety of positions at Bain & Company, a strategy consulting firm. Ms. Perkins received a B.S. in Chemical Engineering from Villanova University and an M.B.A. from Harvard Business School.

Lawrence E. Bloch, M.D., J.D., has served as our President since January 2017, and our Executive Vice President, Chief Financial Officer and Chief Business Officer from July 2012 to December 2016. Prior to joining Infinity, Dr. Bloch served as Chief Executive Officer of NeurAxon, Inc., a privately held biopharmaceutical company, from 2007 to 2011. Previously, he served as Chief Financial Officer and Chief Business Officer of NitroMed, Inc., a publicly held biopharmaceutical company, from 2004 to 2006. From 2000 to 2004, Dr. Bloch served as Chief Financial Officer, and from 1999 to 2002 as Vice President, Business Development, of Applied Molecular Evolution, Inc., a publicly held biopharmaceutical company. Dr. Bloch began his career as an emergency medicine resident physician at Massachusetts General Hospital and Brigham & Woman's Hospital. Dr. Bloch has served as director of NeurAxon, Inc., a privately held biopharmaceutical company, from 2007 to 2011. He holds a J.D. from Harvard Law

School, an M.D. from Harvard Medical School and an M.B.A. from Harvard Business School.

Jeffery L. Kutok, M.D., Ph.D., has served as our Senior Vice President and Chief Scientific Officer since February 2017, our Vice President of Biology and Translational Science from August 2013 to February 2017, our Senior Director of Biology and Translational Science from August 2012 to August 2013, our Senior Director of Molecular Pathology from March 2012 to August 2012, and our Director of Molecular Pathology from January 2011 to March 2012. Prior to joining Infinity, Dr. Kutok was an associate professor of pathology at Harvard Medical School and Brigham and Women's Hospital. His laboratory

focused on translational medicine research and biomarker identification in cancer, and he is an author on over 190 journal articles, reviews and book chapters. Dr. Kutok is board certified in Anatomic Pathology and Hematology and had clinical duties in Hematopathology and Molecular Diagnostics at Brigham and Women's Hospital. Dr. Kutok received his B.S. in biology and his M.D., Ph.D. in medicine and molecular pathology from the State University of New York at Stony Brook. His Ph.D. was earned working in the laboratory of Dr. Barry Coller, M.D. in the field of platelet pathobiology. He was also a post-doctoral fellow at Harvard University in the laboratory of Dr. Gary Gilliland, M.D., Ph.D.

Seth A. Tasker, J.D. has served as our Vice President, General Counsel and Secretary since July 2016, our Deputy General Counsel between March 2015 and July 2016, our Associate General Counsel between March 2013 and March 2015, our Assistant General Counsel between March 2010 and March 2013, and our Corporate Counsel between March 2008 and March 2010. Prior to joining Infinity, Mr. Tasker served in varying levels of responsibility in the legal function at Surface Logix, Inc., a privately hely biopharmaceutical company, from 2001 to 2008. Mr. Tasker holds a B.S. in Microbiology from the University of Vermont, a J.D. from Suffolk University Law School, and an M.B.A. from Suffolk University Sawyer School of Management.

Available Information

Our Internet website is http://www.infi.com. We make available free of charge through our website our annual report on Form 10-K, quarterly reports on Form 10-Q, current reports on Form 8-K and amendments to those reports filed or furnished pursuant to Sections 13(a) and 15(d) of the Securities Exchange Act of 1934, as amended. We make these reports available through our website as soon as reasonably practicable after we electronically file such reports with, or furnish such reports to, the SEC. In addition, we regularly use our website to post information regarding our business, product development programs and governance, and we encourage investors to use our website, particularly the information in the section entitled "Investors/Media," as a source of information about us.

Our Code of Conduct and Ethics and the charters of the Audit, Compensation, Nominating & Corporate Governance and Research & Development Committees of our Board of Directors are all available on our website at http://www.infi.com at the "Investors/Media" section under "Corporate Governance." Stockholders may request a free copy of any of these documents by writing to Investor Relations, Infinity Pharmaceuticals, Inc., 784 Memorial Drive, Cambridge, Massachusetts 02139, U.S.A.

The foregoing references to our website are not intended to, nor shall they be deemed to, incorporate information on our website into this report by reference.

Item 1A. RISK FACTORS

The following risk factors and other information included in this Annual Report on Form 10-K should be carefully considered. The risks and uncertainties described below are not the only risks and uncertainties we face. Additional risks and uncertainties not presently known to us or that we presently deem less significant may also impair our business operations. Please see page 1 of this Annual Report on Form 10-K for a discussion of some of the forward-looking statements that are qualified by these risk factors. If any of the following risks occur, our business, financial condition, results of operations and future growth prospects could be materially and adversely affected.

Risks Related to Our Financial Position and Need for Additional Capital

We have a history of operating losses, expect to incur significant and increasing operating losses in the future, may never become profitable, or if we become profitable, we may not remain profitable.

We have a limited operating history for you to evaluate our business. We have no approved products and have generated no product revenue from sales. We have primarily incurred operating losses. As of December 31, 2016, we

had an accumulated deficit of $625.7 million. Pending any decision to change strategic direction, we expect to continue to spend significant resources to fund IPI-549, the wind-down of duvelisib, and restructuring related expenses. IPI-549 is our selective inhibitor of phosphoinositide-3-kinase, or PI3K, gamma. Duvelisib is a selective inhibitor of PI3K delta and gamma which we licensed to Verastem, Inc, or Verastem. While we may have net income in some periods as the result of non-recurring collaboration revenue, we expect to incur substantial operating losses over the next several years as our clinical trial and drug manufacturing activities continue. In addition, if we proceed to seek and possibly obtain regulatory approval of IPI-549, we would expect to incur significant commercialization expenses for product sales, marketing, manufacturing and distribution. As a result, we expect that our accumulated deficit would also increase significantly.

IPI-549 is under clinical development and may never be approved for sale or generate any revenue. We will not be able to generate product revenue unless and until IPI-549 successfully completes clinical trials and receives regulatory approval. We do not expect to generate revenue from product sales for the foreseeable future. Even if we eventually generate revenues, we may never be profitable, and if we do achieve profitability, we may not be able to sustain or increase profitability on a quarterly or annual basis. Our failure to become and remain profitable would decrease the value of our company and could impair our ability to raise capital, expand our business, maintain our research and development efforts, and cause a decline in the value of our common stock.

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

Developing pharmaceutical products, including conducting preclinical studies and clinical trials, is a very time consuming, expensive and uncertain process that takes years to complete. We will need substantial additional funds to support our planned operations. In the absence of additional funding or business development activities, we believe that our existing cash, cash equivalents and available-for-sale securities at December 31, 2016 will be adequate to satisfy our capital needs into the first quarter of 2019 based on our operating plans.

Our estimate as to how long we expect our existing cash, cash equivalents and available-for-sale securities to be able to continue to fund our operations is based on assumptions that may prove to be wrong, and we could use our available capital resources sooner than we currently expect. Further, changing circumstances, some of which may be beyond our control, could cause us to consume capital significantly faster than we currently anticipate. Our future funding requirements, both short-term and long-term, will depend on many factors, including, but not limited to:

- the scope, progress, results and costs of developing IPI-549, currently in clinical development;
- our ability to realize the planned cost savings benefits of strategic restructurings we effected in 2016, which included a significant reduction in our workforce, in order to preserve capital to support the development of IPI-549;
- our ability to secure alternative leasing or subleasing arrangements for our current lease and to achieve related cost savings;
- the timing of, and the costs involved in, obtaining regulatory approvals for IPI-549;
- our ability to effectively transition the duvelisib program to Verastem;
- the costs involved in preparing, filing, prosecuting, maintaining, defending and enforcing patent claims, including litigation costs and the outcome of such litigation;
- the absence of any breach, acceleration event or event of default under any agreements with third parties;
- the outcome of any lawsuits that could be brought against us;
- the cost of acquiring raw materials for, and of manufacturing, our product candidates is higher than anticipated;
- the cost or quantity required of comparator drugs used in clinical studies increases; and
- a loss in our investments due to general market conditions or other reasons.

Raising additional capital may cause dilution to our stockholders, restrict our operations or require us to relinquish rights to our technologies or product candidates.

We may seek additional funding through public or private financings of equity or debt securities, but such financing may not be available on acceptable terms, if at all. If we raise additional funds through the issuance of additional debt or equity securities, it could result in dilution to our existing stockholders, increased fixed payment obligations and the existence of securities with rights that may adversely affect the rights of our existing stockholders including liquidation or other preferences and anti-dilution protections. If we incur indebtedness, we could become subject to covenants that would restrict our operations and potentially impair our competitiveness, such as limitations on our ability to incur additional debt, make capital expenditures, create liens, redeem stock, declare dividends, and acquire, sell or license intellectual property rights, or other operating restrictions that could adversely impact our ability to conduct our business. Any of these events could significantly harm our business, financial condition and prospects. In addition, securing financing could require a substantial amount of time and attention from our management and may divert a disproportionate amount of their attention away from day-to-day activities, which may adversely affect our management’s ability to oversee the development of our product candidates.

We may also seek additional funds through arrangements with collaborators or other third parties, or through project financing. These arrangements would generally require us to relinquish or encumber rights to some of our technologies or product candidates, and we may not be able to enter into such agreements on acceptable terms, if at all.

If we are unable to obtain additional funding on a timely basis, we may be required to curtail, terminate, sell or license IPI-549 or to scale back, suspend or terminate our business operations.

Risks Related to the Development and Commercialization of IPI-549

In the near term, we are dependent on the success of IPI-549, our only product candidate in development.

Our prospects are substantially dependent on our ability to develop, obtain marketing approval for and successfully commercialize product candidates in one or more disease indications.

We currently have no products approved for sale and are investing substantially all of our efforts and financial resources in the development of IPI-549.

The success of IPI-549 will depend on several factors, including the following:

- initiation and successful enrollment and completion of clinical trials, including in combination with other agents;
- a safety, tolerability and efficacy profile that is satisfactory to the U.S. Food and Drug Administration, or FDA, or any comparable foreign regulatory authority for marketing approval;
- timely receipt of marketing approvals from applicable regulatory authorities;
- the extent of any required post-marketing approval commitments to applicable regulatory authorities;
- establishment of supply arrangements with third-party raw materials suppliers and manufacturers;
- establishment of arrangements with third-party manufacturers to obtain finished drug product that is appropriately packaged for sale;
- adequate ongoing availability of raw materials and drug product for clinical development and any commercial sales;
- obtaining and maintaining patent, trade secret protection and regulatory exclusivity, both in the United States and internationally;
- protection of our rights in our intellectual property portfolio;
- successful launch of commercial sales following any marketing approval;
- a continued acceptable safety profile following any marketing approval;
- commercial acceptance by patients, the medical community and third-party payors; and
- our ability to compete with other therapies.

Many of these factors are beyond our control, including clinical development, the regulatory submission process, potential threats to our intellectual property rights and the manufacturing, marketing and sales efforts of any collaborator. If we are unable to develop, receive marketing approval for and successfully commercialize IPI-549, on our own or with any collaborator, or experience delays as a result of any of these factors or otherwise, our business could be substantially harmed.

IPI-549 remains subject to clinical testing and regulatory approval. This process is highly uncertain, and we may never be able to obtain marketing approval for IPI-549.

To date, we have not obtained approval from the FDA or any foreign regulatory authority to market or sell any of our product candidates. Any product candidates that we seek to advance will be subject to extensive governmental regulations relating to development, clinical trials, manufacturing and commercialization. Rigorous preclinical testing and clinical trials and an extensive regulatory approval process are required in the United States and in many foreign jurisdictions prior to the commercial sale of medicinal products like our product candidates.

For example, we are evaluating IPI-549, our only product candidate, in clinical development. If our Phase 1 clinical trial of IPI-549 is successful, we will need to conduct further clinical trials and will need to apply for regulatory approval before we may market or sell any products based on IPI-549. Satisfaction of these and other regulatory requirements is costly, time consuming, uncertain and subject to unanticipated delays. It is possible that IPI-549 will not obtain marketing approval. Even if IPI-549 has a beneficial effect, that effect may not be detected during clinical evaluation as a result of one or more of a variety of factors, including the size, duration, design, measurements, conduct or analysis of our clinical trials. Conversely, as a

30

result of the same factors, our clinical trials may indicate an apparent positive effect of IPI-549 that is greater than the actual positive effect, if any. Similarly, in our clinical trials we may fail to detect toxicity of or intolerability caused by IPI-549, or mistakenly believe that IPI-549 is toxic or not well tolerated when that is not in fact the case.

IPI-549 must undergo rigorous clinical trials prior to receipt of regulatory approval. Any problems in these clinical trials could delay or prevent commercialization of IPI-549.

We cannot predict whether we will encounter problems with any of our ongoing or planned clinical trials that will cause us or regulatory authorities to delay, suspend, or discontinue clinical trials or to delay the analysis of data from ongoing clinical trials. Any of the following could delay or disrupt the clinical development of IPI-549:

- unfavorable results of discussions with the FDA or comparable foreign authorities regarding the scope or design of our clinical trials;
- delays in receiving, or the inability to obtain, required approvals from institutional review boards or other reviewing entities at clinical sites selected for participation in our clinical trials;
- delays in enrolling patients into clinical trials;
- a lower than anticipated retention rate of patients in clinical trials;
- the need to repeat or discontinue clinical trials as a result of inconclusive or negative results or unforeseen complications in testing or because the results of later trials may not confirm positive results from earlier preclinical studies or clinical trials;
- inadequate supply, delays in distribution or deficient quality of, or inability to purchase or manufacture drug product, comparator drugs or other materials necessary to conduct our clinical trials;
- unfavorable FDA or other foreign regulatory inspection and review of a clinical trial site, Infinity, or an Infinity vendor, or records of any clinical or preclinical investigation;
- serious and unexpected drug-related side effects experienced by participants in our clinical trials, which may occur even if they were not observed in earlier trials or only observed in a limited number of participants;
- a finding that the trial participants are being exposed to unacceptable health risks;
- the placement by the FDA or a foreign regulatory authority of a clinical hold on a trial; or
- any restrictions on, or post-approval commitments with regard to, any regulatory approval we ultimately obtain that render the product candidate not commercially viable.

We may suspend, or the FDA or other applicable regulatory authorities may require us to suspend, clinical trials of IPI-549 at any time if we or they believe the patients participating in such clinical trials, or in independent third-party clinical trials for drugs based on similar technologies, are being exposed to unacceptable health risks or for other reasons.

The delay, suspension or discontinuation of any of our clinical trials, or a delay in the analysis of clinical data for IPI-549, for any of the foregoing reasons, could adversely affect our ability to obtain regulatory approval for and to commercialize IPI-549, increase our operating expenses and have a material adverse effect on our financial results.

Adverse events or undesirable side effects caused by, or other unexpected properties of, IPI-549, alone or in combination with other agents, may be identified during development and could delay or prevent IPI-549 marketing approval or limit its use.

Adverse events or undesirable side effects caused by, or other unexpected properties of, IPI-549 could cause us, any collaborators, an institutional review board or regulatory authorities to interrupt, delay or halt clinical trials of IPI-549 and could result in a more restrictive label or the delay or denial of marketing approval by the FDA or comparable foreign regulatory authorities. If IPI-549 is associated with adverse events or undesirable side effects or has properties that are unexpected, we, or any collaborators, may need to abandon development or limit development of IPI-549 to certain uses or subpopulations in which the undesirable side effects or other characteristics are less prevalent, less severe or more acceptable from a risk-benefit perspective. Many compounds that initially showed promise in clinical or earlier stage testing have later been found to cause undesirable or unexpected side effects that prevented further development of the compound.

If we, or any future collaborators, experience any of a number of possible unforeseen events in connection with clinical trials of IPI-549, potential clinical development, marketing approval or commercialization of IPI-549 could be

delayed or prevented.

We, or any future collaborators, may experience numerous unforeseen events during, or as a result of, clinical trials that could delay or prevent clinical development, marketing approval or commercialization of IPI-549, including:

- regulators or institutional review boards may not authorize us, any collaborators or our or their investigators to commence a clinical trial or conduct a clinical trial at a prospective trial site;
- we, or any collaborators, may have delays in reaching or fail to reach agreement on acceptable clinical trial contracts or clinical trial protocols with prospective trial sites;
- clinical trials of IPI-549 may produce unfavorable or inconclusive results;
- we, or any collaborators, may decide, or regulators may require us or them, to conduct additional clinical trials or abandon IPI-549;
- the number of patients required for clinical trials of IPI-549 may be larger than we, or any collaborators, anticipate, patient enrollment in these clinical trials may be slower than we, or any collaborators, anticipate or participants may drop out of these clinical trials at a higher rate than we, or any collaborators, anticipate;
- the cost of planned clinical trials of IPI-549 may be greater than we anticipate;
- our third-party contractors or those of any collaborators, including those manufacturing IPI-549 or components or ingredients thereof or conducting clinical trials on our behalf or on behalf of any collaborators, may fail to comply with regulatory requirements or meet their contractual obligations to us or any collaborators in a timely manner or at all;
- patients that enroll in a clinical trial may misrepresent their eligibility to do so or may otherwise not comply with the clinical trial protocol, resulting in the need to drop the patients from the clinical trial, increase the needed enrollment size for the clinical trial or extend the clinical trial's duration;
- we, or any collaborators, may have to delay, suspend or terminate clinical trials of IPI-549 for various reasons, including a finding that the participants are being exposed to unacceptable health risks, undesirable side effects or other unexpected characteristics of IPI-549;
- regulators or institutional review boards may require that we, or any collaborators, or our or their investigators suspend or terminate clinical research for various reasons, including noncompliance with regulatory requirements or their standards of conduct, a finding that the participants are being exposed to unacceptable health risks, undesirable side effects or other unexpected characteristics of IPI-549 or findings of undesirable effects caused by a chemically or mechanistically similar product or product candidate;
- the FDA or comparable foreign regulatory authorities may disagree with our, or any collaborators', clinical trial designs or our or their interpretation of data from preclinical studies and clinical trials;
- the FDA or comparable foreign regulatory authorities may fail to approve or subsequently find fault with the manufacturing processes or facilities of third-party manufacturers with which we, or any collaborators, enter into agreements for clinical and commercial supplies;
- the supply or quality of raw materials or manufactured product candidates or other materials necessary to conduct clinical trials of IPI-549 may be insufficient, inadequate or not available at an acceptable cost, or we may experience interruptions in supply; and
- the approval policies or regulations of the FDA or comparable foreign regulatory authorities may significantly change in a manner rendering our clinical data insufficient to obtain marketing approval.

Product development costs for us, or any collaborators, will increase if we, or they, experience delays in testing or pursuing marketing approvals and we, or they, may be required to obtain additional funds to complete clinical trials and prepare for possible commercialization of IPI-549. We do not know whether any clinical trials will begin as planned, will need to be restructured, or will be completed on schedule or at all. Significant preclinical study or clinical trial delays also could shorten any periods during which we, or any collaborators, may have the exclusive right to commercialize IPI-549 or allow our competitors, or the competitors of any current or future collaborators, to bring products to market before we, or any collaborators, do and impair our ability, or the ability of any collaborators, to successfully commercialize IPI-549 and may harm our business and results of operations. In addition, many of the factors that lead to clinical trial delays may ultimately lead to the denial of marketing approval of IPI-549, or, in the event that our clinical trials remain unable to demonstrate meaningful clinical benefit, our failure to reach the marketing approval stage at all.

Results of preclinical studies and early clinical trials may not be successful, and even if they are successful, may not be predictive of results of future late-stage clinical trials.

We are in early-stage clinical development for IPI-549. The outcome of preclinical studies and early clinical trials may not be predictive of the success of later clinical trials, and interim results of clinical trials do not necessarily predict success in future clinical trials. Many companies in the pharmaceutical and biotechnology industries have suffered significant setbacks in late-stage clinical trials after achieving positive results in earlier development, and we could face similar setbacks. The design of a clinical trial can determine whether its results will support approval of a product and flaws in the design of a clinical trial may not become apparent until the clinical trial is well advanced. We may be unable to design and execute a clinical trial to support marketing approval. In addition, preclinical and clinical data are often susceptible to varying interpretations and analyses. Many companies that believed their product candidates performed satisfactorily in preclinical studies and clinical trials have nonetheless failed to obtain marketing approval for the product candidates. Even if we, or any collaborators, believe that the results of clinical trials for IPI-549 warrant marketing approval, the FDA or comparable foreign regulatory authorities may disagree and may not grant marketing approval of IPI-549.

In some instances, there can be significant variability in safety or efficacy results between different clinical trials of the same product candidate due to numerous factors, including changes in trial procedures set forth in protocols, differences in the size and type of the patient populations, changes in and adherence to the dosing regimen and other clinical trial protocols and the rate of dropout among clinical trial participants. If we fail to receive positive results in clinical trials of IPI-549, the development timeline and regulatory approval and commercialization prospects for IPI-549 and, correspondingly, our business and financial prospects, would be negatively impacted.

Our inability to enroll sufficient numbers of patients in our clinical trials, or any delays in patient enrollment, could result in increased costs and longer development periods for our product candidates.

Clinical trials require sufficient patient enrollment, which is a function of many factors, including:

- the size and nature of the patient population;
- the severity of the disease under investigation;
- the nature and complexity of the trial protocol, including eligibility criteria for the trial;
- the number of clinical trial sites and the proximity of patients to those sites;
- standard of care in disease under investigation;
- the commitment of clinical investigators to identify eligible patients;
- competing studies or trials; and
- clinicians' and patients' perceptions as to the potential advantages and risks of the drug being studied in relation to other available therapies, including any new drugs that may be approved for the indications we are investigating.

Our failure to enroll patients in a clinical trial could delay the initiation or completion of the clinical trial beyond current expectations. In addition, the FDA or other foreign regulatory authorities could require us to conduct clinical trials with a larger number of patients than has been projected for any of our product candidates. As a result of these factors, we may not be able to enroll a sufficient number of patients in a timely or cost-effective manner.

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

- the inclusion of a placebo arm in a trial;
- possible inactivity or low activity of the product candidate being tested at one or more of the dose levels being tested;
- the occurrence of adverse side effects, whether or not related to the product candidate; and
- the availability of numerous alternative treatment options, including clinical trials evaluating competing product candidates, that may induce patients to discontinue their participation in the trial.

A delay in our clinical trial activities could adversely affect our ability to obtain regulatory approval for and to commercialize our product candidates, increase our operating expenses, and have a material adverse effect on our financial results.

We have never obtained marketing approval for a product candidate, and we may be unable to obtain, or may be delayed in obtaining, marketing approval for IPI-549.

We have never obtained marketing approval for a product candidate. It is possible that the FDA may refuse to accept for substantive review any new drug applications, or NDAs, that we submit for IPI-549 or may conclude after review

of our

data that our application is insufficient to obtain marketing approval of IPI-549. If the FDA does not accept or approve our NDAs for IPI-549, it may require that we conduct additional clinical trials, preclinical studies or manufacturing validation studies and submit that data before it will reconsider our applications. Depending on the extent of these or any other FDA-required trials or studies, approval of any NDA or application that we submit may be delayed by several years, or may require us to expend more resources than we have available. It is also possible that additional trials or studies, if performed and completed, may not be considered sufficient by the FDA to approve our NDAs. Any delay in obtaining, or an inability to obtain, marketing approvals would prevent us from commercializing IPI-549 or any companion diagnostics, generating revenues and achieving and sustaining profitability. If any of these outcomes occurs, we may be forced to abandon our development efforts for IPI-549, which could significantly harm our business.

Even if IPI-549 receives marketing approval, we or others may later discover that the product is less effective than previously believed or causes undesirable side effects that were not previously identified, which could compromise our ability, or that of any future collaborator, to market IPI-549, and we could become subject to costly and damaging product liability claims.

Even if we receive regulatory approval for IPI-549, we will have tested it in only a small number of patients in carefully defined subsets and over a limited period of time during our clinical trials. If our applications for marketing are approved and more patients begin to use our products, or patients use IPI-549 for a longer period of time, IPI-549 might be less effective than indicated by our clinical trials. Furthermore, new risks and side effects associated with IPI-549 may be discovered or previously observed risks and side effects may become more prevalent and/or clinically significant.

In addition, supplemental clinical trials that may be conducted on a drug following its initial approval may produce findings that are inconsistent with the trial results previously submitted to regulatory authorities. As a result, regulatory authorities may revoke their approvals, or we may be required to conduct additional clinical trials, make changes in labeling of IPI-549 (including a “black box” warning or a contraindication) or the manner in which it is administered, reformulate IPI-549 or make changes and obtain new approvals for our and our suppliers’ manufacturing facilities. We also might have to withdraw or recall IPI-549 from the marketplace, and regulators might seize IPI-549. We might be subject to fines, injunctions, or the imposition of civil or criminal penalties. Any safety concerns with respect to IPI-549 may also result in a significant drop in the potential sales of IPI-549, damage to our reputation in the marketplace, or result in our and our collaborators’ becoming subject to lawsuits, including class actions. Any of these results could decrease or prevent any sales of our approved product or substantially increase the costs and expenses of commercializing and marketing our product and could negatively impact our stock price.

Even if IPI-549 receives marketing approval, it may fail to achieve the degree of market acceptance by physicians, patients, third-party payors and others in the medical community necessary for commercial success, in which case we may not be able to generate significant revenues from product sales to become profitable.

Even if IPI-549 obtains regulatory approval, it may not gain market acceptance among physicians, patients, managed care organizations, third-party payors, and the medical community for a variety of reasons including:

- timing of our receipt of any marketing approvals, the terms of any such approvals and the countries in which any such approvals are obtained;
- timing of market introduction of competitive products;
- lower demonstrated clinical safety or efficacy, or less convenient or more difficult route of administration, compared to competitive products;
- lack of cost-effectiveness;
- lack of reimbursement from government payors, managed care plans and other third-party payors;
- prevalence and severity of side effects;
- potential advantages of alternative treatment methods;
- whether it is designated under physician treatment guidelines as a first, second or third line therapy;
- changes in the standard of care for targeted indications;

- limitations or warnings, including distribution or use restrictions, contained in the product's approved labeling;
- safety concerns with similar products marketed by others;
- the reluctance of the target population to try new therapies and of physicians to prescribe those therapies;

- the lack of success of our physician education programs; and
- ineffective sales, marketing and distribution support.

If IPI-549 received marketing approval but fails to achieve market acceptance, we would not be able to generate significant revenue, which may adversely impact our ability to become profitable.

Even if we receive regulatory approvals for marketing IPI-549 or other product candidates we may develop in the future, we could lose our regulatory approvals and our business would be adversely affected if we, our collaborators, or our contract manufacturers fail to comply with continuing regulatory requirements.

The FDA and other regulatory agencies continue to review products even after they receive initial approval. If we receive approval to commercialize any product candidates, the manufacturing, marketing and sale of these drugs will be subject to continuing regulation, including compliance with quality systems regulations, the FDA's current good manufacturing practices, or cGMPs, adverse event requirements and prohibitions on promoting a product for unapproved uses. Enforcement actions resulting from our failure to comply with government and regulatory requirements could result in fines, suspension of approvals, withdrawal of approvals, product recalls, product seizures, mandatory operating restrictions, criminal prosecution, civil penalties and other actions that could impair the manufacturing, marketing and sale of any product candidates and our ability to conduct our business.

If we are unable to establish sales, marketing and distribution capabilities or enter into sales, marketing and distribution arrangements with third parties, we may not be successful in commercializing any product candidates if approved.

We do not have a sales, marketing or distribution infrastructure and have no experience in the sale, marketing or distribution of pharmaceutical products. To achieve commercial success for any approved product, we must either develop a sales and marketing organization or outsource these functions to third parties. The development of sales, marketing and distribution capabilities would require substantial resources, would be time consuming and could delay any product launch. If the commercial launch of a product candidate for which we recruit a sales force and establish marketing and distribution capabilities is delayed or does not occur for any reason, we could have prematurely or unnecessarily incurred these commercialization costs. This may be costly, and our investment could be lost if we cannot retain or reposition our sales and marketing personnel. In addition, we may not be able to hire or retain a sales force in the United States that is sufficient in size or has adequate expertise in the medical markets that we choose to target. If we are unable to establish or retain a sales force and marketing and distribution capabilities, our operating results may be adversely affected. If a potential partner has development or commercialization expertise that we believe is particularly relevant to one of our products, then we may seek to collaborate with that potential partner even if we believe we could otherwise develop and commercialize the product independently.

As a result of entering into any such arrangements with third parties to perform sales, marketing and distribution services, our product revenues or the profitability of these product revenues may be lower, perhaps substantially lower, than if we were to directly market and sell products in those markets. Furthermore, we may be unsuccessful in entering into the necessary arrangements with third parties or may be unable to do so on terms that are favorable to us. In addition, we may have little or no control over such third parties, and any of them may fail to devote the necessary resources and attention to sell and market our products effectively.

If we do not establish sales, marketing and distribution capabilities, either on our own or in collaboration with third parties, we will not be successful in commercializing any of our product candidates that receive marketing approval.

Our competitors and potential competitors may develop products that make IPI-549 less attractive or obsolete.

Immuno-oncology is a highly competitive and rapidly changing segment of the pharmaceutical industry. Many large pharmaceutical and biotechnology companies, academic institutions, governmental agencies and other public and private research organizations are pursuing the development of novel drugs that target various oncology diseases. We currently face, and expect to continue to face, intense and increasing competition as new products enter the market and advanced technologies become available.

Our competitors may commence and complete clinical testing of their product candidates, obtain regulatory approvals and begin commercialization of their products sooner than we and/or our collaborators may for IPI-549. These competitive products may have superior safety or efficacy, have more attractive pharmacologic properties, or may be manufactured less expensively than IPI-549. Mergers and acquisitions in the pharmaceutical and biotechnology

industries may result in even more resources being concentrated among a smaller number of our competitors. Smaller or early stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies. 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, the development of 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 IPI-549 or achieve a competitive position in the market. This would adversely affect our ability to generate revenues.

Even if we, or any future collaborators, are able to commercialize IPI-549, the product may become subject to unfavorable pricing regulations, third-party payor reimbursement practices or healthcare reform initiatives, any of which could harm our business.

The commercial success of IPI-549 will depend substantially, both domestically and abroad, on the extent to which the costs of IPI-549 will be paid by third-party payors, including government health care programs and private health insurers. If coverage is not available, or reimbursement is limited, we, or any future collaborators, may not be able to successfully commercialize IPI-549. Even if coverage is provided, the approved reimbursement amount may not be high enough to allow us, or any future collaborators, to establish or maintain pricing sufficient to realize a sufficient return on our or their investments. In the United States, no uniform policy of coverage and reimbursement for products exists among third-party payors and coverage and reimbursement levels for products can differ significantly from payor to payor. As a result, the coverage determination process is often a time consuming and costly process that may require us to provide scientific and clinical support for the use of our products to each payor separately, with no assurance that coverage and adequate reimbursement will be applied consistently or obtained in the first instance.

There is significant uncertainty related to third-party payor coverage and reimbursement of newly approved drugs. Marketing approvals, pricing and reimbursement for new drug products vary widely from country to country. Some countries require approval of the sale price of a drug before it can be marketed. In many countries, the pricing review period begins after marketing or product licensing approval is granted. In some foreign markets, prescription pharmaceutical pricing remains subject to continuing governmental control even after initial approval is granted. As a result, we, or any future collaborators, might obtain marketing approval for a product in a particular country, but then be subject to price regulations that delay commercial launch of the product, possibly for lengthy time periods, which may negatively impact the revenues we are able to generate from the sale of the product in that country. Adverse pricing limitations may hinder our ability or the ability of any future collaborators to recoup our or their investment in IPI-549, even if IPI-549 obtains marketing approval.

Patients who are provided medical treatment for their conditions generally rely on third-party payors to reimburse all or part of the costs associated with their treatment. Therefore, our ability, and the ability of any future collaborators, to commercialize successfully IPI-549 will depend in part on the extent to which coverage and adequate reimbursement for IPI-549 and related treatments will be available from third-party payors. Third-party payors decide which medications they will cover and establish reimbursement levels. The healthcare industry is acutely focused on cost containment, both in the United States and elsewhere. Government authorities and other third-party payors have attempted to control costs by limiting coverage and the amount of reimbursement for particular medications, which could affect our ability or that of any future collaborators to sell IPI-549 profitably. These payors may not view IPI-549 as cost-effective, and coverage and reimbursement may not be available to our customers, or those of any future collaborators, or may not be sufficient to allow IPI-549 to be marketed on a competitive basis. Cost-control initiatives could cause us, or any future collaborators, to decrease the price we, or they, might establish for IPI-549, which could result in lower than anticipated product revenues. If the prices for IPI-549 decrease or if governmental and other third-party payors do not provide coverage or adequate reimbursement, our prospects for revenue and profitability will suffer.

There may also be delays in obtaining coverage and reimbursement for newly approved drugs, and coverage may be more limited than the indications for which the drug is approved by the FDA or comparable foreign regulatory authorities. Moreover, eligibility for reimbursement does not imply that any drug will be paid for in all cases or at a rate that covers our costs, including research, development, manufacture, sale and distribution. Reimbursement rates may vary, by way of example, according to the use of the product and the clinical setting in which it is used. Reimbursement rates may also be based on reimbursement levels already set for lower cost drugs or may be

incorporated into existing payments for other services.

In addition, increasingly, third-party payors are requiring higher levels of evidence of the benefits and clinical outcomes of new technologies and are challenging the prices charged. Further, the net reimbursement for drug products may be subject to additional reductions if there are changes to laws that presently restrict imports of drugs from countries where they may be sold at lower prices than in the United States. An inability to promptly obtain coverage and adequate payment rates from both government-funded and private payors for IPI-549 could significantly harm our operating results, our ability to raise capital needed to commercialize IPI-549 and our overall financial condition.

If the FDA or comparable foreign regulatory authorities approve generic versions of IPI-549 that receive marketing approval, or such authorities do not grant IPI-549 appropriate periods of data exclusivity before approving generic versions of IPI-549, the sales of IPI-549 could be adversely affected.

Once an NDA is approved, the product covered thereby becomes a "reference-listed drug" in the FDA's publication, "Approved Drug Products with Therapeutic Equivalence Evaluations," or the Orange Book. Manufacturers may seek approval of generic versions of reference-listed drugs through submission of abbreviated new drug applications, or ANDAs, in the United States. In support of an ANDA, a generic manufacturer need not conduct clinical trials. Rather, the applicant generally must show that its product has the same active ingredient(s), dosage form, strength, route of administration and conditions of use or labeling as the reference-listed drug and that the generic version is bioequivalent to the reference-listed drug, meaning it is absorbed in the body at the same rate and to the same extent. Generic products may be significantly less costly to bring to market than the reference-listed drug and companies that produce generic products are generally able to offer them at lower prices. Thus, following the introduction of a generic drug, a significant percentage of the sales of any branded product or reference-listed drug may be typically lost to the generic product.

The FDA may not approve an ANDA for a generic product until any applicable period of non-patent exclusivity for the reference-listed drug has expired. The Federal Food, Drug, and Cosmetic Act, or FDCA, provides a period of five years of non-patent exclusivity for a new drug containing a new chemical entity, or NCE. Specifically, in cases where such exclusivity has been granted, an ANDA may not be filed with the FDA until the expiration of five years unless the submission is accompanied by a Paragraph IV certification that a patent covering the reference-listed drug is either invalid or will not be infringed by the generic product, in which case the applicant may submit its application four years following approval of the reference-listed drug. When the composition of matter patents underlying our product candidates expire, it is possible that another applicant could obtain approval to produce generic versions of our product candidates. If any product we develop does not receive five years of NCE exclusivity, the FDA may approve generic versions of such product three years after its date of approval, subject to the requirement that the ANDA applicant certifies to any patents listed for our products in the Orange Book. Manufacturers may seek to launch these generic products following the expiration of the applicable marketing exclusivity period, even if we still have patent protection for our product.

We may have significant product liability exposure that may harm our business and our reputation.

We face exposure to significant product liability or other claims if IPI-549 is alleged to have caused harm. These risks are inherent in the testing, manufacturing and marketing of human medicinal products. Although we do not currently commercialize any products, claims could be made against us based on the use of IPI-549 or duvelisib in clinical trials. We currently have clinical trial insurance and will seek to obtain product liability insurance prior to the commercial launch of IPI-549. Our insurance may not, however, provide adequate coverage against potential liabilities. Furthermore, clinical trial and product liability insurance is becoming increasingly expensive. As a result, we may be unable to maintain current amounts of insurance coverage or obtain additional or sufficient insurance at a reasonable cost. If we are sued for any injury caused by IPI-549, our liability could exceed our insurance coverage and our total assets, and we would need to divert management attention to our defense. Claims against us, regardless of their merit or potential outcome, may also generate negative publicity or hurt our ability to recruit investigators and patients to our clinical trials, obtain physician acceptance of IPI-549, or expand our business.

Risks Related to Our Dependence on Third Parties

If a collaborator terminates or fails to perform its obligations under agreements with us, the development and commercialization of our product candidates could be delayed or terminated.

In October 2016, we entered into an exclusive license agreement with Verastem to develop and commercialize products based on duvelisib. We may in the future seek other third-party collaborators. The success of a strategic alliance with any partner is largely dependent on the resources, efforts, technology and skills brought to such alliance by such partner. The benefits of such alliances will be reduced or eliminated if any such partner:

- decides not to devote the necessary resources because of internal constraints, such as limited personnel with the requisite scientific or commercial expertise, limited cash resources or specialized equipment limitations;
-

decides not to pursue development and commercialization of the program or to continue or renew development or commercialization programs, based on clinical trial results, changes in the collaborators' strategic focus or available funding, the belief that other product candidates may have a higher likelihood of obtaining regulatory approval or potential to generate a greater return on investment, or external factors, such as an acquisition, that divert resources or create competing priorities;

- does not perform its obligations as expected;
- does not have sufficient resources necessary or is otherwise unable to carry the program through clinical development, regulatory approval and commercialization;
- cannot obtain the necessary regulatory approvals;
- delays clinical trials, provides insufficient funding for a clinical trial program, stops a clinical trial or abandons the program, repeats or conducts new clinical trials or requires a new formulation of the program for clinical testing;
- independently develops, or develops with third parties, products that compete directly or indirectly with the program;
- does not commit sufficient resources to the marketing and distribution of such product or products;
- does not properly maintain or defend our intellectual property rights or uses our proprietary information in such a way as to invite litigation that could jeopardize or invalidate our intellectual property or proprietary information or expose us to potential litigation;
- infringes the intellectual property rights of third parties, which may expose us to litigation and potential liability; or
- terminates the collaboration prior to its completion.

If such partner were to terminate its arrangements with us, as was the case with AbbVie Inc., or AbbVie, or breach such arrangements, or fail to maintain the financial resources necessary to continue financing its portion of development, manufacturing, and commercialization costs, as applicable, we may not have the financial resources or capabilities necessary to continue development and commercialization of the product candidate on our own. Consequently, the development and commercialization of the affected product candidate could be delayed, curtailed or terminated, and we may find it difficult to attract a new collaborator for such product candidate. For example, as a result of AbbVie's termination of our strategic collaboration, we are not entitled to receive payments for any milestone that was not achieved prior to AbbVie’s delivery to us of its termination notice, and neither party has any financial obligation to the other, other than pursuant to the wind-down plan.

Disputes and difficulties in these types of relationships are common, often due to priorities changing over time, conflicting priorities or conflicting interests. Merger and acquisition activity may exacerbate these conflicts. Much of the potential revenue from alliances consists of payments contingent upon the achievement of specified milestones and royalties payable on sales of any successfully developed drugs. Any such contingent revenue will depend upon our, and our collaborators’, ability to successfully develop, launch, market and sell new drugs. In some cases, we will not be involved in some or all of these processes, and we will depend entirely on our collaborators.

If any future collaborator fails to develop or effectively commercialize a product candidate that is the subject of our strategic alliance with them, we may not be able to develop and commercialize such product candidate independently, and our financial condition and operations would be negatively impacted.

We might seek to establish collaborations in the future and, if we are not able to establish them on commercially reasonable terms, we may have to alter our development and commercialization plans.

In the future, we might seek out one or more other collaborators for the development and commercialization of IPI-549. Likely collaborators may include large and mid-size pharmaceutical companies, regional and national pharmaceutical companies and biotechnology companies. In addition, if we are able to obtain marketing approval for IPI-549 from foreign regulatory authorities, we might enter into strategic relationships with international biotechnology or pharmaceutical companies for the commercialization of IPI-549 outside of the United States.

We would face significant competition in seeking appropriate collaborators. Whether we reach a definitive agreement for an additional collaboration will depend, among other things, upon our assessment of the collaborator’s resources and expertise, the terms and conditions of the proposed collaboration, and the proposed collaborator’s evaluation of a number of factors. Those factors may include the potential differentiation of IPI-549 from competing product candidates, design or results of clinical trials, the likelihood of approval by the FDA or comparable foreign regulatory authorities and the regulatory pathway for any such approval, the potential market for IPI-549, the costs and complexities of manufacturing and delivering the product to patients and the potential of competing products. The collaborator may also consider alternative product candidates or technologies for similar indications that may be available for collaboration and whether such a collaboration could be more attractive than the one with us for IPI-549.

38

Additional collaborations would be complex and time consuming to negotiate and document.

Any collaboration agreements that we enter into in the future may contain restrictions on our ability to enter into potential collaborations or to otherwise develop IPI-549.

Further, there have been a significant number of recent business combinations among large pharmaceutical companies that have resulted in a reduced number of potential future collaborators. We may not be able to negotiate collaborations on a timely basis, on acceptable terms, or at all. If we are unable to do so, we may have to curtail the development of IPI-549, reduce or delay its development, delay its potential commercialization or reduce the scope of any sales or marketing activities, or increase our expenditures and undertake development or commercialization activities at our own expense.

We rely on third parties to conduct our clinical trials, and those third parties may not perform satisfactorily.

We rely on third parties such as contract research organizations, medical institutions and external investigators to enroll qualified patients, conduct our clinical trials and provide services in connection with such clinical trials, and we intend to rely on these and other similar entities in the future. Our reliance on these third parties for clinical development activities reduces our control over these activities. Accordingly, these third-party contractors may not complete activities on schedule, or may not conduct our clinical trials in accordance with regulatory requirements or the trial design. If these third parties do not successfully carry out their contractual obligations or meet expected deadlines, we may be required to replace them. Replacing a third-party contractor may result in a delay of the affected trial and unplanned costs. If this were to occur, our ability to obtain regulatory approval for and to commercialize IPI-549 could be delayed.

In addition, we are responsible for ensuring that each of our clinical trials is conducted in accordance with the general investigational plan and protocol for the trial. The FDA requires us to comply with certain standards, referred to as good clinical practices, for conducting, recording and reporting the results of clinical trials to assure that data and reported results are credible and accurate and that the rights, integrity and confidentiality of trial participants are protected. Our reliance on third parties that we do not control does not relieve us of these responsibilities and requirements. If any of our trial investigators or third-party contractors does not comply with good clinical practices, we may not be able to use the data and reported results from the trial. If this noncompliance were to occur, our ability to obtain regulatory approval for and to commercialize IPI-549 could be delayed.

We currently rely on third-party manufacturers to produce our preclinical and clinical drug supplies, and we may also rely upon third-party manufacturers to produce commercial supplies of IPI-549.

IPI-549 requires precise, high quality manufacturing. The third-party manufacturers on which we rely may not be able to comply with cGMPs, and other applicable government regulations and corresponding foreign standards. These regulations govern manufacturing processes and procedures and the implementation and operation of systems to control and assure the quality of products. The FDA and foreign regulatory authorities may, at any time, audit or inspect a manufacturing facility to ensure compliance with cGMPs and other quality standards. Any failure by our contract manufacturers to achieve and maintain high manufacturing and quality control standards could result in the inability of IPI-549 to be released for use in one or more countries. In addition, such a failure could result in, among other things, patient injury or death, product liability claims, penalties or other monetary sanctions, the failure of regulatory authorities to grant marketing approval of IPI-549, delays, suspension or withdrawal of approvals, license revocation, seizures or recalls of IPI-549, operating restrictions and/or criminal prosecution, any of which could significantly and adversely affect supply of IPI-549 and seriously hurt our business.

Contract manufacturers may also encounter difficulties involving production yields or delays in performing their services. We do not have control over third-party manufacturers' performance and compliance with applicable regulations and standards. If, for any reason, our manufacturers cannot perform as agreed, we may be unable to replace such third-party manufacturers in a timely manner, and the production of IPI-549 would be interrupted, resulting in delays in clinical trials and additional costs. Switching manufacturers may be difficult because the number of potential manufacturers is limited, the demand for such services is high and, depending on the type of material manufactured at the contract facility, the change in contract manufacturer must be submitted to and/or approved by the FDA and comparable regulatory authorities outside of the United States. In addition, a new manufacturer would have to be educated in, or develop substantially equivalent processes for, production of our product candidates after receipt

of regulatory approval. It may be difficult or impossible for us to find a replacement manufacturer on acceptable terms quickly, or at all.

To date, IPI-549 has been manufactured for preclinical testing and clinical trials primarily by third-party manufacturers. If the FDA or other regulatory agencies approve IPI-549 for commercial sale, we expect that we would continue to rely, at least initially, on third-party manufacturers to produce commercial quantities of IPI-549. These manufacturers may not be able to successfully increase the manufacturing capacity for IPI-549 in a timely or economical manner, or at all. Significant scale-up of manufacturing might entail changes in the manufacturing process that have to be submitted to or

approved by the FDA or other regulatory agencies. If contract manufacturers engaged by us are unable to successfully increase the manufacturing capacity for IPI-549, or we are unable to establish our own manufacturing capabilities, the commercial launch of any approved products may be delayed or there may be a shortage in supply.

Risks Related to Our Intellectual Property

If we fail to obtain or maintain necessary or useful intellectual property rights, we could encounter substantial delays in the research, development and commercialization of IPI-549.

We currently have rights to certain intellectual property, through licenses from third parties, to develop IPI-549 and other product candidates that we may in the future develop under our PI3K inhibitor program. In addition, we have rights to certain intellectual property, through licenses from third parties, that we have exclusively licensed to Verastem to research, develop, manufacture and commercialize duvelisib. We may decide to license additional third-party technology that we deem necessary or useful for our development of IPI-549. However, we may be unable to acquire or in-license any compositions, methods of use, processes or other intellectual property rights from third parties that we identify as necessary for IPI-549 at a reasonable cost, or at all. The licensing or acquisition of third-party intellectual property rights is a competitive area, and several more established companies may pursue strategies to license or acquire third-party intellectual property rights that we may consider attractive. These established companies may have a competitive advantage over us due to their size, capital resources and greater clinical development and commercialization capabilities. In addition, companies that perceive us to be a competitor may be unwilling to assign or license rights to us.

We sometimes collaborate with non-profit and academic institutions to accelerate our preclinical research or development under written agreements with these institutions. Typically, these institutions provide us with an option to negotiate a license to any of the institution's rights in technology resulting from the collaboration. Regardless of such option, we may be unable to negotiate a license within the specified timeframe or under terms that are acceptable to us or we may decide not to execute such option if we believe such license is not necessary to pursue our program. If we are unable or opt not to do so, the institution may offer the intellectual property rights to other parties, potentially blocking our ability to pursue our program.

If we do not obtain or maintain these intellectual property rights which we require, we could encounter substantial delays in developing and commercializing IPI-549 while we attempt to develop alternative technologies, methods and product candidates, which we may not be able to accomplish. If we are ultimately unable to do so, we may be unable to develop or commercialize IPI-549, which could harm our business significantly.

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

We are party to several license agreements under which we license patent rights and other intellectual property related to our business, including an amended and restated development and license agreement with Takeda under which we obtained rights to discover, develop and commercialize pharmaceutical products targeting the delta and/or gamma isoforms of PI3K, including IPI-549 and duvelisib. We may enter into additional license agreements in the future. Our license agreements impose, and we expect that future license agreements will impose, various diligence, milestone payment, royalty, insurance and other obligations on us. If we fail to comply with our obligations under these licenses, our licensors may have the right to terminate these license agreements, in which event we might not be able to market IPI-549 that is covered by these agreements, or our licensors may convert the license to a non-exclusive license, which could adversely affect the value of IPI-549 being developed under the license agreement. Termination of these license agreements or reduction or elimination of our licensed rights may also result in our having to negotiate new or reinstated licenses with less favorable terms. If we fail to use diligent efforts to develop and commercialize products licensed under the Takeda Agreement, for example, or if Verastem materially breaches the Verastem Agreement, we could lose our license rights under the Takeda Agreement, including rights to IPI-549.

Our intellectual property licenses with third parties may be subject to disagreements over contract interpretations, which could narrow the scope of our rights to the relevant intellectual property or technology or increase our financial or other obligations to our licensors.

The agreements under which we currently license intellectual property or technology from third parties are complex, and certain provisions in such agreements may be susceptible to multiple interpretations. The resolution of any contract interpretation disagreement that may arise could narrow what we believe to be the scope of our rights to the relevant intellectual property or technology, or increase what we believe to be our financial or other obligations under the relevant agreement, either of which could harm our business, financial condition, results of operations and prospects.

Our success depends substantially upon our ability to obtain and maintain intellectual property protection for IPI-549. We own or hold exclusive licenses to a number of U.S. and foreign patents and patent applications directed to IPI-549. Our success depends on our ability to obtain patent protection both in the United States and in other countries for IPI-549, our methods of manufacture and our methods of use. Our ability to protect IPI-549 from unauthorized or infringing use by third parties depends substantially on our ability to obtain and enforce our patents.

Due to evolving legal standards relating to the patentability, validity and enforceability of patents covering pharmaceutical inventions and molecular diagnostics and the claim scope of these patents, our ability to obtain and enforce patents that may issue from any pending or future patent applications is uncertain and involves complex legal, scientific and factual questions. The standards that the United States Patent and Trademark Office, or USPTO, and its foreign counterparts use to grant patents are not always applied predictably or uniformly and are subject to change. To date, no consistent policy has emerged regarding the breadth of claims allowed in pharmaceutical or molecular diagnostics patents. Thus, we cannot guarantee that any patents will issue from any pending or future patent applications owned by or licensed to us. Even if patents do issue, we cannot guarantee that the claims of these patents will be held valid or enforceable by a court of law, will provide us with any significant protection against competitive products or will afford us a commercial advantage over competitive products.

The U.S. Congress passed the Leahy-Smith America Invents Act, or the America Invents Act, which became effective in March 2013. The America Invents Act reforms United States patent law in part by changing the standard for patent approval for certain patents from a “first to invent” standard to a “first to file” standard and developing a post-grant review system. This new law changes United States patent law in a way that may severely weaken our ability to obtain patent protection in the United States. Additionally, recent judicial decisions establishing new case law and a reinterpretation of past case law, as well as regulatory initiatives, may make it more difficult for us to protect our intellectual property. Issued patents that we have or may obtain or license may not provide us with any meaningful protection, prevent competitors from competing with us or otherwise provide us with any competitive advantage. Our competitors may be able to circumvent our patents by developing similar or alternative technologies or products in a non-infringing manner.

If we do not obtain adequate intellectual property protection for our products in the United States, competitors could duplicate them without repeating the extensive testing that we will have been required to undertake to obtain approval by the FDA. Regardless of any patent protection, under the current statutory framework, the FDA is prohibited by law from approving any generic version of any of our products for up to five years after it has approved our product. Upon the expiration of that period, or if that time period is altered, the FDA could approve a generic version of our product unless we have patent protection sufficient for us to block that generic version. Without sufficient patent protection, the applicant for a generic version of our product would only be required to conduct a relatively inexpensive study to show that its product is bioequivalent to our product and would not have to repeat the studies that we conducted to demonstrate that the product is safe and effective.

In the absence of adequate patent protection in other countries, competitors may similarly be able to obtain regulatory approval in those countries for products that duplicate IPI-549. The laws of some foreign jurisdictions do not protect intellectual property rights to the same extent as in the United States. Many companies have encountered significant difficulties in protecting and defending such rights in foreign jurisdictions. Some of our development efforts may be performed in China, India and other countries outside of the United States through third-party contractors. We may not be able to monitor and assess intellectual property developed by these contractors effectively; therefore, we may not be able to appropriately protect this intellectual property and could lose valuable intellectual property rights. In addition, the legal protection afforded to inventors and owners of intellectual property in countries outside of the United States may not be as protective of intellectual property rights as in the United States, and we may, therefore, be unable to acquire and protect intellectual property developed by these contractors to the same extent as if these development activities were being conducted in the United States. If we encounter difficulties in protecting our intellectual property rights in foreign jurisdictions, our business prospects could be substantially harmed.

In addition, we rely on intellectual property assignment agreements with our collaborators, vendors, employees, consultants, clinical investigators, scientific advisors and other collaborators to grant us ownership of new intellectual property that is developed by them. These agreements may not result in the effective assignment to us of that

intellectual property.

Other agreements through which we license patent rights may not give us control over patent prosecution or maintenance, so that we may not be able to control which claims or arguments are presented and may not be able to secure, maintain, or successfully enforce necessary or desirable patent protection from those patent rights. If we are unable to obtain control over patent prosecution in these other agreements, we cannot be certain that patent prosecution and maintenance activities by our licensors have been or will be conducted in compliance with applicable laws and regulations or will result in valid and enforceable patents.

We, or any future partners, collaborators or licensees, may fail to identify patentable aspects of inventions made in the course of development and commercialization activities before it is too late to obtain patent protection for them. Therefore, we may miss potential opportunities to strengthen our patent position.

It is possible that defects of form in the preparation or filing of our patents or patent applications may exist, or may arise in the future, for example with respect to proper priority claims, inventorship, claim scope or patent term adjustments. If we or our partners, collaborators, licensees, or licensors, whether current or future, fail to establish, maintain or protect such patents and other intellectual property rights, such rights may be reduced or eliminated. If our partners, collaborators, licensees or licensors, are not fully cooperative or disagree with us as to the prosecution, maintenance or enforcement of any patent rights, such patent rights could be compromised. If there are material defects in the form, preparation, prosecution, or enforcement of our patents or patent applications, such patents may be invalid and/or unenforceable, and such applications may never result in valid, enforceable patents. Any of these outcomes could impair our ability to prevent competition from third parties, which may have an adverse impact on our business. As a result, our ownership of key intellectual property could be compromised.

Confidentiality agreements may not adequately prevent disclosure of trade secrets and other proprietary information.

To protect our proprietary technology, we rely in part on confidentiality agreements with our vendors, collaborators, employees, consultants, scientific advisors, clinical investigators and other collaborators. We generally require each of these individuals and entities to execute a confidentiality agreement at the commencement of a relationship with us. These agreements may not effectively prevent disclosure of confidential information and may not provide an adequate remedy in the event of unauthorized disclosure or misuse of confidential information or other breaches of the agreements.

In addition, we may rely on trade secrets to protect our technology, especially where we do not believe patent protection is appropriate or obtainable. Trade secrets are, however, difficult to protect. Others may independently discover our trade secrets and proprietary information, and in such case we could not assert any trade secret rights against such party. Enforcing a claim that a party illegally obtained and is using our trade secrets is difficult, expensive and time consuming, and the outcome is unpredictable. In addition, courts outside of the United States may be less willing to protect trade secrets. Costly and time-consuming litigation could be necessary to seek to enforce and determine the scope of our proprietary rights and could result in a diversion of management's attention, and failure to obtain or maintain trade secret protection could adversely affect our competitive business position.

Patent interference, opposition or similar proceedings relating to our intellectual property portfolio are costly, and an unfavorable outcome could prevent us from commercializing IPI-549.

Patent applications in the United States are maintained in confidence for up to 18 months after their filing. In some cases, however, patent applications remain confidential in the USPTO for the entire time prior to issuance as a U.S. patent. Similarly, publication of discoveries in the scientific or patent literature often lags behind actual discoveries. Consequently, we cannot be certain that we were the first to invent, or the first to file patent applications on, IPI-549 or its therapeutic use. In the event that a third party has also filed a U.S. patent application relating to IPI-549 or a similar invention, we may have to participate in interference or derivation proceedings declared by the USPTO or the third party to determine priority of invention in the United States. An adverse decision in an interference or derivation proceeding may result in the loss of rights under a patent or patent application. In addition, the cost of interference proceedings could be substantial.

Claims by third parties of intellectual property infringement are costly and distracting, and could deprive us of valuable rights we need to develop or commercialize IPI-549.

Our commercial success will depend on whether there are third-party patents or other intellectual property relevant to our potential products that may block or hinder our ability to develop and commercialize IPI-549. We may not have identified all U.S. and foreign patents or published applications that may adversely affect our business either by blocking our ability to manufacture or commercialize our drugs or by covering similar technologies that adversely affect the applicable market. In addition, we may undertake research and development with respect to IPI-549, even when we are aware of third-party patents that may be relevant to IPI-549, on the basis that we may challenge or license such patents. There are no assurances that such licenses will be available on commercially reasonable terms, or at all. If such licenses are not available, we may become subject to patent litigation and, while we cannot predict the

outcome of any litigation, it may be expensive and time consuming. If we are unsuccessful in litigation concerning patents owned by third parties, we may be precluded from selling IPI-549.

While we are not currently aware of any litigation or third-party claims of intellectual property infringement related to IPI-549, the biopharmaceutical industry is characterized by extensive litigation regarding patents and other intellectual property rights. Other parties may obtain patents and claim that the use of our technologies infringes these patents or that we are

employing their proprietary technology without authorization. We could incur substantial costs and diversion of management and technical personnel in defending against any claims that the manufacture and sale of our potential products or use of our technologies infringes any patents, or defending against any claim that we are employing any proprietary technology without authorization. The outcome of patent litigation is subject to uncertainties that cannot be adequately quantified in advance, including the demeanor and credibility of witnesses and the identity of the adverse party, especially in pharmaceutical patent cases that may turn on the testimony of experts as to technical facts upon which experts may reasonably disagree. In the event of a successful claim of infringement against us, we may be required to:

- pay substantial damages;
- stop developing, manufacturing and/or commercializing IPI-549;
- develop non-infringing product candidates, technologies and methods; and
- obtain one or more licenses from other parties, which could result in our paying substantial royalties or the granting of cross-licenses to our technologies.

If any of the foregoing were to occur, we may be unable to commercialize IPI-549, or we may elect to cease certain of our business operations, either of which could severely harm our business.

We may undertake infringement or other legal proceedings against third parties, causing us to spend substantial resources on litigation and exposing our own intellectual property portfolio to challenge.

Competitors may infringe our patents. To prevent infringement or unauthorized use, we may need to file infringement suits, which are expensive and time-consuming. In an infringement proceeding, a court may decide that one or more of our patents is invalid, unenforceable, or both. Even if the validity of our patents is upheld, a court may refuse to stop the other party from using the technology at issue on the ground that the other party's activities are not covered by our patents. In this case, third parties may be able to use our patented technology without paying licensing fees or royalties. Policing unauthorized use of our intellectual property is difficult, and we may not be able to prevent misappropriation of our proprietary rights, particularly in countries where the laws may not protect such rights as fully as in the United States. In addition, third parties may affirmatively challenge our rights to, or the scope or validity of, our patent rights.

Patent terms may be inadequate to protect our competitive position on our products for an adequate amount of time. Given the amount of time required for the development, testing and regulatory review of new product candidates, patents protecting such candidates might expire before or shortly after such candidates are commercialized. We expect to seek extensions of patent terms in the United States and, if available, in other countries where we are prosecuting patents. In the United States, the Drug Price Competition and Patent Term Restoration Act of 1984 permits a patent term extension of up to five years beyond the normal expiration of the patent, which is limited to the approved indication (or any additional indications approved during the period of extension). However, the applicable authorities, including the FDA and the USPTO in the United States, and any equivalent regulatory authority in other countries, may not agree with our assessment of whether such extensions are available, and may refuse to grant extensions to our patents, or may grant more limited extensions than we request. If this occurs, our competitors may be able to take advantage of our investment in development and clinical trials by referencing our clinical and preclinical data and launch their product earlier than might otherwise be the case.

We may be subject to claims by third parties asserting that our employees or we have misappropriated their intellectual property, or claiming ownership of what we regard as our own intellectual property.

Many of our employees and our licensors' employees, including our senior management, were previously employed at universities or at other biotechnology or pharmaceutical companies, some of which may be competitors or potential competitors. Some of these employees, including each member of our senior management, executed proprietary rights, non-disclosure and non-competition agreements, or similar agreements, in connection with such previous employment. Although we try to ensure that our employees do not use the proprietary information or know-how of others in their work for us, we may be subject to claims that we or these employees have used or disclosed intellectual property, including trade secrets or other proprietary information, of any such third party. Litigation may be necessary to defend against such claims. If we fail in defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights or personnel or sustain damages. Such intellectual property rights could

be awarded to a third party, and we could be required to obtain a license from such third party to commercialize our technology or products. Such a license may not be available on commercially reasonable terms or at all. Even if we are successful in defending against such claims, litigation could result in substantial costs and be a distraction to management.

In addition, while we typically require our employees, consultants and contractors who may be involved in the development of intellectual property to execute agreements assigning such intellectual property to us, we may be unsuccessful

in executing such an agreement with each party who in fact develops intellectual property that we regard as our own, which may result in claims by or against us related to the ownership of such intellectual property. If we fail in prosecuting or defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights. Even if we are successful in prosecuting or defending against such claims, litigation could result in substantial costs and be a distraction to our senior management and scientific personnel.

Obtaining and maintaining our patent protection depends on compliance with various procedural, document submission, fee payment and other requirements imposed by governmental patent agencies, and our patent protection could be reduced or eliminated for non-compliance with these requirements.

The USPTO and various foreign governmental patent agencies require compliance with a number of procedural, documentary, fee payment and other provisions during the patent process. There are situations in which non-compliance can result in abandonment or lapse of a patent or patent application, resulting in partial or complete loss of patent rights in the relevant jurisdiction. If we fail to comply with these requirements, competitors might be able to enter the market earlier than would otherwise have been the case, which could decrease our revenue from that product.

Risks Related to Regulatory Approval and Marketing of IPI-549 and Other Legal Compliance Matters

Even if we complete the necessary preclinical studies and clinical trials, the regulatory approval process is expensive, time-consuming and uncertain and may prevent us from obtaining approvals for the commercialization of IPI-549. If we or our collaborators are not able to obtain, or if there are delays in obtaining, required regulatory approvals, we or they will not be able to commercialize IPI-549, and our ability to generate revenue will be materially impaired.

IPI-549 and the activities associated with its development and commercialization, including its design, testing, manufacture, safety, efficacy, record keeping, labeling, storage, approval, advertising, promotion, sale and distribution, export and import, are subject to comprehensive regulation by the FDA and other regulatory agencies in the United States and by the European Medicines Agency and comparable regulatory authorities in other countries. Failure to obtain marketing approval for IPI-549 will prevent us from commercializing IPI-549. We and our collaborators have not received approval to market IPI-549 from regulatory authorities in any jurisdiction. We have only limited experience in filing and supporting the applications necessary to gain marketing approvals and expect to rely on third-party contract research organizations to assist us in this process.

Securing marketing approval requires the submission of extensive preclinical and clinical data and supporting information to the various regulatory authorities for each therapeutic indication to establish the product candidate’s safety and efficacy. Securing regulatory approval also requires the submission of information about the product manufacturing process to, and inspection of manufacturing facilities by, the relevant regulatory authority. IPI-549 may not be effective, may be only moderately effective or may prove to have undesirable or unintended side effects, toxicities or other characteristics that may preclude our obtaining marketing approval or prevent or limit commercial use.

The process of obtaining marketing approvals, both in the United States and abroad, is expensive, may take many years if additional clinical trials are required, if approval is obtained at all, and can vary substantially based upon a variety of factors, including the type, complexity and novelty of the product candidates involved. Changes in marketing approval policies during the development period, changes in or the enactment of additional statutes or regulations, or changes in regulatory review for each submitted product application, may cause delays in the approval or rejection of an application. The FDA and comparable authorities in other countries have substantial discretion in the approval process and may refuse to accept any application or may decide that our data is insufficient for approval and require additional preclinical, clinical or other studies. In addition, varying interpretations of the data obtained from preclinical and clinical testing could delay, limit or prevent marketing approval of IPI-549. Any marketing approval we or our collaborators ultimately obtain may be limited or subject to restrictions or post-approval commitments that render the approved product not commercially viable.

Accordingly, if we or our collaborators experience delays in obtaining approval or if we or they fail to obtain approval of IPI-549, the commercial prospects for IPI-549 may be harmed, and our ability to generate revenues will be materially impaired.

Failure to obtain marketing approval in foreign jurisdictions would prevent IPI-549 from being marketed in such jurisdictions.

In order to market and sell our medicines in the European Union and many other jurisdictions, we or our third party collaborators must obtain separate marketing approvals and comply with numerous and varying regulatory requirements. The approval procedure varies among countries and can involve additional testing. The time required to obtain approval may differ substantially from that required to obtain FDA approval. The regulatory approval process outside the United States generally

includes all of the risks associated with obtaining FDA approval. In addition, in many countries outside the United States, a product must be approved for reimbursement before the product can be approved for sale in that country. We or our third party collaborators may not obtain approvals from regulatory authorities outside the United States on a timely basis, if at all. Approval by the FDA does not ensure approval by regulatory authorities in other countries or jurisdictions, and approval by one regulatory authority outside the United States does not ensure approval by regulatory authorities in other countries or jurisdictions or by the FDA. We may not be able to file for marketing approvals and may not receive necessary approvals to commercialize IPI-549 in any market.

Even if we or our collaborators obtain marketing approvals for IPI-549, the terms of approvals and ongoing regulation of IPI-549 may limit how we manufacture and market IPI-549, which could impair our ability to generate revenue.

Once marketing approval has been granted, an approved product and its manufacturer and marketer are subject to ongoing review and extensive regulation. We, and any collaborators, must therefore comply with requirements concerning advertising and promotion for IPI-549. Promotional communications with respect to prescription drugs are subject to a variety of legal and regulatory restrictions and must be consistent with the information in the product's approved labeling. Thus, we and any collaborators will not be able to promote any products we develop for indications or uses for which they are not approved.

In addition, manufacturers of approved products and those manufacturers' facilities are required to comply with extensive FDA requirements, including ensuring that quality control and manufacturing procedures conform to cGMPs applicable to drug manufacturers or quality assurance standards applicable to medical device manufacturers, which include requirements relating to quality control and quality assurance as well as the corresponding maintenance of records and documentation and reporting requirements. We, any contract manufacturers we may engage in the future, our current or future collaborators and their contract manufacturers will also be subject to other regulatory requirements, including submissions of safety and other post-marketing information and reports, registration and listing requirements, requirements regarding the distribution of samples to physicians, recordkeeping, and costly post-marketing studies or clinical trials and surveillance to monitor the safety or efficacy of the product such as the requirement to implement a risk evaluation and mitigation strategy.

Accordingly, assuming we, or any of our collaborators, receive marketing approval for IPI-549, we, our collaborators, and our and their contract manufacturers will continue to expend time, money and effort in all areas of regulatory compliance, including manufacturing, production, product surveillance and quality control.

If we, and any collaborators, are not able to comply with post-approval regulatory requirements, we, and our collaborators, could have the marketing approvals for our products withdrawn by regulatory authorities and our, or any collaborators', ability to market any future products could be limited, which could adversely affect our ability to achieve or sustain profitability. Further, the cost of compliance with post-approval regulations may have a negative effect on our operating results and financial condition.

IPI-549 could be subject to restrictions or withdrawal from the market and we may be subject to substantial penalties if we fail to comply with regulatory requirements or if we experience unanticipated problems with IPI-549, when and if it is approved.

Any product candidate for which we or our collaborators obtain marketing approval, along with the manufacturing processes, post-approval clinical data, labeling, advertising and promotional activities for such product, will be subject to continual requirements of and review by the FDA and other regulatory authorities. These requirements include submissions of safety and other post-marketing information and reports, registration and listing requirements, cGMP requirements relating to quality control and manufacturing, quality assurance and corresponding maintenance of records and documents, and requirements regarding the distribution of samples to physicians and recordkeeping. Even if marketing approval of IPI-549 is granted, the approval may be subject to limitations on the indicated uses for which the product may be marketed or to the conditions of approval, or contain requirements for costly post-marketing testing and surveillance to monitor the safety or efficacy of the medicine, including the requirement to implement a risk evaluation and mitigation strategy.

The FDA and other agencies, including the Department of Justice, or the DOJ, closely regulate and monitor the post-approval marketing and promotion of products to ensure that they are marketed and distributed only for the approved indications and in accordance with the provisions of the approved labeling. The FDA and DOJ impose

stringent restrictions on manufacturers' communications regarding off-label use and if we do not market our products for their approved indications, we may be subject to enforcement action for off-label marketing. Violations of the Federal Food, Drug, and Cosmetic Act and other statutes, including the False Claims Act, relating to the promotion and advertising of prescription drugs may lead to investigations and enforcement actions alleging violations of federal and state health care fraud and abuse laws, as well as state consumer protection laws.

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

- restrictions on such products, manufacturers or manufacturing processes;
- restrictions on the labeling or marketing of a product;
- restrictions on distribution or use of a product;
- requirements to conduct post-marketing studies or clinical trials;
- warning letters or untitled letters;
- withdrawal of the products from the market;
- refusal to approve pending applications or supplements to approved applications that we submit;
- recall of products;
- damage to relationships with any potential collaborators;
- unfavorable press coverage and damage to our reputation;
- fines, restitution or disgorgement of profits or revenues;
- suspension or withdrawal of marketing approvals;
- refusal to permit the import or export of our products;
- product seizure;
- injunctions or the imposition of civil or criminal penalties; and
- litigation involving patients using our products.

Non-compliance with European Union requirements regarding safety monitoring or pharmacovigilance, and with requirements related to the development of products for the pediatric population, can also result in significant financial penalties. Similarly, failure to comply with the European Union's requirements regarding the protection of personal information can also lead to significant penalties and sanctions.

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

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

- the federal Anti-Kickback Statute prohibits, among other things, persons from knowingly and willfully soliciting, offering, receiving or providing remuneration, directly or indirectly, in cash or in kind, to induce or reward, or in return for, either the referral of an individual for, or the purchase, order or recommendation or arranging of, any good or service, for which payment may be made under a federal healthcare program such as Medicare and Medicaid;
- the federal False Claims Act imposes criminal and civil penalties, including through civil whistleblower or qui tam actions, against individuals or entities for, among other things, knowingly presenting, or causing to be presented, false or fraudulent claims for payment by a federal healthcare program or making a false statement or record material to payment of a false claim or avoiding, decreasing or concealing an obligation to pay money to the federal government, with potential liability including mandatory treble damages and significant per-claim penalties, currently set at $5,500 to $11,000 per false claim;
- the federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, imposes criminal and civil liability for executing a scheme to defraud any healthcare benefit program or making false statements relating to healthcare matters;
- HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act and its implementing regulations, also imposes obligations, including mandatory contractual terms, with respect to safeguarding the privacy, security and transmission of individually identifiable health information;

46

- the federal Physician Payments Sunshine Act requires applicable manufacturers of covered drugs to report payments and other transfers of value to physicians and teaching hospitals; and
- analogous state and foreign laws and regulations, such as state anti-kickback and false claims laws and transparency statutes, may apply to sales or marketing arrangements and claims involving healthcare items or services reimbursed by non-governmental third party payors, including private insurers.

Some state laws require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government and may require drug manufacturers to report information related to payments and other transfers of value to physicians and other healthcare providers or marketing expenditures. State and foreign laws also govern the privacy and security of health information in some circumstances, many of which differ from each other in significant ways and often are not preempted by HIPAA, thus complicating compliance efforts.

If our operations are found to be in violation of any of the laws described above or any governmental regulations that apply to us, we may be subject to penalties, including civil and criminal penalties, damages, fines and the curtailment or restructuring of our operations. Any penalties, damages, fines, curtailment or restructuring of our operations could adversely affect our financial results. We are developing and implementing a corporate compliance program designed to ensure that we will market and sell any future products that we successfully develop from our product candidates in compliance with all applicable laws and regulations, but we cannot guarantee that this program will protect us from governmental investigations or other actions or lawsuits stemming from a failure to be in compliance with such laws or regulations. If any such actions are instituted against us and we are not successful in defending ourselves or asserting our rights, those actions could have a significant impact on our business, including the imposition of significant fines or other sanctions.

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

Current and future legislation may increase the difficulty and cost for us and any collaborators to obtain marketing approval of IPI-549 and affect the price we, or they, may obtain.

In the United States and some foreign jurisdictions, there have been a number of legislative and regulatory changes and proposed changes regarding the healthcare system that could, among other things, prevent or delay marketing approval of IPI-549, restrict or regulate post-approval activities and affect our ability, or the ability of any collaborators, to profitably sell any products for which we, or they, obtain marketing approval. We expect that current laws, as well as other healthcare reform measures that may be adopted in the future, may result in more rigorous coverage criteria and in additional downward pressure on the price that we, or any collaborators, may receive for any approved products.

For example, in March 2010, President Obama signed into law the Patient Protection and Affordable Care Act, as amended by the Health Care Education Reconciliation Act, or the ACA. Among the provisions of the ACA of potential importance to our business and IPI-549 are the following:

- an annual, non-deductible fee on any entity that manufactures or imports specified branded prescription drugs and biologic agents;
- an increase in the statutory minimum rebates a manufacturer must pay under the Medicaid Drug Rebate Program;
- a new methodology by which rebates owed by manufacturers under the Medicaid Drug Rebate Program are calculated for drugs that are inhaled, infused, instilled, implanted or injected;
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expansion of healthcare fraud and abuse laws, including the civil False Claims Act and the federal Anti-Kickback Statute, new government investigative powers and enhanced penalties for noncompliance;

- a new Medicare Part D coverage gap discount program, in which manufacturers must agree to offer 50% point-of-sale discounts off negotiated prices of applicable brand drugs to eligible beneficiaries during their coverage gap period, as a condition for the manufacturer's outpatient drugs to be covered under Medicare Part D;

- extension of manufacturers' Medicaid rebate liability to individuals enrolled in Medicaid managed care organizations;
- expansion of eligibility criteria for Medicaid programs;
- expansion of the entities eligible for discounts under the Public Health Service pharmaceutical pricing program;
- new requirements to report certain financial arrangements with physicians and teaching hospitals;
- a new requirement to annually report drug samples that manufacturers and distributors provide to physicians;
- a new Patient-Centered Outcomes Research Institute to oversee, identify priorities in, and conduct comparative clinical effectiveness research, along with funding for such research;
- a new Independent Payment Advisory Board, or IPAB, which has authority to recommend certain changes to the Medicare program to reduce expenditures by the program that could result in reduced payments for prescription drugs; and
- established the Center for Medicare and Medicaid Innovation within CMS to test innovative payment and service delivery models.

Other legislative changes have been proposed and adopted since the ACA was enacted. These changes include the Budget Control Act of 2011, which, among other things, led to aggregate reductions to Medicare payments to providers of up to 2% per fiscal year that started in 2013 and, due to subsequent legislation, will continue until 2025. In addition, the American Taxpayer Relief Act of 2012, among other things, reduced Medicare payments to several providers and increased the statute of limitations period for the government to recover overpayments to providers from three to five years. Moreover, the Medicare Access and CHIP Reauthorization Act of 2015, among other things, introduced the Quality Payment Program under which Medicare physicians will be required to either participate in an Advanced Alternative Payment Model, or AAPM, and assume some risk for patient outcomes, or participate in the Merit-Based Incentive Payment System, or MIPS, which will provide an incentive compensation structure that will rate physicians in part based on cost of services. These new laws may result in additional reductions in Medicare and other healthcare funding and otherwise affect the prices we may obtain for any of our product candidates for which we may obtain regulatory approval or the frequency with which any such product candidate is prescribed or used.

We expect that the ACA, as well as other healthcare reform measures that may be adopted in the future, may result in additional reductions in Medicare and other healthcare funding, more rigorous coverage criteria, new payment methodologies and additional downward pressure on the price that we receive for any approved product and/or the level of reimbursement physicians receive for administering any approved product we might bring to market. Reductions in reimbursement levels may negatively impact the prices we receive or the frequency with which our products are prescribed or administered. Any reduction in reimbursement from Medicare or other government programs may result in a similar reduction in payments from private payors.

In addition, with the new Administration and Congress, there will likely be additional legislative changes, including repeal and replacement of certain provisions of the ACA. It remains to be seen, however, precisely what the new legislation will provide, when it will be enacted and what impact it will have on the availability of healthcare and containing or lowering the cost of healthcare. Such reforms could have an adverse effect on anticipated revenue from product candidates that we may successfully develop and for which we may obtain marketing approval and may affect our overall financial condition and ability to develop or commercialize product candidates. For example, the President and congressional leaders have expressed interest in repealing certain ACA provisions and replacing them with alternatives that may be less costly and provide state Medicaid programs and private health plans more flexibility. It is possible that these repeal and replacement initiatives, if enacted into law, could ultimately result in fewer individuals having health insurance coverage or in individuals having insurance coverage with less generous benefits. The scope of potential future legislation to repeal and replace ACA provisions is highly uncertain in many respects, and it is possible that some of the ACA provisions that generally are not favorable for the research-based pharmaceutical industry could also be repealed along with ACA coverage expansion provisions.

Moreover, legislative and regulatory proposals have been made to expand post-approval requirements and restrict sales and promotional activities for pharmaceutical products. We cannot be sure whether additional legislative changes will be enacted, or whether the FDA regulations, guidance or interpretations will be changed, or what the impact of such changes on the marketing approvals of our product candidates, if any, may be. In addition, increased scrutiny by the United States Congress of the FDA's approval process may significantly delay or prevent marketing approval, as well as subject us and any collaborators to more stringent product labeling and post-marketing testing and other requirements.

Governments outside the United States tend to impose strict price controls, which may adversely affect our revenues, if any.

In some countries, such as the countries of the European Union, the pricing of prescription pharmaceuticals is subject to governmental control and access. In these countries, pricing negotiations with governmental authorities can take considerable time after the receipt of marketing approval for a product. To obtain reimbursement or pricing approval in some countries, we, or any current or future collaborators, may be required to conduct a clinical trial that compares the cost-effectiveness of our product to other available therapies. If reimbursement of our products is unavailable or limited in scope or amount, or if pricing is set at unsatisfactory levels, our business could be materially harmed.

We are subject to U.S. and foreign anti-corruption and anti-money laundering laws with respect to our operations and non-compliance with such laws can subject us to criminal and/or civil liability and harm our business.

We are subject to the U.S. Foreign Corrupt Practices Act of 1977, as amended, or the FCPA, the U.S. domestic bribery statute contained in 18 U.S.C. § 201, the U.S. Travel Act, the USA PATRIOT Act, and possibly other state and national anti-bribery and anti-money laundering laws in countries in which we conduct activities. Anti-corruption laws are interpreted broadly and prohibit companies and their employees, agents, third-party intermediaries, joint venture partners and collaborators from authorizing, promising, offering, or providing, directly or indirectly, improper payments or benefits to recipients in the public or private sector. We may have direct or indirect interactions with officials and employees of government agencies or government-affiliated hospitals, universities, and other organizations. In addition, we may engage third party intermediaries to promote our clinical research activities abroad and/or to obtain necessary permits, licenses, and other regulatory approvals. We can be held liable for the corrupt or other illegal activities of these third-party intermediaries, our employees, representatives, contractors, partners, and agents, even if we do not explicitly authorize or have actual knowledge of such activities.

We cannot assure you that our employees and third party intermediaries will comply with such anti-corruption laws. Noncompliance with anti-corruption and anti-money laundering laws could subject us to whistleblower complaints, investigations, sanctions, settlements, prosecution, other enforcement actions, disgorgement of profits, significant fines, damages, other civil and criminal penalties or injunctions, suspension and/or debarment from contracting with certain persons, the loss of export privileges, reputational harm, adverse media coverage, and other collateral consequences. If any subpoenas, investigations, or other enforcement actions are launched, or governmental or other sanctions are imposed, or if we do not prevail in any possible civil or criminal litigation, our business, results of operations and financial condition could be materially harmed. In addition, responding to any action will likely result in a materially significant diversion of management's attention and resources and significant defense and compliance costs and other professional fees. In certain cases, enforcement authorities may even cause us to appoint an independent compliance monitor which can result in added costs and administrative burdens.

We are subject to governmental export and import controls that could impair our ability to compete in international markets due to licensing requirements and subject us to liability if we are not in compliance with applicable laws.

Our products and solutions are subject to export control and import laws and regulations, including the U.S. Export Administration Regulations, U.S. Customs regulations, and various economic and trade sanctions regulations administered by the U.S. Treasury Department's Office of Foreign Assets Controls. Exports of our products and solutions outside of the United States must be made in compliance with these laws and regulations. If we fail to comply with these laws and regulations, we and certain of our employees could be subject to substantial civil or criminal penalties, including the possible loss of export or import privileges; fines, which may be imposed on us and responsible employees or managers; and, in extreme cases, the incarceration of responsible employees or managers. In addition, changes in our products or solutions or changes in applicable export or import laws and regulations may create delays in the introduction, provision, or sale of our products and solutions in international markets, prevent customers from using our products and solutions or, in some cases, prevent the export or import of our products and solutions to certain countries, governments or persons altogether. Any limitation on our ability to export, provide, or sell our products and solutions could adversely affect our business, financial condition and results of operations.

If we fail to comply with environmental, health and safety laws and regulations, we could become subject to fines or penalties or incur costs that could harm our business.

We are subject to numerous environmental, health and safety laws and regulations, including those governing laboratory procedures and the handling, use, storage, treatment and disposal of hazardous materials and wastes. From time to time and in the future, our operations may involve the use of hazardous and flammable materials, including chemicals and biological materials, and may also produce hazardous waste products. Even if we contract with third parties for the disposal of these materials and waste products, we cannot completely eliminate the risk of contamination or injury resulting from these

materials. In the event of contamination or injury resulting from the use or disposal of our hazardous materials, we could be held liable for any resulting damages, and any liability could exceed our resources. We also could incur significant costs associated with civil or criminal fines and penalties for failure to comply with such laws and regulations.

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

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

Unfavorable global economic conditions could adversely affect our business, financial condition or results of operations.

Our results of operations could be adversely affected by general conditions in the global economy and in the global financial markets. The most recent global financial crisis caused extreme volatility and disruptions in the capital and credit markets. A severe or prolonged economic downturn, such as the most recent global financial crisis, could result in a variety of risks to our business, including weakened demand for our product candidates and our ability to raise additional capital when needed on acceptable terms, if at all. This is particularly true in the European Union, which is undergoing a continued severe economic crisis. A weak or declining economy could strain our suppliers, possibly resulting in supply disruption, or cause delays in payments for our services by third-party payors or our collaborators. Any of the foregoing could harm our business and we cannot anticipate all of the ways in which the current economic climate and financial market conditions could adversely impact our business.

Security breaches may disrupt our operations and harm our operating results.

Our network security and data recovery measures may not be adequate to protect against computer viruses, break-ins and similar disruptions from unauthorized tampering with our computer systems. The misappropriation, theft, sabotage or any other type of security breach with respect to any of our proprietary and confidential information that is electronically stored, including research or clinical data, could have a material adverse impact on our business, operating results and financial condition. Additionally, any break-in or trespass of our facilities that results in the misappropriation, theft, sabotage or any other type of security breach with respect to our proprietary and confidential information, including research or clinical data, or that results in damage to our research and development equipment and assets, could have a material adverse impact on our business, operating results and financial condition.

Our employees may engage in misconduct or other improper activities, including non-compliance with regulatory standards and requirements, which could cause significant liability for us and harm our reputation.

We are exposed to the risk of employee fraud or other misconduct, including intentional failures to comply with FDA regulations or similar regulations of comparable foreign regulatory authorities, provide accurate information to the FDA or comparable foreign regulatory authorities, comply with manufacturing standards we have established, comply with federal and state healthcare fraud and abuse laws and regulations and similar laws and regulations established and enforced by comparable foreign regulatory authorities, report financial information or data accurately or disclose unauthorized activities to us. Employee misconduct could also involve the improper use of information obtained in the course of clinical trials, which could result in regulatory sanctions and serious harm to our reputation. It is not always possible to identify and deter employee misconduct, and the precautions we take to detect and prevent this activity may not be effective in controlling unknown or unmanaged risks or losses or in protecting us from governmental investigations or other actions or lawsuits stemming from a failure to be in compliance with such laws, standards or regulations. If any such actions are instituted against us, and we are not successful in defending ourselves or asserting our rights, those actions could have a significant impact on our business and results of operations, including the imposition of significant fines or other sanctions.

Risks Related to Employee Matters and Managing Growth

If we are not able to retain key personnel and advisors, we may not be able to operate our business successfully.

We are highly dependent on our executive leadership team. All of these individuals are employees-at-will, which means that neither Infinity nor the employee is obligated to a fixed term of service and that the employment relationship may be terminated by either Infinity or the employee at any time, without notice and whether or not cause or good reason exists for

such termination. The loss of the services of any of these individuals might impede the achievement of our research, development and commercialization objectives. We do not maintain “key person” insurance on any of our employees.
Retaining qualified scientific and business personnel is also critical to our success. Our industry has experienced a high rate of turnover of management personnel in recent years. If we lose one or more of our executive officers or other key employees, our ability to implement our business strategy successfully could be seriously harmed. This competition is particularly intense near our headquarters in Cambridge, Massachusetts. We may not be able to attract or retain these personnel on acceptable terms given the competition among numerous pharmaceutical and biotechnology companies for similar personnel. In addition, as a result of our restructurings throughout 2016, we may face additional challenges in retaining our existing senior management and key employees for our company as our business needs change.
We also experience competition in the hiring of scientific personnel from universities and research institutions. In addition, we rely on consultants and advisors, including scientific and clinical advisors, to assist us in formulating our research and development strategy. Our consultants and advisors may be employed by other entities, have commitments under consulting or advisory contracts with third parties that limit their availability to us, or both.
We may undertake strategic acquisitions in the future, and any difficulties from integrating acquired businesses, products, product candidates and technologies could adversely affect our business and our stock price.
We may acquire additional businesses, products, product candidates, or technologies that complement or augment our existing business. We may not be able to integrate any acquired businesses, products, product candidates or technologies successfully or operate any acquired business profitably. Integrating any newly acquired business, product, product candidate, or technology could be expensive and time-consuming. Integration efforts often place a significant strain on managerial, operational and financial resources and could prove to be more difficult or expensive than we expect. The diversion of the attention of our management to, and any delay or difficulties encountered in connection with, any future acquisitions we may consummate could result in the disruption of our ongoing business or inconsistencies in standards, controls, procedures and policies that could adversely affect our ability to maintain relationships with customers, suppliers, collaborators, employees and others with whom we have business dealings.
We may need to raise additional funds through public or private debt or equity financings to acquire any businesses, products, product candidates, or technologies which may result in, among other things, dilution for stockholders or the incurrence of indebtedness.
As part of our efforts to acquire businesses, products, product candidates and technologies or to enter into other significant transactions, we conduct business, legal and financial due diligence in an effort to identify and evaluate material risks involved in the transaction. We will also need to make certain assumptions regarding acquired product candidates, including, among other things, development costs, the likelihood of receiving regulatory approval and the market for such product candidates. If we are unsuccessful in identifying or evaluating all such risks or our assumptions prove to be incorrect, we might not realize some or all of the intended benefits of the transaction. If we fail to realize intended benefits from acquisitions we may consummate in the future, our business and financial results could be adversely affected.
In addition, we will likely incur significant expenses in connection with our efforts, if any, to consummate acquisitions. These expenses may include fees and expenses for investment bankers, attorneys, accountants and other advisers in connection with our efforts and could be incurred whether or not an acquisition is consummated. Even if we consummate a particular acquisition, we may incur as part of such acquisition substantial closure costs associated with, among other things, elimination of duplicate operations and facilities. In such case, the incurrence of these costs could adversely affect our financial results for particular quarterly or annual periods.
Risks Related to Our Common Stock
Our common stock may have a volatile trading price and low trading volume.
The market price of our common stock has been and we expect it to continue to be subject to significant fluctuations.
Some of the factors that may cause the market price of our common stock to fluctuate include:
- the results of our current and any future clinical trials of IPI-549;
- the timing and costs associated with the wind-down of our involvement with duvelisib;
- future sales of, and the trading volume in, our common stock;

- announcements of strategic transactions relating to our programs or our company;
- our entry into key agreements, including those related to the acquisition or in-licensing of new programs, or the termination of key agreements, including our amended and restated development and license agreement with Takeda or the Verastem Agreement;

- the results and timing of regulatory reviews relating to the approval of IPI-549;
- the initiation of, material developments in, or conclusion of litigation, including but not limited to litigation to enforce or defend any of our intellectual property rights or to defend product liability claims;
- the failure of IPI-549, if approved, to achieve commercial success;
- the results of clinical trials conducted by others on drugs that would compete with IPI-549;
- the regulatory approval of drugs that would compete with IPI-549;
- issues in manufacturing IPI-549;
- the loss of key employees;
- changes in estimates or recommendations, or publication of inaccurate or unfavorable research about our business, by securities analysts who cover our common stock;
- future financings through the issuance of equity or debt securities or otherwise;
- healthcare reform measures, including changes in the structure of healthcare payment systems;
- our cash position and period-to-period fluctuations in our financial results; and
- general and industry-specific economic and/or capital market conditions.

Moreover, the stock markets in general have experienced substantial volatility that has often been unrelated to the operating performance of individual companies. These broad market fluctuations may also adversely affect the trading price of our common stock.

In the past, when the market price of a stock has been volatile, as our stock price may be, holders of that stock have occasionally brought securities class action litigation against the company that issued the stock. If any of our stockholders were to bring a lawsuit of this type against us, even if the lawsuit is without merit, negative publicity could be generated, and we could incur substantial costs defending the lawsuit. A stockholder lawsuit could also divert the time and attention of our management.

If we fail to meet the requirements for continued listing on the NASDAQ Global Select Market, our common stock could be delisted from trading, which would decrease the liquidity of our common stock and our ability to raise additional capital.

Our common stock is currently listed for quotation on the NASDAQ Global Select Market. We are required to meet specified requirements in order to maintain our listing on the NASDAQ Global Select Market, including, among other things, a minimum bid price of $1.00 per share. Our bid price has been below $3.00 per share since June 2016. If our bid price falls further to below $1.00 per share for 30 consecutive business days, we will receive a deficiency notice from NASDAQ advising us that we have 180 days to regain compliance by maintaining a minimum bid price of at least $1.00 for a minimum of ten consecutive business days. Under certain circumstances, NASDAQ could require that the minimum bid price exceed $1.00 for more than ten consecutive days before determining that a company complies.

If we fail to satisfy the NASDAQ Global Select Market’s continued listing requirements, we may transfer to the NASDAQ Capital Market, which generally has lower financial requirements for initial listing, to avoid delisting, or, if we fail to meet its listing requirements, the OTC Bulletin Board. A transfer of our listing to the NASDAQ Capital Market or having our common stock trade on the OTC Bulletin Board could adversely affect the liquidity of our common stock. Any such event could make it more difficult to dispose of, or obtain accurate quotations for the price of, our common stock, and there also would likely be a reduction in our coverage by securities analysts and the news media, which could cause the price of our common stock to decline further. We may also face other material adverse consequences in such event, such as negative publicity, a decreased ability to obtain additional financing, diminished investor and/or employee confidence, and the loss of business development opportunities, some or all of which may contribute to a further decline in our stock price.

The estimates and judgments we make, or the assumptions on which we rely, in preparing our consolidated financial statements could prove inaccurate.

Our consolidated financial statements have been prepared in accordance with accounting principles generally accepted in the United States. The preparation of these consolidated financial statements requires us to make estimates and judgments that affect the reported amounts of our assets, liabilities, revenues and expenses. Such estimates and judgments include those related to revenue recognition, impairment of long-lived assets, restructuring, accrued

expenses, assumptions in the valuation of stock-based compensation and income taxes. We base our estimates and judgments on historical experience, facts and circumstances known to us and on various assumptions that we believe to be reasonable under the circumstances. These estimates and judgments, or the assumptions underlying them, may change over time or prove inaccurate. If this is the case, we

may be required to restate our financial statements, which could in turn subject us to securities class action litigation. Defending against such potential litigation relating to a restatement of our financial statements would be expensive and would require significant attention and resources of our management. Moreover, our insurance to cover our obligations with respect to the ultimate resolution of any such litigation may be inadequate. As a result of these factors, any such potential litigation could have a material adverse effect on our financial results and cause our stock price to decline.

If we are not able to maintain effective internal control under Section 404 of the Sarbanes-Oxley Act, our business and stock price could be adversely affected.

Section 404 of the Sarbanes-Oxley Act of 2002 requires us, on an annual basis, to review and evaluate our internal control and requires our independent auditors to attest to the effectiveness of our internal control over financial reporting. Any failure by us to maintain the effectiveness of our internal control in accordance with the requirements of Section 404 of the Sarbanes-Oxley Act, which could be impacted by our restructuring or employee turnover, as such requirements exist today or may be modified, supplemented or amended in the future, could have a material adverse effect on our business, operating results and stock price.

We might not be able to utilize a significant portion of our net operating loss carryforwards and research and development tax credit carryforwards.

We have incurred significant net losses since our inception and cannot guarantee when, if ever, we will become profitable. To the extent that we continue to generate federal and state taxable losses, unused net operating loss and tax credit carryforwards will carry forward to offset future taxable income. These net operating loss and tax credit carryforwards could expire unused and be unavailable to offset future income tax liabilities. In addition, under Section 382 of the Internal Revenue Code of 1986, as amended, and corresponding provisions of state law, if a corporation undergoes an “ownership change,” which is generally defined as a greater than 50% change, by value, in its equity ownership over a three-year period, the corporation’s ability to use its pre-change net operating loss carryforwards and other pre-change tax attributes to offset its post-change income may be limited. We may experience ownership changes in the future as a result of subsequent shifts in our stock ownership, some of which may be outside of our control. In addition, we have not conducted a detailed study to document whether our historical activities qualify to support the research and development credit carryforwards. A detailed study could result in adjustment to our research and development credit carryforwards. If we determine that an ownership change has occurred and our ability to use our historical net operating loss and tax credit carryforwards is materially limited, or if our research and development carryforwards are adjusted, it would harm our future operating results by effectively increasing our future tax obligations.

We do not anticipate paying cash dividends, so you must rely on stock price appreciation for any return on your investment.

We anticipate retaining any future earnings for reinvestment in our research and development programs and growing infrastructure and personnel to support our commercialization efforts. Therefore, we do not anticipate paying cash dividends in the future. As a result, only appreciation of the price of our common stock will provide a return to stockholders. Investors seeking cash dividends should not invest in our common stock.

Our executive officers, directors and major shareholders may be able to exert significant control over the company, which may make an acquisition of us difficult.

To our knowledge, based on the number of shares of our common stock outstanding on March 1, 2017 stockholders beneficially owning 5% or more of our common stock, as well as our executive officers, directors, and their respective affiliates, beneficially owned in the aggregate approximately 48% of our common stock. These stockholders have the ability to influence our company through this ownership position. For example, as a result of this concentration of ownership, these stockholders, if acting together, may have the ability to affect the outcome of matters submitted to our stockholders for approval, including the election and removal of directors, changes to our equity compensation plans and any merger or similar transaction. This concentration of ownership may, therefore, harm the market price of our common stock by:

- delaying, deferring or preventing a change in control of Infinity;
- impeding a merger, consolidation, takeover or other business combination involving Infinity; or

- discouraging a potential acquirer from making a tender offer or otherwise attempting to obtain control of Infinity.

Anti-takeover provisions in our organizational documents and Delaware law may make an acquisition of us difficult. We are incorporated in Delaware. Anti-takeover provisions of Delaware law and our organizational documents may make a change in control more difficult. Also, under Delaware law, our Board of Directors may adopt additional anti-takeover

measures. For example, our charter authorizes our Board of Directors to issue up to 1,000,000 shares of undesignated preferred stock and to determine the terms of those shares of stock without any further action by our stockholders. If our Board of Directors exercises this power, it could be more difficult for a third party to acquire a majority of our outstanding voting stock. Our charter and bylaws also contain provisions limiting the ability of stockholders to call special meetings of stockholders.

Our stock incentive plan generally permits our Board of Directors to provide for acceleration of vesting of options granted under that plan in the event of certain transactions that result in a change of control. If our Board of Directors uses its authority to accelerate vesting of options, this action could make an acquisition more costly, and it could prevent an acquisition from going forward.

Moreover, because we are incorporated in Delaware, we are governed by the provisions of Section 203 of the Delaware General Corporation Law statute, which generally prohibits a person who owns in excess of 15% of our outstanding voting stock from engaging in a transaction with us for a period of three years after the date on which such person acquired in excess of 15% of our outstanding voting common stock, unless the transaction is approved by our Board of Directors and holders of at least two-thirds of our outstanding voting stock, excluding shares held by such person. The prohibition against such transactions does not apply if, among other things, prior to the time that such person became an interested stockholder, our Board of Directors approved the transaction in which such person acquired 15% or more of our outstanding voting stock. The existence of the foregoing provisions could limit the price that investors might be willing to pay in the future for shares of our common stock.

Our investments are subject to risks that may cause losses and affect the liquidity of these investments.

As of December 31, 2016, we had $92.1 million in cash, cash equivalents and available-for-sale securities. We historically have invested these amounts in money market funds, corporate obligations, U.S. government-sponsored enterprise obligations, U.S. Treasury securities and mortgage-backed securities meeting the criteria of our investment policy, which prioritizes the preservation of our capital. Corporate obligations may include obligations issued by corporations in countries other than the United States, including some issues that have not been guaranteed by governments and government agencies. Our investments are subject to general credit, liquidity, market and interest rate risks and instability in the global financial markets. We may realize losses in the fair value of these investments or a complete loss of these investments. In addition, should our investments cease paying or reduce the amount of interest paid to us, our interest income would suffer. These market risks associated with our investment portfolio may have a material adverse effect on our financial results and the availability of cash to fund our operations.

Item 1B. Unresolved Staff Comments

None.

Item 2. Properties

On September 25, 2014, we entered into a lease covering 61,000 square feet of office space located at 784 Memorial Drive. The lease expires on March 31, 2025, and contains two separate five-year options to extend its term to 2035. We currently lease space to subtenants in 784 Memorial Drive totaling approximately 12,000 square feet.

Item 3. Legal Proceedings

We are not a party to any material legal proceedings.

Item 4. Mine Safety Disclosures

Not applicable.

PART II

Item 5. Market for Registrant’s Common Equity, Related Stockholder Matters and Issuer Purchases of Equity Securities

Market Information

Our common stock is traded on the NASDAQ Global Select Market under the symbol “INFI.” The following table sets forth the range of high and low sales prices for our common stock for the quarterly periods indicated, as reported by NASDAQ. Such quotations represent inter-dealer prices without retail mark up, mark down or commission and may not necessarily represent actual transactions.

	2016		2015	
	High	Low	High	Low
First quarter	$8.16	$4.75	$17.42	$13.66
Second quarter	6.63	1.24	15.44	10.23
Third quarter	1.80	1.24	11.13	7.56
Fourth quarter	1.65	0.84	10.85	7.19

Holders
As of March 1, 2017, there were 51 holders of record of our common stock.

Dividends
We have never paid cash dividends on our common stock, and we do not expect to pay any cash dividends in the foreseeable future.

Comparative Stock Performance Graph
The information included under the heading “Comparative Stock Performance Graph” included in this Item 5 of Part II of this Annual Report on Form 10-K shall not be deemed to be “soliciting material” or subject to Regulation 14A or 14C, shall not be deemed “filed” for purposes of Section 18 of the Securities Exchange Act of 1934, as amended, which we refer to as the Exchange Act, or otherwise subject to the liabilities of that section, nor shall it be deemed incorporated by reference in any filing under the Securities Act of 1933, as amended, or the Exchange Act.

The graph below shows a comparison of cumulative total stockholder returns from December 31, 2011 through December 31, 2016 for our common stock, the NASDAQ Stock Market (U.S.) Index and the NASDAQ Biotechnology Index. The graph assumes that $100 was invested in our common stock and in each index on December 31, 2011, and that all dividends were reinvested. No cash dividends have been declared or paid on our common stock.

The stockholder returns shown on the graph below are not necessarily indicative of future performance, and we will not make or endorse any predictions as to future stockholder returns.

Item 6. Selected Financial Data

The following financial data should be read in conjunction with our consolidated financial statements and related notes appearing elsewhere in this report. Amounts below are in thousands, except for shares and per share amounts.

	Year Ended December 31,				
	2016	2015	2014	2013	2012
Statement of Operations Data:					
Collaboration revenue	$18,723	$109,066	$164,995	$—	$47,114
Operating expenses:					
Research and development(1)	119,611	199,109	143,633	99,760	118,595
General and administrative(1)	42,219	37,065	29,285	27,916	27,882
Total operating expenses	161,830	236,174	172,918	127,676	146,477
Gain on AbbVie Opt-Out (2)	112,216	—	—	—	—
Gain on termination of Purdue entities alliance	—	—	—	—	46,555
Loss from operations	(30,891)	(127,108)	(7,923)	(127,676)	(52,808)
Other income (expense), net	790	(933)	(9,310)	896	(1,349)
Income from Massachusetts tax incentive award	—	—	—	—	193
Loss before income taxes	(30,101)	(128,041)	(17,233)	(126,780)	(53,964)
Income taxes	—	(335)	(183)	—	—
Net loss	$(30,101)	$(128,376)	$(17,416)	$(126,780)	$(53,964)
Basic and diluted loss per common share	$(0.61)	$(2.62)	$(0.36)	$(2.64)	$(1.70)
Basic and diluted weighted average number of common shares outstanding	49,608,234	49,083,479	48,561,653	47,936,001	31,711,264

	As of December 31,				
	2016	2015	2014	2013	2012
Selected Balance Sheet Data:					
Cash, cash equivalents and available-for-sale securities, including long-term	$92,064	$245,231	$333,245	$214,468	$326,635
Working capital	77,797	184,641	289,691	202,735	311,086
Total assets	125,655	288,821	369,144	230,710	335,660
Due to Takeda, less current portion(3)	—	—	—	6,456	6,252
Construction liability(4)	—	—	15,456	—	—
Financing obligation(5)	19,591	20,007	—	—	—
Accumulated deficit	(625,689)	(595,588)	(467,212)	(449,796)	(323,016)
Total stockholders' equity	82,454	98,557	209,472	201,275	310,205

(1)During the year ended December 31, 2016, we recorded $21.2 million of expense related to restructuring activities of which $13.6 million is recorded in research and development expense and $7.6 million is recorded in general and administrative expense.

(2)On June 24, 2016, AbbVie delivered to us a written notice that AbbVie was exercising its right to terminate the AbbVie Agreement unilaterally upon 90 days' written notice, which we refer to as the AbbVie Opt-Out. The gain on AbbVie Opt-Out was non-recurring and due to the written notice of termination received from AbbVie on June 24, 2016. The AbbVie Opt-Out was irrevocable, and we had no obligation to continue to provide AbbVie any services related to Duvelisib Products after June 24, 2016. The termination of the AbbVie Agreement became effective on September 23, 2016. See Note 12 of the consolidated financial statements.

(3)During the year ended December 31, 2012, we recorded $14.4 million in research and development expense related to the fair value of a release payment of $15 million, payable in installments, pursuant to the amended and restated agreement with Takeda Pharmaceuticals Company Limited, or Takeda. We paid $1.7 million, $6.7 million and the final $6.7 million of this $15 million release payment during the years ended December 31, 2012, December 31, 2014, and December 31, 2015, respectively.

(4)In September 2014, we entered into a lease agreement with BHX, LLC, as trustee of 784 Realty Trust, for the lease of office space at 784 Memorial Drive, Cambridge, Massachusetts. Upon lease commencement, building construction

was initiated, and we were involved in the construction project. We are deemed for accounting purposes to be the owner of the

building during the construction period. As of December 31, 2014, we recorded building and accumulated construction costs of approximately $16.0 million and a construction liability of approximately $15.5 million. See Note 11 of the consolidated financial statements.
(5)In June 2015, the construction of 784 Memorial Drive, Cambridge, Massachusetts was substantially complete, and the leased premises, which we refer to as the Leased Premises, was available for occupancy. The construction-in-progress was then placed in service, and the construction liability was reclassified to a financing obligation as the transaction did not qualify for sale-leaseback accounting due to our continuing involvement. At December 31, 2016 and 2015, we held building and accumulated construction costs net of accumulated depreciation of approximately $22.0 million and $23.0 million, respectively, and a financing obligation of approximately $19.6 million and $20.0 million, respectively. See Note 11 of the consolidated financial statements.

Item 7. Management's Discussion and Analysis of Financial Condition and Results of Operations
The following discussion of our financial condition and results of operations should be read in conjunction with our consolidated financial statements and related notes included elsewhere in this report. Some of the information contained in this discussion and analysis and set forth elsewhere in this report, including information with respect to our plans and strategy for our business, includes forward-looking statements that involve risks and uncertainties. You should review the section titled "Risk Factors" in Part I, Item 1A of this report for a discussion of important factors that could cause actual results to differ materially from the results described in or implied by the forward-looking statements contained in the following discussion and analysis.

Overview
We are an innovative biopharmaceutical company dedicated to developing best-in-class medicines for patients with difficult-to-treat diseases. We combine proven scientific expertise with a passion for developing novel small molecule drugs that target disease pathways for potential applications in oncology. We are focusing our efforts on our lead product candidate, IPI-549, an orally administered, clinical-stage, immuno-oncology product candidate that selectively inhibits the enzyme phosphoinositide-3-kinase-gamma, or PI3K-gamma.

IPI-549 is currently being studied in a Phase 1, first-in-human clinical trial that is expected to enroll approximately 175 patients with advanced solid tumors. The study includes a dose-escalation phase to evaluate the safety, tolerability, pharmacokinetics, and pharmacodynamics of IPI-549 as a monotherapy, as well as a dose-escalation phase evaluating IPI-549 in combination with nivolumab, also known as Opdivo. Nivolumab is a checkpoint inhibitor therapy being commercialized by Bristol-Myers Squibb, or BMS, that targets a receptor in the human body called programmed death receptor 1, or PD-1. If supported by data from the initial portion of the study, a Phase 1b portion would investigate IPI-549 in patients with selected solid tumors, including non-small cell lung cancer, melanoma and squamous cell carcinoma of the head and neck, whose tumors have shown initial resistance or subsequently have developed resistance to immune checkpoint therapy.

We have primarily incurred operating losses since inception. Our net loss was $30.1 million, $128.4 million and $17.4 million for the years ended December 31, 2016, 2015 and 2014, respectively. As of December 31, 2016, we had an accumulated deficit of $625.7 million. As we have no approved products, we have not generated any revenue from product sales and, to date, all our revenue has been generated under research collaboration agreements. As of December 31, 2016, we had approximately $92.1 million in cash, cash equivalents and available-for-sale securities. We will need substantial additional funds to support our planned operations. In the absence of additional funding or business development activities, we believe that our existing cash, cash equivalents and available-for-sale securities at December 31, 2016 will be adequate to satisfy our capital needs into the first quarter of 2019 based on planned levels of spending. We have not included any of the $28 million of potential future Verastem, Inc., or Verastem, milestone payments in this forecast.

We expect to continue to spend significant resources to fund the development and potential commercialization of IPI-549, and we expect to incur significant operating losses for the foreseeable future. We expect to incur substantial operating losses over the next several years as our clinical trial and drug manufacturing activities increase. In addition, in connection with seeking and possibly obtaining regulatory approval of any of our product candidates, we expect to incur significant commercialization expenses for product sales, marketing, manufacturing and distribution. As a result, we expect that our accumulated deficit will also increase significantly.

Financial Overview
Revenue

To date, all of our revenue has been generated under research collaboration agreements. The terms of these research collaboration agreements may include payment to us of non-refundable, upfront license fees, funding or reimbursement of research and development efforts, milestone payments if specified objectives are achieved, and/or royalties on product sales. In the future, we may generate revenue from a combination of product sales, research and development support services and milestone payments in connection with strategic relationships, as well as royalties resulting from the sales of products developed under licenses of our intellectual property. We expect that any potential future revenue we generate will fluctuate from year to year as a result of the timing and amount of license fees, research and development reimbursement, milestone and other payments earned under our collaborative or strategic relationships and the amount and timing of payments that we earn upon the sale of our products, to the extent any are successfully commercialized.

Research and Development Expense

We are a drug development company. Our research and development expense has historically consisted primarily of the following:

- compensation of personnel associated with research and development activities;
- clinical testing costs, including payments made to contract research organizations;
- costs of comparator drugs used in clinical studies;
- costs of purchasing laboratory supplies and materials;
- costs of manufacturing product candidates for preclinical testing and clinical studies;
- costs associated with the licensing of research and development programs;
- preclinical testing costs, including costs of toxicology studies;
- fees paid to external consultants;
- fees paid to professional service providers for independent monitoring and analysis of our clinical trials;
- costs for collaboration partners to perform research activities, including development milestones for which a payment is due when achieved;
- depreciation of equipment; and
- allocated costs of facilities.

General and Administrative Expense

General and administrative expense primarily consists of compensation of personnel in executive, finance, accounting, legal, information technology infrastructure, corporate communications, corporate development, human resources and commercial functions. Other costs include facilities costs not otherwise included in research and development expense, early commercial efforts and professional fees for legal and accounting services. General and administrative expense also consists of the costs of maintaining our intellectual property portfolio.

Other Income and Expense

Investment and other income typically consists of interest earned on cash, cash equivalents and available-for-sale securities, net of interest expense, amortization of warrants and other revenue and loss. During the year ended December 31, 2016, we recognized net $0.9 million in other income primarily related to the sale of assets. Interest expense is currently related to the 784 Memorial Drive lease (see Note 11 of our consolidated financial statements).

Critical Accounting Policies and Significant Judgments and Estimates

The following discussion and analysis of our financial condition and results of operations is based on our consolidated financial statements, which have been prepared in accordance with accounting principles generally accepted in the United States. The preparation of these financial statements requires us to make judgments, estimates and assumptions that affect the amounts reported in the financial statements and accompanying notes. On an ongoing basis, we evaluate our estimates, including those related to revenue recognition, accrued expenses and assumptions in the valuation of stock-based compensation. We base our estimates on historical experience and on various other assumptions that we believe to be reasonable under the circumstances. Actual results could differ from those estimates. Differences

between actual and estimated results have not been material and have been adjusted in the period they become known. We believe that the following accounting policies and estimates are most critical to understanding and evaluating our reported financial results. Please refer to Note 2 to our consolidated financial statements included in this report for a description of our significant accounting policies.

Revenue Recognition

To date, all of our revenue has been generated under research collaboration agreements, and all our revenue during 2016 and 2015 was derived from our strategic alliance with AbbVie Inc., or AbbVie. The terms of these research collaboration

agreements may include payment to us of non-refundable, upfront license fees, funding or reimbursement of research and development efforts, milestone payments if specified objectives are achieved, and/or royalties on product sales. We evaluate all deliverables within an arrangement to determine whether or not they provide value on a stand-alone basis. Based on this evaluation, the deliverables are separated into units of accounting. For each unit of accounting identified within an arrangement, we determine the period over which the performance obligation occurs. Revenue is then recognized using the proportional performance method. The proportional performance method is used when the level of effort to complete the performance obligations under an arrangement can be reasonably estimated. We recognize revenue based upon our best estimate of the selling price for each element when there is no other means to determine the fair value of that item and allocate the consideration based on the relative values. The process for determining the best estimate of the selling price involves significant judgment and estimates.

At the inception of each agreement that includes milestone payments, we evaluate whether each milestone is substantive on the basis of the contingent nature of the milestone. This evaluation includes an assessment of whether:

- the consideration is commensurate with either (1) our performance to achieve the milestone, or (2) the enhancement of the value of the delivered item(s) as a result of a specific outcome resulting from our performance to achieve the milestone,
- the consideration relates solely to past performance, and
- the consideration is reasonable relative to all of the deliverables and payment terms within the arrangement.

In making this assessment, we evaluate factors such as the clinical, regulatory, commercial and other risks that must be overcome to achieve the respective milestone, the level of effort and investment required, and whether the milestone consideration is reasonable relative to all deliverables and payment terms in the arrangement. We recognize revenues related to substantive milestones in full in the period in which the substantive milestone is achieved. If a milestone payment is not considered substantive, we recognize the amount associated with the applicable milestone based on the period over which the performance obligation occurs for each deliverable in the arrangement.

We will recognize royalty revenue, if any, based upon actual and estimated net sales by the licensee of licensed products in licensed territories, in the period the sales occur. We have not recognized any royalty revenue to date.

In the event of an early termination of a collaboration agreement, any deferred revenue is recognized in the period in which all our obligations under the agreement have been fulfilled.

Accrued Expenses

As part of the process of preparing financial statements, we are required to estimate accrued expenses. This process involves identifying services that have been performed on our behalf and estimating the level of service performed and the associated cost incurred for such service as of each balance sheet date. Examples of services for which we must estimate accrued expenses include contract service fees paid to contract manufacturers in conjunction with pharmaceutical development work and to contract research organizations in connection with clinical trials and preclinical studies. In connection with these service fees, our estimates are most affected by our understanding of the status and timing of services provided. The majority of our service providers invoice us in arrears for services performed. In the event that we do not identify certain costs that have been incurred by our service providers, or if we under- or over-estimate the level of services performed or the costs of such services in any given period, our reported expenses for such period would be too low or too high, respectively. We often rely on subjective judgments to determine the date on which certain services commence, the level of services performed on or before a given date and the cost of such services. We make these judgments based upon the facts and circumstances known to us. Our estimates of expenses in future periods may be under- or over-accrued.

Stock-Based Compensation

We expense the fair value of employee stock options and other equity compensation. We use our judgment in determining the fair value of our equity instruments, including in selecting the inputs we use for the Black-Scholes valuation model. Equity instrument valuation models are by their nature highly subjective. Any significant changes in any of our judgments, including those used to select the inputs for the Black-Scholes valuation model, could have a significant impact on the fair value of the equity instruments granted and the associated compensation charge we record in our financial statements.

Results of Operations

The following table summarizes our results of operations for the years ended December 31, 2016, 2015 and 2014, in thousands, together with the change in each item as a percentage.

	2016	% Change	2015	% Change	2014
Collaboration revenue	$18,723	(83)%	$109,066	(34)%	$164,995
Research and development expense:					
Programs	(119,611)	(18)%	(146,609)	14 %	(128,633)
Takeda payments	—	(100)%	(52,500)	250 %	(15,000)
Total research and development expense	(119,611)	(40)%	(199,109)	39 %	(143,633)
General and administrative expense	(42,219)	14 %	(37,065)	27 %	(29,285)
Gain on AbbVie Opt-Out (note 12)	112,216	— %	—	— %	—
Interest expense	(1,225)	(10)%	(1,368)	(86)%	(9,649)
Investment and other income	2,015	363 %	435	28 %	339
Income taxes	—	(100)%	(335)	83 %	(183)

Revenue

Our revenue during the year ended December 31, 2016 consisted of approximately:

- $18.7 million of revenue related to development and committee services we performed under our collaboration agreement with AbbVie.

Our revenue during the year ended December 31, 2015 consisted of approximately:

- $75.2 million related to license revenue recognized as part of the $130 million enrollment milestone payment received from our collaboration agreement with AbbVie; and
- $33.9 million of revenue related to development and committee services we performed under our collaboration agreement with AbbVie.

Our revenue during the year ended December 31, 2014 consisted of approximately:

- $159.1 million related to license revenue recognized as part of the $275 million upfront payment received from our collaboration agreement with AbbVie; and
- $5.9 million of revenue related to development and committee services we performed under our collaboration agreement with AbbVie.

We recognized license revenue upon execution of the arrangement. Revenue related to development services and committee services was recognized using the proportionate performance method as services were provided over the estimated service period of approximately five years. We recorded the remaining amount related to development and committee services of $35.4 million and $95.5 million as short-term and long-term deferred revenue, respectively, as of December 31, 2015. Following the notification of the termination of the AbbVie Agreement, the remaining deferred revenue of $112.2 million as of June 24, 2016 was recorded as the gain on AbbVie Opt-Out. See Note 12 of our consolidated financial statements for details on the AbbVie Agreement and the AbbVie Opt-Out.

Gain on AbbVie Opt-Out

The gain on AbbVie Opt-Out was non-recurring and due to the written notice of termination received from AbbVie on June 24, 2016. The AbbVie Opt-Out was irrevocable, and we had no obligation to continue to provide AbbVie any services related to Duvelisib Products after June 24, 2016. The termination of the AbbVie Agreement became effective on September 23, 2016.

Research and Development Expense

Research and development expenses represented approximately 74% of our total operating expenses for the year ended December 31, 2016, 84% of our total operating expenses for the year ended December 31, 2015, and 83% of our total operating expenses for the year ended December 31, 2014.

The decrease in research and development expense for the year ended December 31, 2016 compared to the year ended December 31, 2015 was primarily attributable to:

- $52.5 million payment in 2015 to exercise the option purchased from Takeda Pharmaceutical Company Limited, or Takeda, in connection with the 2014 amendment of our development and license agreement with Takeda;
- $22.0 million decrease in clinical development expenses related to duvelisib, an oral, dual inhibitor of the delta and gamma isoforms of PI3K, including charges from AbbVie for costs incurred by AbbVie for other than the AbbVie Studies and for our share of the AbbVie Studies; and

- $13.2 million decrease in compensation due to the decrease in headcount resulting from restructuring activities in 2016.

These decreases were partially offset by $13.6 million of expense related to restructuring activities. See Note 13 of the consolidated financial statements for additional information on the restructurings.

The increase in research and development expense for the year ended December 31, 2015 compared to the year ended December 31, 2014 was primarily attributable to:

- $52.5 million payment to exercise the option purchased from Takeda in connection with the 2014 amendment of our development and license agreement with Takeda;
- $10.0 million increase in clinical development expenses related to duvelisib, including charges from AbbVie for costs incurred by AbbVie for other than the AbbVie Studies and for our share of the AbbVie Studies; and
- $4.8 million increase in compensation expense primarily due to hiring of additional personnel.

We began to track and accumulate costs by major program starting on January 1, 2006. These expenses primarily relate to payroll and related expenses for personnel working on the programs, process development and manufacturing, preclinical toxicology studies, clinical trial costs and allocated costs of facilities. During the year ended December 31, 2016, 2015 and 2014, and from January 1, 2006 through December 31, 2016, we estimate that we incurred the following expenses by program:

Program	Year Ended December 31, 2016	Year Ended December 31, 2015	Year Ended December 31, 2014	January 1, 2006 to December 31, 2016
	(in millions)			
PI3K Inhibitor(1)	$116.6	$ 189.6	$ 120.8	$ 589.0
Hsp90 inhibitor	—	0.1	1.6	137.8
Hedgehog pathway inhibitor	—	—	0.1	164.1

(1)Includes both duvelisib and IPI-549. Includes an upfront license fee of $13.5 million in 2010, $4 million in development milestones in 2011, $14.4 million recorded as fair value for the release payment for the amended and restated Takeda agreement and $6 million in development milestones in 2012, $10 million development milestone payment and a $5 million option fee payment in 2014, as well as a $52.5 million payment related to the exercise of an option to Takeda in 2015.

We expect expenses related to our PI3K program to decrease as a result of our Verastem Agreement related to duvelisib. See Note 12 of our consolidated financial statements for details on the Verastem Agreement. Upon entry into the Verastem Agreement, Verastem assumed financial responsibility for activities that were part of our ongoing duvelisib program. We have financial responsibility for the shutdown of certain specified clinical studies up to a maximum of $4.5 million. We will continue clinical development of IPI-549. We do not believe that the historical costs associated with our lead drug development programs are indicative of the future costs associated with these programs, nor represent what any other future drug development programs we initiate may cost. Due to the variability in the length of time and scope of activities necessary to develop a product candidate and uncertainties related to our cost estimates and our ability to obtain marketing approval for our product candidates, accurate and meaningful estimates of the total costs required to bring our product candidates to market are not available.

Because of the risks inherent in drug development, we cannot reasonably estimate or know:

- the nature, timing and estimated costs of the efforts necessary to complete the development of our programs;
- the completion dates of these programs; or
- the period in which material net cash inflows are expected to commence, if at all, from the programs described above and any potential future product candidates.

There is significant uncertainty regarding our ability to successfully develop any product candidates. These risks include the uncertainty of:

- the scope, rate of progress and cost of our clinical trials that we are currently running or may commence in the future;
- the scope and rate of progress of our preclinical studies and other research and development activities;
- clinical trial results;
- the cost of establishing clinical supplies of any product candidates;
- the cost and availability of comparator drugs;
- the cost of filing, prosecuting, defending and enforcing any patent claims and other intellectual property rights relating to our programs under development;

- the terms and timing of any strategic alliance, licensing and other arrangements that we have or may establish in the future relating to our programs under development;
- the cost and timing of regulatory approvals; and
- the effect of competing technological and market developments.

General and Administrative Expense

The increase in general and administrative expense for the year ended December 31, 2016 as compared to the year ended December 31, 2015 was primarily attributable to an increase of $7.6 million due to restructuring related costs, partially offset by a decrease in organizational support of $0.8 million due to the reduction in employee headcount during the year. See Note 13 of the consolidated financial statements for additional information on the restructurings.

The increase in general and administrative expense for the year ended December 31, 2015 as compared to the year ended December 31, 2014 was primarily attributable to an increase of $3.8 million in compensation expense, primarily due to hiring of additional personnel as well as an increase of $1.7 million in consulting expense and $1.1 million in market research expense.

Interest Expense

Interest expense for the year ended December 31, 2016 is due to the financing obligation related to our 784 Memorial Drive lease.

Interest expense for the year ended December 31, 2015 is due to the financing obligation related to our 784 Memorial Drive lease and the amortization of the loan commitment asset recognized under our facility agreement with affiliates of Deerfield Management Company, L.P., or Deerfield, which terminated in February 2015.

Investment and Other Income

Investment and other income increased in the year ended December 31, 2016 as compared to the year ended December 31, 2015 primarily as a result of a net gain on the sale of fixed assets of $0.9 million and due to additional income from subleases at 784 Memorial Drive.

Investment and other income increased in the year ended December 31, 2015 as compared to the year ended December 31, 2014 primarily as a result of income from subleases at 784 Memorial Drive.

Income Taxes

We did not incur any income tax expense during the year ended December 31, 2016.

Our income tax expense increased for the year ended December 31, 2015 as compared to the year ended December 31, 2014 due to the alternative minimum tax effect of the upfront payment and the milestone payment received in connection with the collaboration agreement with AbbVie that we entered into on September 2, 2014.

Liquidity and Capital Resources

We have not generated any revenue from product sales to date, and we do not expect to generate any such revenue for the foreseeable future, if at all. We have instead relied on the proceeds from sales of equity securities, debt, interest on investments, up-front license fees, expense reimbursement, and milestones and cost sharing under our collaborations to fund our operations. Our available-for-sale debt securities primarily trade in liquid markets, and the average days to maturity of our portfolio, as of December 31, 2016, is less than six months. Because our product candidate is in an early stage of clinical development and the outcome of our effort is uncertain, we cannot estimate the actual amounts necessary to successfully complete the development and commercialization of our product candidate or whether, or when, we may achieve profitability.

Our significant capital resources are as follows:

	December 31, 2016	December 31, 2015
	(in thousands)	
Cash, cash equivalents and available-for-sale securities	$92,064	$245,231
Working capital	77,797	184,641

	Year Ended December 31,		
	2016	2015	2014
	(in thousands)		
Cash (used in) provided by:			
Operating activities	$(154,356)	$(83,653)	$117,715
Takeda payments (included in operating activities above)	—	(59,167)	(21,667)
Investing activities	40,329	(37,903)	117,853
Capital expenditures (included in investing activities above)	(661)	(6,426)	(1,362)
Financing activities	(83)	2,321	3,723

Cash Flows

The principal use of cash in operating activities in all periods presented was related to our research and development programs. Our cash flow used in operating activities for the year ended December 31, 2016 compared to the year ended December 31, 2015 increased primarily due to increased operating expenses, including restructuring activities, as well as the absence of additional collaborative funding received in 2016. AbbVie paid us a $275 million upfront payment during the year ended December 31, 2014, and a $130 million milestone payment in November 2015 associated with the completion of enrollment in our clinical trial DYNAMO™ in September 2015.

Our cash flow used in operating activities for the year ended December 31, 2015 compared to the year ended December 31, 2014, increased primarily due to increased operating expenses, including a $52.5 million payment in March 2015 to Takeda associated with the exercise of an option that we purchased in July 2014 to eliminate our obligation to pay Takeda a tiered 7% to 11% royalty with respect to worldwide net sales in oncology indications of products containing or comprised of duvelisib and $6.7 million related to the final installment on a release payment. During the year ended December 31, 2014, we paid Takeda a $10 million milestone payment for the initiation of the first Phase 3 study for duvelisib, a $6.7 million release payment and a $5 million option payment.

Our cash flow used in operating activities in future periods may vary significantly due to various factors, including potential cash inflows from future collaboration agreements and potential cash outflows for licensing new programs from third parties. We cannot be certain whether and when we may enter into any such collaboration agreements or in-licenses.

Our investing activities for the years ended December 31, 2016, 2015 and 2014 included purchases and proceeds from maturities and sales of available-for-sale securities and purchases and proceeds from sales of property and equipment. Our investing activities for the year ended December 31, 2016 included $66.5 million in purchases of available-for-sale securities, proceeds of $93.4 million from maturities of available-for-sale securities and proceeds of $12.0 million from the sale of available-for-sale securities. We also received proceeds of $2.1 million related to the sale of property and equipment in 2016.

Net cash from financing activities for the year ended December 31, 2016 included $0.3 million of proceeds from issuances of common stock from stock option exercises related to stock incentive plans and $18,000 of proceeds from issuances of common stock related to our employee stock purchase plan, which were partially offset by $0.4 million of payments on the financing obligation related to our 784 Memorial Drive lease.

Net cash from financing activities for the year ended December 31, 2015 included $1.9 million of proceeds from issuances of common stock from stock option exercises related to stock incentive plans and $1.0 million of proceeds from issuances of common stock related to our employee stock purchase plan, which were partially offset by $0.5 million of payments on the construction liability and financing obligation related to our 784 Memorial Drive lease.

Net cash from financing activities for the year ended December 31, 2014 included $3.9 million of proceeds from issuances of common stock from stock option exercises related to stock incentive plans, $1.0 million related to restricted cash held on deposit with a bank to collateralize a letter of credit in the name of our facility lessor in accordance with our facility lease agreement, $0.8 million of proceeds from issuances of common stock related to our employee stock purchase plan, $0.5 million related to a decrease in restricted cash held on deposit with a bank to collateralize a letter of credit in the name of our facility lessor in accordance with our amended facility lease agreement and $0.4 million of transaction costs related to the facility agreement with Deerfield.

We will need substantial additional funds to support our planned operations. In the absence of additional funding or business development activities, we believe that our existing cash, cash equivalents and available-for-sale securities will be

adequate to satisfy our capital needs into the first quarter of 2019. We have not included any of the $28 million of potential future Verastem milestone payments in this forecast. We do not expect to generate significant revenue from product sales unless and until we obtain regulatory approval of and commercialize one of our current or future product candidates. Until we can generate sufficient levels of cash from operations, and because sufficient funds may not be available to us when needed from collaborations, we expect that we will be required to continue to fund our operations in part through the sale of debt or equity securities or through licensing select programs or partial economic rights that include up-front, royalty and/or milestone payments. Our need to raise additional funds may be accelerated if our research and development expenses exceed our current expectations, if we acquire a third party, or if we acquire or license rights to additional product candidates or new technologies from one or more third parties. Our need to raise additional funds may also be accelerated for other reasons, including, without limitation, if:

- our product candidates require more extensive clinical or preclinical testing than we currently expect;
- we advance our product candidates into clinical trials for more indications than we currently expect;
- we advance more of our product candidates than expected into costly later stage clinical trials;
- we advance more preclinical product candidates than expected into early stage clinical trials;
- we acquire additional business, technologies, products or product candidates;
- the cost of acquiring raw materials for, and of manufacturing, our product candidates is higher than anticipated;
- the cost or quantity required of comparator drugs used in clinical studies increases;
- we are required, or consider it advisable, to acquire or license intellectual property rights from one or more third parties; or
- we experience a loss in our investments due to general market conditions or other reasons.

Historically, we have relied on our strategic alliances for a significant portion of our research and development funding needs. Mundipharma and Purdue provided us approximately $260 million in research and development funding during the term of our strategic alliance. AbbVie provided us approximately $405 million in research and development funding through the termination of our strategic alliance in September 2016.

We have received $244.8 million of net proceeds from our public stock offerings. We may continue to seek additional funding through public or private financings of equity and/or debt securities, but such financings may not be available on acceptable terms, if at all. In addition, the terms of our financings may be dilutive to, or otherwise adversely affect, holders of our common stock, and such terms may impact our ability to make capital expenditures or incur additional debt.

We may also seek additional funds through arrangements with collaborators or other third parties, or through project financing. These arrangements would generally require us to relinquish or encumber rights to some of our technologies or product candidates, and we may not be able to enter into such agreements on acceptable terms, if at all. If we are unable to obtain additional funding on a timely basis, we may be required to curtail or terminate some or all of our development programs or to scale back, suspend or terminate our business operations.

Organizational Restructuring

In June 2016, we reported the top line data from DYNAMO, a registration-focused Phase 2 monotherapy study evaluating the efficacy and safety of duvelisib in patients with refractory indolent non-Hodgkin lymphoma, or iNHL. The study met its primary endpoint with an overall response rate of 46%, all of which were partial responses, among 129 patients with iNHL. On June 24, 2016, AbbVie delivered to us a written notice of the AbbVie Opt-Out.

June 2016 Restructurings

As a result of our discussions with AbbVie regarding our collaboration and the subsequent AbbVie Opt-Out, our Board of Directors approved a strategic restructuring in order to preserve our resources as we determine future strategic plans, which included significant employee headcount reductions during June 2016. We recognized $8.3 million and $4.5 million in total restructuring charges for the year ended December 31, 2016 in research and development expenses and general and administrative expenses, respectively.

We continue to evaluate the lease for the facility that we currently occupy. See Note 11 to our consolidated financial statements for information regarding our facility lease termination at 780/790 Memorial Drive. If we pursue and successfully restructure the 784 Memorial Drive facility lease in 2017, we could potentially incur additional charges upon our exit from the space. Such potential future charges could include further impairments and lease exit payments related to our office space at 784 Memorial Drive in Cambridge, Massachusetts. At December 31, 2016, the accompanying consolidated balance sheets reflect the 784 Memorial Drive building and accumulated construction costs net of accumulated depreciation of $22.0 million and a total financing obligation of approximately $19.6 million.

In June 2016, we reduced our employee headcount by approximately 66% compared to our employee headcount as of December 31, 2015. We have existing severance plans which outline contractual termination benefits. We recognized all contractual severance and benefits outlined in the plan when termination was probable and reasonably estimable in accordance with FASB ASC Topic 712, Compensation - Nonretirement Postemployment Benefits.

Approximately $1.9 million of expense was recorded during the year ended December 31, 2016 related to the write-off of prepaid expenses that were not expected to continue and other payments that were due as a result of early terminations.

We identified and recorded the impairment of approximately $0.4 million in furniture and fixtures during the year ended December 31, 2016.

In performing the recoverability test for the 780/790 Memorial Drive asset group, we concluded that the asset group was not recoverable. We recorded an impairment charge of $0.8 million related to 780/790 Memorial Drive assets, including the related tenant improvement allowance (see Note 11), after comparing the fair value (using probability weighted scenarios with discounted cash flows) to the asset group’s carrying value, for the year ended December 31, 2016.

In performing the recoverability test for the 784 Memorial Drive asset group, we concluded that the asset group was not recoverable. We had an independent appraisal performed for the 784 Memorial building and improvements. We concluded no impairment was needed as the fair market value (considering the cost approach, sales comparison approach and the income approach) exceeded the asset group’s carrying value.

September 2016 Restructuring

As a result of our progress on strategic initiatives with duvelisib, our Board of Directors approved further headcount reductions during September 2016. The September 2016 restructuring reduced our employee headcount by approximately 4% compared to our employee headcount as of December 31, 2015. Included in the table below, we recognized $0.3 million and $0.2 million in total restructuring charges for the year ended December 31, 2016 in research and development expenses and general and administrative expenses, respectively, related to the September restructuring.

October 2016 Restructuring

On October 28, 2016, our Board of Directors approved a strategic restructuring in connection with and subject to the entry into the Verastem Agreement. The restructuring included workforce reductions of 19 positions across the organization representing approximately 9% compared to our employee headcount as of December 31, 2015. Included in the table below, we recognized $2.6 million and $2.0 million in total restructuring charges for the year ended December 31, 2016 in research and development expenses and general and administrative expenses, respectively, related to the October restructuring.

Summary Table

The following table summarizes the impact of the June 2016, September 2016 and October 2016 restructuring activities on our operating expenses and payments for the year ended December 31, 2016 and the current liability remaining on our balance sheet as of December 31, 2016, in thousands:

	Charges incurred during the year ended December 31, 2016 (in thousands)	Amounts paid through December 31, 2016	Less non-cash charges during the year ended December 31, 2016	Amounts accrued at December 31, 2016
Employee severance, benefits and related costs for work force reduction	$ 17,960	$ 9,516	$ 1,552	$ 6,892
Long-lived asset impairment	1,324	—	1,324	—

Contract termination, prepaid expense write-offs and other related costs	1,891	821	1,042	28
Total restructuring	$ 21,175	$ 10,337	$ 3,918	$ 6,920

During the year ended December 31, 2016, we recorded $21.2 million of expense related to restructuring activities of which $13.6 million is recorded in research and development expense and $7.6 million is recorded in general and administrative expense. We are obligated to continue to pay the remaining amounts accrued through the third quarter of 2017.

At-the-Market Facility

In May 2016, we entered into an at-the-market sales agreement, or Sales Agreement, with Cantor Fitzgerald & Co., or Cantor Fitzgerald, as agent, pursuant to which we may from time to time, at our option, offer and sell shares of our common stock having an aggregate offering price of up to $50 million through Cantor Fitzgerald, acting as our sales agent. Cantor Fitzgerald will be entitled to a commission of 3.0% of the aggregate gross proceeds from sales of shares of our common stock under the Sales Agreement. Sales of shares of our common stock under the Sales Agreement may be made by any method permitted by law that is deemed an "at the market" offering as defined in Rule 415 under the Securities Act of 1933, as amended, including sales made through the Nasdaq Global Select Market, on any other existing trading market for our common stock or to or through a market maker. We may also authorize Cantor Fitzgerald to sell shares in privately negotiated transactions. As of December 31, 2016, we had not used the at-the-market facility. We have no obligation to sell shares of our common stock and cannot provide any assurances that we will issue any shares pursuant to the Sales Agreement. We may also suspend the offering of shares of our common stock upon notice and subject to other conditions.

Contractual Obligations

As of December 31, 2016, we had the following contractual obligations, excluding contingent milestone payments:

	Payments Due by Period (in thousands)						
Contractual Obligations	Total	2017	2018	2019	2020	2021	2022 and beyond
784 facility	$18,079	$2,044	$2,044	$2,044	$2,227	$2,287	$ 7,433
Total contractual cash obligations	$18,079	$2,044	$2,044	$2,044	$2,227	$2,287	$ 7,433

The above table does not include contracts with contract research organizations as they are generally cancellable, with notice, at our option. In addition, we have obligations to make milestone payments under our license agreement with Takeda. For a description of these obligations, please see our description of our license agreement with Takeda under the heading "Strategic Alliances—Takeda" in Part I, Item 1 of this report. We are obligated to pay to Takeda up to $5 million in remaining success-based milestones for the development of a product candidate, and up to $165 million in success-based milestones for the approval and commercialization of one distinct product. Because the achievement of these milestones had not occurred as of December 31, 2016, such contingencies have not been recorded in our financial statements.

During the year ended December 31, 2014, we entered into a lease agreement for the lease of office space at 784 Memorial Drive, Cambridge, Massachusetts. Upon lease commencement, building construction was initiated. We were involved in the construction project and were deemed for accounting purposes to be the owner of the building during the construction period. The construction was substantially complete, and the Leased Premises was available for occupancy in June 2015. The construction-in-progress was then placed in service, and the asset was transferred to building and building improvements. At December 31, 2016 and 2015, the accompanying consolidated balance sheet reflects the building and accumulated construction costs net of accumulated depreciation of approximately $22.0 million and $23.0 million, respectively, and a financing obligation of approximately $19.6 million and $20.0 million at December 31, 2016 and 2015, respectively (see Note 11 of the financial statements).

Amounts related to contingent milestone payments are not considered contractual obligations as they are contingent on the successful achievement of certain development, regulatory approval and commercial milestones, which may not be achieved.

Off-Balance Sheet Arrangements

Since inception, we have not engaged in any off-balance sheet financing activities, including the use of structured finance, special purpose entities or variable interest entities.

Inflation

We do not believe that inflation has had a significant impact on our revenues or results of operations since inception.

New Accounting Pronouncements

See Note 2 to our consolidated financial statements included in Part II, Item 8, “Financial Statements and Supplementary Data,” of this Annual Report on Form 10-K for a description of recent accounting pronouncements applicable to our business.

Item 7A. Quantitative and Qualitative Disclosures about Market Risk

Our interest income is sensitive to changes in the general level of U.S. interest rates, particularly since a significant portion of our investments are in money market funds, corporate obligations, and U.S. government-sponsored enterprise obligations. We do not enter into investments for trading or speculative purposes. Our cash is deposited in and invested through highly rated financial institutions in North America. Our marketable securities are subject to interest rate risk and will fall in value if market interest rates increase.

A hypothetical 100 basis point increase in interest rates would result in an approximately $25,000 decrease in the fair value of our investments as of December 31, 2016, as compared to an approximately $0.4 million decrease as of December 31, 2015. We have the ability to hold our fixed income investments until maturity and, therefore, we do not expect our operating results or cash flows to be affected to any significant degree by the effect of a change in market interest rates on our investments.

Item 8. Financial Statements and Supplementary Data

Report of Independent Registered Public Accounting Firm
The Board of Directors and Stockholders of
Infinity Pharmaceuticals, Inc.

We have audited the accompanying consolidated balance sheets of Infinity Pharmaceuticals, Inc. as of December 31, 2016 and 2015, and the related consolidated statements of operations and comprehensive loss, stockholders' equity and cash flows for each of the three years in the period ended December 31, 2016. These financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on these financial statements based on our audits.

We conducted our audits in accordance with the standards of the Public Company Accounting Oversight Board (United States). Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the financial statements are free of material misstatement. An audit includes examining, on a test basis, evidence supporting the amounts and disclosures in the financial statements. An audit also includes assessing the accounting principles used and significant estimates made by management, as well as evaluating the overall financial statement presentation. We believe that our audits provide a reasonable basis for our opinion.

In our opinion, the financial statements referred to above present fairly, in all material respects, the consolidated financial position of Infinity Pharmaceuticals, Inc. at December 31, 2016 and 2015, and the consolidated results of its operations and its cash flows for each of the three years in the period ended December 31, 2016, in conformity with U.S. generally accepted accounting principles.

We also have audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States), Infinity Pharmaceuticals, Inc.'s internal control over financial reporting as of December 31, 2016, based on criteria established in Internal Control-Integrated Framework issued by the Committee of Sponsoring Organizations of the Treadway Commission (2013 framework) and our report dated March 14, 2017 expressed an unqualified opinion thereon.

/s/ ERNST & YOUNG LLP
Boston, Massachusetts
March 14, 2017

INFINITY PHARMACEUTICALS, INC.
Consolidated Balance Sheets
(in thousands, except share and per share amounts)

	December 31,	
	2016	2015
Assets		
Current assets:		
Cash and cash equivalents	$74,060	$188,170
Available-for-sale securities	18,004	57,061
Restricted cash	1,152	—
Prepaid expenses and other current assets	8,444	9,466
Total current assets	101,660	254,697
Property and equipment, net	23,424	28,240
Restricted cash, less current portion	530	1,681
Long-term receivable (note 11)	—	1,821
Other assets	41	2,382
Total assets	$125,655	$288,821
Liabilities and stockholders' equity		
Current liabilities:		
Accounts payable	$2,413	$9,628
Accrued expenses	21,008	24,604
Deferred revenue, current	—	35,408
Financing obligation, current (note 11)	442	416
Total current liabilities	23,863	70,056
Deferred revenue, less current portion	—	95,531
Deferred rent, less current portion (note 11)	183	4,632
Financing obligation, less current portion (note 11)	19,149	19,591
Other liabilities	6	454
Total liabilities	43,201	190,264
Commitments and contingencies (note 11)		
Stockholders' equity:		
Preferred Stock, $0.001 par value; 1,000,000 shares authorized, no shares issued and outstanding at December 31, 2016 and 2015	—	—
Common Stock, $0.001 par value; 100,000,000 shares authorized, 50,374,871 and 49,305,136 shares issued and outstanding at December 31, 2016 and December 31, 2015, respectively	50	49
Additional paid-in capital	708,096	694,051
Accumulated deficit	(625,689)	(595,588)
Accumulated other comprehensive income (loss)	(3)	45
Total stockholders' equity	82,454	98,557
Total liabilities and stockholders' equity	$125,655	$288,821

The accompanying notes are an integral part of these consolidated financial statements.

INFINITY PHARMACEUTICALS, INC.
Consolidated Statements of Operations and Comprehensive Loss
(in thousands, except share and per share amounts)

	Years Ended December 31,		
	2016	2015	2014
Collaboration revenue	$18,723	$109,066	$164,995
Operating expenses:			
Research and development	119,611	199,109	143,633
General and administrative	42,219	37,065	29,285
Total operating expenses	161,830	236,174	172,918
Gain on AbbVie Opt-Out (note 12)	112,216	—	—
Loss from operations	(30,891)	(127,108)	(7,923)
Other income (expense):			
Interest expense	(1,225)	(1,368)	(9,649)
Investment and other income	2,015	435	339
Total other income (expense)	790	(933)	(9,310)
Loss before income taxes	(30,101)	(128,041)	(17,233)
Income taxes	—	(335)	(183)
Net loss	$(30,101)	$(128,376)	$(17,416)
Basic and diluted loss per common share	$(0.61)	$(2.62)	$(0.36)
Basic and diluted weighted average number of common shares outstanding	49,608,234	49,083,479	48,561,653
Other comprehensive loss:			
Net unrealized holding losses on available-for-sale securities arising during the period	$(48)	$(69)	$(42)
Comprehensive loss	$(30,149)	$(128,445)	$(17,458)

The accompanying notes are an integral part of these consolidated financial statements.

INFINITY PHARMACEUTICALS, INC.
Consolidated Statements of Cash Flows
(in thousands)

	Years Ended December 31,		
	2016	2015	2014
Operating activities			
Net loss	$(30,101)	$(128,376)	$(17,416)
Adjustments to reconcile net loss to net cash provided by (used in) operating activities:			
Non-cash gain on AbbVie Opt-Out (note 12)	(112,216)	—	—
Depreciation	3,418	2,292	1,773
Stock-based compensation, including 401(k) match	13,714	14,700	12,588
Impairment of property and equipment	771	—	—
Gain on sale of fixed assets	(876)	—	—
Non-cash interest expense on amount Due to Takeda	—	—	211
Amortization of loan commitment asset	—	647	9,649
Net amortization of premium/discount on available-for-sale securities	159	272	1,257
Other, net	(2)	(162)	83
Changes in operating assets and liabilities:			
Prepaid expenses and other assets	5,208	933	(494)
Accounts payable, accrued expenses and other liabilities	(20,418)	10,517	6,815
Due to Takeda	—	(6,667)	(6,667)
Deferred revenue	(18,723)	20,934	110,005
Deferred rent	4,710	1,257	(89)
Net cash provided by (used in) operating activities	(154,356)	(83,653)	117,715
Investing activities			
Purchases of property and equipment	(661)	(6,426)	(1,362)
Proceeds from sale of assets	2,140	—	—
Purchases of available-for-sale securities	(66,503)	(121,456)	(21,789)
Proceeds from maturities of available-for-sale securities	93,400	89,515	141,004
Proceeds from sales of available-for-sale securities	11,953	464	—
Net cash provided by (used in) investing activities	40,329	(37,903)	117,853
Financing activities			
Proceeds from issuances of common stock related to stock incentive plans, net	314	1,866	3,881
Proceeds from issuances of common stock related to employee stock purchase plan	18	964	836
Payments on construction liability	—	(273)	—
Payments on financing obligation	(415)	(236)	—
Restricted cash	—	—	(548)
Deferred transaction costs	—	—	(446)
Net cash provided by (used in) financing activities	(83)	2,321	3,723
Net increase (decrease) in cash and cash equivalents	(114,110)	(119,235)	239,291
Cash and cash equivalents at beginning of period	188,170	307,405	68,114
Cash and cash equivalents at end of period	$74,060	$188,170	$307,405
Supplemental cash flow information			
Cash paid for interest	$1,225	$721	$—
Cash paid for income taxes	$5	$885	$—
Supplemental schedule of noncash investing and financing activities			
Loan commitment asset	$—	$—	$9,850
Facility fee	$—	$—	$1,500

Warrants issued	$—	$—	$8,350
Construction liability	$—	$—	$15,456
Reclassification to financing obligation	$—	$19,273	$—
Property and equipment in accrued expenses	$—	$65	$—
Increase in property and equipment for amount paid by landlord	$—	$5,059	$797

The accompanying notes are an integral part of these consolidated financial statements.

INFINITY PHARMACEUTICALS, INC.
Consolidated Statements of Stockholders' Equity
(in thousands, except share amounts)

	Common Stock		Additional Paid-in Capital	Accumulated Deficit	Accumulated Other Comprehensive Income (Loss)	Total Stockholders' Equity
	Shares	Amount				
Balance at December 31, 2013	48,227,838	$ 48	$ 650,867	$ (449,796)	$ 156	$ 201,275
Exercise of stock options	523,954		3,881			3,881
Valuation of initial warrants			8,350			8,350
Stock-based compensation expense			11,878			11,878
401(k) plan match issued in common stock	50,464		710			710
Issuance of common stock related to employee stock purchase plan	76,572	1	835			836
Unrealized loss on marketable securities					(42)	(42)
Net loss				(17,416)		(17,416)
Balance at December 31, 2014	48,878,828	$ 49	$ 676,521	$ (467,212)	$ 114	$ 209,472
Exercise of stock options	225,578		1,796			1,796
Stock-based compensation expense			13,844			13,844
401(k) plan match issued in common stock	68,235		856			856
Issuance of common stock related to employee stock purchase plan	124,358		964			964
Issuance of common stock for services	8,137		70			70
Unrealized loss on marketable securities					(69)	(69)
Net loss				(128,376)		(128,376)
Balance at December 31, 2015	49,305,136	$ 49	$ 694,051	$ (595,588)	$ 45	$ 98,557

The accompanying notes are an integral part of these consolidated financial statements.

INFINITY PHARMACEUTICALS, INC.
Consolidated Statements of Stockholders' Equity (Continued)
(in thousands, except share amounts)

	Common Stock		Additional Paid-in Capital	Accumulated Deficit	Accumulated Other Comprehensive Income (Loss)	Total Stockholders' Equity
	Shares	Amount				
Balance at December 31, 2015	49,305,136	$ 49	$ 694,051	$ (595,588)	$ 45	$ 98,557
Exercise of stock options	67,077		373			373
Stock-based compensation expense			11,937			11,937
401(k) plan match issued in common stock	295,596		619			619
Issuance of common stock related to employee stock purchase plan	15,860		18			18
Vesting of restricted stock and other, net	691,202	1	1,098			1,099
Unrealized loss on marketable securities					(48)	(48)
Net loss				(30,101)		(30,101)
Balance at December 31, 2016	50,374,871	$ 50	$ 708,096	$ (625,689)	$ (3)	$ 82,454

The accompanying notes are an integral part of these consolidated financial statements.

INFINITY PHARMACEUTICALS, INC.
Notes to Consolidated Financial Statements
1. Organization
Infinity Pharmaceuticals, Inc. is an innovative biopharmaceutical company dedicated to developing best-in-class medicines to patients with difficult-to-treat diseases. As used throughout these audited, consolidated financial statements, the terms “Infinity,” “we,” “us,” and “our” refer to the business of Infinity Pharmaceuticals, Inc. and its wholly-owned subsidiaries.

2. Summary of Significant Accounting Policies
Basis of Presentation
These consolidated financial statements include the accounts of Infinity and its wholly-owned subsidiaries. We have eliminated all significant intercompany accounts and transactions in consolidation.

The preparation of consolidated financial statements in accordance with generally accepted accounting principles requires our management to make estimates and judgments that may affect the reported amounts of assets, liabilities, revenues and expenses, and related disclosure of contingent assets and liabilities. On an ongoing basis, we evaluate our estimates and judgments. We base our estimates on historical experience and on various other assumptions that are believed to be reasonable, the results of which form the basis for making judgments about the carrying values of assets and liabilities. Actual results may differ from these estimates under different assumptions or conditions.

Cash Equivalents and Available-For-Sale Securities
Cash equivalents and available-for-sale securities primarily consist of money market funds, U.S. government-sponsored enterprise obligations, corporate obligations and mortgage-backed securities. Corporate obligations include obligations issued by corporations in countries other than the United States, including some obligations that have not been guaranteed by governments and government agencies. We consider all highly liquid investments with maturities of three months or less at the time of purchase to be cash equivalents. Cash equivalents, which consist of money market funds, corporate obligations and U.S. government-sponsored enterprise obligations, are stated at fair value. They are also readily convertible to known amounts of cash and have such short-term maturities that each presents insignificant risk of change in value due to changes in interest rates. Our classification of cash equivalents is consistent with prior periods.

We determine the appropriate classification of marketable securities at the time of purchase and reevaluate such designation at each balance sheet date. We have classified all of our marketable securities at December 31, 2016 and 2015 as “available-for-sale.” We carry available-for-sale securities at fair value, with the unrealized gains and losses reported in accumulated other comprehensive income (loss), which is a separate component of stockholders’ equity.

We adjust the cost of available-for-sale debt securities for amortization of premiums and accretion of discounts to maturity. We include such amortization and accretion in investment and other income. The cost of securities sold is based on the specific identification method. We include in investment income interest and dividends on securities classified as available-for-sale.

We conduct periodic reviews to identify and evaluate each investment that is in an unrealized loss position in order to determine whether an other-than-temporary impairment exists. An unrealized loss exists when the current fair value of an individual security is less than its amortized cost basis. Unrealized losses on available-for-sale debt securities that are determined to be temporary, and not related to credit loss, are recorded, net of tax, in accumulated other comprehensive income (loss).

For available-for-sale debt securities in an unrealized loss position, we perform an analysis to assess whether we intend to sell or whether we would more likely than not be required to sell the security before the expected recovery of the amortized cost basis. Where we intend to sell a security, or may be required to do so, the security's decline in fair value is deemed to be other-than-temporary, and the full amount of the unrealized loss is recorded within earnings as an impairment loss.

Regardless of our intent to sell a security, we perform additional analysis on all securities in an unrealized loss position to evaluate losses associated with the creditworthiness of the security. Credit losses are identified where we do not expect to receive cash flows sufficient to recover the amortized cost basis of a security and are recorded within earnings as an impairment loss.

We will need substantial additional funds to support our planned operations. In the absence of additional funding or business development activities, we believe that our existing cash, cash equivalents and available-for-sale securities at December 31, 2016 will be adequate to satisfy our capital needs based on planned levels of spending into the first quarter of 2019. We have not included any of the future potential $28 million of Verastem Inc., or Verastem, milestone payments in this forecast (see Note 12). For more information, refer to the section titled “Liquidity and Capital Resources” in Item 7, Management’s Discussion and Analysis of Financial Condition and Results of Operations.

Concentration of Risk

Cash and cash equivalents are primarily maintained with two major financial institutions in the United States. Deposits at banks may exceed the insurance provided on such deposits. Generally, these deposits may be redeemed upon demand and, therefore, bear minimal risk. Financial instruments that potentially subject us to concentration of credit risk primarily consist of available-for-sale securities. Available-for-sale securities consist of U.S. government-sponsored enterprise obligations, investment grade corporate obligations and mortgage-backed securities. Our investment policy, which has been approved by our Board of Directors, limits the amount that we may invest in any one issuer of investments, thereby reducing credit risk concentrations.

Segment Information

We operate in one business segment, which focuses on drug development. We make operating decisions based upon performance of the enterprise as a whole and utilize our consolidated financial statements for decision making.

All of our revenues to date have been generated under research collaboration agreements. Revenue associated with the amortization of the deferred revenue associated with the grant of licenses to, and research and development services provided to, AbbVie Inc., or AbbVie, accounted for all of our revenue during the years ended December 31, 2014, 2015 and 2016.

Property and Equipment

Property and equipment are stated at cost. Depreciation is recorded using the straight-line method over the estimated useful lives of the applicable assets. Assets included in construction-in-progress are not depreciated until placed into service. Application development costs incurred for computer software developed or obtained for internal use are capitalized. Upon sale or retirement, the cost and related accumulated depreciation are eliminated from the respective account, and the resulting gain or loss, if any, is included in current operations. Amortization of leasehold improvements, building improvements and capital leases is recorded as depreciation expense and included in research and development and general and administrative expense, as applicable. Repairs and maintenance charges that do not increase the useful life of the assets are charged to operations as incurred. Property and equipment are depreciated over the following periods:

Laboratory equipment	5 years
Computer equipment and software	3 to 5 years
Leasehold improvements	Shorter of lease term or useful life of asset
Building and building improvements	10 to 50 years, less estimated residual value at the end of the financing obligation term
Furniture and fixtures	7 to 10 years

Impairment of Long-Lived Assets

We evaluate our long-lived assets for potential impairment. Potential impairment is assessed when there is evidence that events or changes in circumstances have occurred that indicate that the carrying amount of a long-lived asset may not be recovered. Recoverability of these assets is assessed based on undiscounted expected future cash flows from the

assets, considering a number of factors, including past operating results, budgets and economic projections, market trends and product development cycles. An impairment in the carrying value of each asset is assessed when the undiscounted expected future cash flows, including its eventual residual value, derived from the asset are less than its carrying value. Impairments, if any, are recognized in earnings. An impairment loss would be recognized in an amount equal to the excess of the carrying amount over the undiscounted expected future cash flows.

Fair Value Measurements

We define fair value as the price that would be received to sell an asset or paid to transfer a liability in an orderly transaction between market participants at the measurement date. We determine fair value based on the assumptions market participants use when pricing the asset or liability. We also use the fair value hierarchy that prioritizes the information used to develop these assumptions.

We value our available-for-sale securities utilizing third-party pricing services. The pricing services use many observable market inputs to determine value, including benchmark yields, reportable trades, broker/dealer quotes, issuer spreads, two-sided markets, benchmark securities, bids, offers, reference data, new issue data, monthly payment information and collateral performance. We validate the prices provided by our third-party pricing services by understanding the models used, obtaining market values from other pricing sources and confirming that those securities trade in active markets.

Revenue Recognition

To date, all of our revenue has been generated under research collaboration agreements, and all our revenue during 2016, 2015 and 2014 was derived from our strategic alliance with AbbVie. The terms of these research collaboration agreements may include payment to us of non-refundable, upfront license fees, funding or reimbursement of research and development efforts, milestone payments if specified objectives are achieved, and/or royalties on product sales. We evaluate all deliverables within an arrangement to determine whether or not they provide value on a stand-alone basis. Based on this evaluation, the deliverables are separated into units of accounting. For each unit of accounting identified within an arrangement, we determine the period over which the performance obligation occurs. Revenue is then recognized using the proportional performance method. The proportional performance method is used when the level of effort to complete the performance obligations under an arrangement can be reasonably estimated. We recognize revenue based upon our best estimate of the selling price for each element when there is no other means to determine the fair value of that item and allocate the consideration based on the relative values. The process for determining the best estimate of the selling price involves significant judgment and estimates.

At the inception of each agreement that includes milestone payments, we evaluate whether each milestone is substantive on the basis of the contingent nature of the milestone. This evaluation includes an assessment of whether:

- the consideration is commensurate with either (1) our performance to achieve the milestone, or (2) the enhancement of the value of the delivered item(s) as a result of a specific outcome resulting from our performance to achieve the milestone,
- the consideration relates solely to past performance, and
- the consideration is reasonable relative to all of the deliverables and payment terms within the arrangement.

In making this assessment, we evaluate factors such as the clinical, regulatory, commercial and other risks that must be overcome to achieve the respective milestone, the level of effort and investment required, and whether the milestone consideration is reasonable relative to all deliverables and payment terms in the arrangement. We recognize revenues related to substantive milestones in full in the period in which the substantive milestone is achieved. If a milestone payment is not considered substantive, we recognize the amount associated with the applicable milestone based on the period over which the performance obligation occurs for each deliverable in the arrangement.

We will recognize royalty revenue, if any, based upon actual and estimated net sales by the licensee of licensed products in licensed territories in the period the sales occur. We have not recognized any royalty revenue to date.

Income Taxes

We use the liability method to account for income taxes. Deferred tax assets and liabilities are determined based on differences between financial reporting and income tax basis of assets and liabilities, as well as net operating loss and tax credit carryforwards, and are measured using the enacted tax rates and laws that will be in effect when the differences reverse. Deferred tax assets are reduced by a valuation allowance to reflect the uncertainty associated with

their ultimate realization. The effect of a change in tax rate on deferred taxes is recognized in income or loss in the period that includes the enactment date.

We use our judgment for the financial statement recognition and measurement of a tax position taken or expected to be taken in a tax return. We recognize any material interest and penalties related to unrecognized tax benefits in income tax expense.

Due to the uncertainty surrounding the realization of the net deferred tax assets in future periods, we have recorded a full valuation allowance against our otherwise recognizable net deferred tax assets as of December 31, 2016 and 2015.

Basic and Diluted Net Loss per Common Share

Basic net loss per share is based upon the weighted average number of common shares outstanding during the period. Diluted net loss per share is based upon the weighted average number of common shares outstanding during the period plus the effect of additional weighted average common equivalent shares outstanding during the period when the effect of adding such shares is dilutive. Common equivalent shares result from the assumed exercise of outstanding stock options and the exercise of outstanding warrants (the proceeds of which are then assumed to have been used to repurchase outstanding stock using the treasury stock method). In addition, the assumed proceeds under the treasury stock method include the average unrecognized compensation expense of stock options that are in-the-money. This results in the "assumed" buyback of additional shares, thereby reducing the dilutive impact of stock options. The two-class method is used for outstanding warrants as the warrants are considered to be participating securities, and such method is more dilutive than the treasury stock method. The following outstanding shares of common stock equivalents were excluded from the computation of net loss per share attributable to common stockholders for the periods presented because including them would have been antidilutive:

	At December 31,		
	2016	2015	2014
Stock options	6,067,945	8,265,577	6,577,296
Warrants	1,000,000	1,000,000	1,000,000
Unvested restricted stock	797,111	—	—

Comprehensive Loss

Comprehensive loss is comprised of net loss and other comprehensive income (loss). Other comprehensive income (loss) is comprised of unrealized holding gains and losses arising during the period on available-for-sale securities that are not other-than-temporarily impaired. During the year ended December 31, 2016, there were no material reclassifications out of accumulated other comprehensive income (loss).

Stock-Based Compensation Expense

For awards granted to employees and directors, including our 2013 Employee Stock Purchase Plan, or ESPP, we measure stock-based compensation cost at the grant date based on the estimated fair value of the award and recognize it as expense over the requisite service period on a straight-line basis. We record the expense of services rendered by non-employees based on the estimated fair value of the stock option as of the respective vesting date. We use the Black-Scholes valuation model in determining the fair value of all equity awards. For awards with performance conditions, we estimate the likelihood of satisfaction of the performance conditions, which affects the period over which the expense is recognized. When the performance conditions related to these awards are determined to be probably, we recognize the expense over the requisite service period. We have no awards with market conditions.

Research and Development Expense

Research and development expense consists of expenses incurred in performing research and development activities, including salaries and benefits, overhead expenses including facilities expenses, materials and supplies, preclinical expenses, clinical trial and related clinical manufacturing expenses, comparator drug expenses, stock-based compensation expense, depreciation of equipment, contract services, and other outside expenses. We also include as research and development expense upfront license payments related to acquired technologies which have not yet reached technological feasibility and have no alternative use. We expense research and development costs as they are incurred. Prepaid comparator drug expenses are capitalized and then recognized as expense when title transfers to us. We have been a party to collaboration agreements in which we were reimbursed for work performed on behalf of the collaborator, as well as one in which we reimbursed the collaborator for work it had performed. We record all appropriate expenses under our collaborations as research and development expense. If the arrangement provides for reimbursement of research and development expenses incurred by us, we evaluate the terms of the arrangement to determine whether the reimbursement should be recorded as revenue or as an offset to research and development

expense. If the arrangement provides for us to reimburse the collaborator for research and development expenses or for the achievement of a development milestone for which a payment is due, we record the reimbursement or the achievement of the development milestone as research and development expense.

New Accounting Pronouncements

In May 2014, the Financial Accounting Standards Board, or FASB, issued Accounting Standard Update, or ASU, No. 2014-9, Revenue from Contracts with Customers, or ASU No. 2014-9, which supersedes all existing revenue recognition requirements, including most industry-specific guidance. The new standard requires a company to recognize revenue when it transfers goods or services to customers in an amount that reflects the consideration that the company expects to receive for those goods or services. ASU No. 2014-9 was originally effective for interim and annual periods beginning after December 15, 2016. In August 2015, the FASB issued a one-year deferral of the effective date of this standard to annual reporting periods, and interim reporting periods within those years, beginning after December 15, 2017. Entities are allowed to adopt the standard as of the original effective date. The standard allows for two transition methods - full retrospective, in which the standard is applied to each prior reporting period presented or modified retrospective, in which the cumulative effect of initially applying the standard recognized at the date of initial adoption. We expect to elect the modified retrospective approach and are continuing to evaluate the impact that ASU No. 2014-09 may have on our consolidated financial statements in connection with collaboration and license agreements.

In February 2016, the FASB issued ASU No. 2016-02, Leases, or ASU No. 2016-02, which requires lessees to recognize the assets and liabilities arising from leases on the balance sheet. ASU No. 2016-02 is effective for fiscal years beginning after December 15, 2018, including interim periods within those fiscal years. Early adoption is permitted. We are currently evaluating the method of adoption and the potential impact that ASU No. 2016-02 may have on our financial position and results of operations.

In March 2016, the FASB issued ASU No. 2016-09, Improvements to Employee Share-Based Payment Accounting, or ASU No. 2016-09, which simplifies several aspects of the accounting for share-based payment transactions, including the income tax consequences, classification of awards as either equity or liabilities and classification on the statement of cash flows. ASU No. 2016-09 is effective for annual periods beginning after December 15, 2016, and for interim periods within those annual periods. Early adoption is permitted in any interim or annual period. The Company plans to change how it accounts for forfeitures upon adoption and does not expected to have a material impact on the Company’s consolidated financial statements.

In August 2016, the FASB issued ASU No. 2016-15, Statement of Cash Flows: Classification of Certain Cash Receipts and Cash Payments, or ASU No. 2016-15. The new standard clarifies classification of certain cash receipts and cash payments on the statement of cash flows to reduce existing diversity in practice. The new accounting guidance will be effective on January 1, 2018. We are currently evaluating the method of adoption and the potential impact that ASU No. 2016-15 may have on our financial position and results of operations.

Recently Adopted Accounting Pronouncements

In August 2014, the FASB issued ASU No. 2014-15, Disclosure of Uncertainties about an Entity’s Ability to Continue as a Going Concern, or ASU No. 2014-15, which provides guidance on determining when and how to disclose going concern uncertainties in the financial statements. The new standard requires management to perform interim and annual assessments of an entity’s ability to continue as a going concern. ASU No. 2014-15 is effective for the annual period ending after December 15, 2016, and for annual periods and interim periods thereafter. We adopted ASU No. 2014-15 for the year ending December 31, 2016 and no additional disclosures were required upon adoption based on our existing cash resources and our planned level of spending.

In January 2017, the FASB issued ASU No. 2017-01, Clarifying the Definition of a Business, or ASU No. 2017-01, which clarifies the definition of a business with the objective of adding guidance to assist entities with evaluating whether transactions should be accounted for as acquisitions (or disposals) of assets or businesses. The new accounting guidance is effective for annual periods beginning after December 15, 2017, including interim periods within those periods. Early adoption is permitted. We early adopted ASU No. 2017-01 as of October 1, 2016 and applied this new guidance to our analysis of the Verastem Agreement (Note 12).

3. Stock-Based Compensation

Under each of the stock incentive plans described below, stock option awards made to new employees upon commencement of employment typically provide for vesting of 25% of the shares underlying the award at the end of the first year of service with the remaining 75% of the shares underlying the award vesting ratably on a monthly basis over the following three-year period subject to continued service. Annual grants to existing employees typically provide for monthly vesting over four years. In addition, under each plan, all options granted expire no later than ten years after the date of grant.

2010 Stock Incentive Plan

Our 2010 Stock Incentive Plan, or the 2010 Plan, was approved by our stockholders in May 2010. The 2010 Plan provides for the grant of incentive stock options intended to qualify under Section 422 of the Internal Revenue Code of 1986, as amended, or IRC, as well as nonstatutory stock options, stock appreciation rights, restricted stock, restricted stock units and other stock-based and cash-based awards. Up to 9,785,000 shares of our common stock may be issued pursuant to awards granted under the 2010 Plan, plus an additional amount of our common stock underlying awards issued under the 2000 Stock Incentive Plan, or the 2000 Plan, that expire or are canceled without the holders receiving any shares under those awards. As of December 31, 2016, an aggregate of 5,126,304 shares of our common stock were reserved for issuance upon the exercise of outstanding awards or achievement of awards with performance conditions, and up to 3,288,112 shares of common stock may be issued pursuant to awards granted under the 2010 Plan.

2000 Stock Incentive Plan

The 2000 Stock Incentive Plan, or the 2000 Plan, provided for the grant of stock options intended to qualify as incentive stock options under the IRC, as well as nonstatutory stock options and restricted stock. As of December 31, 2016, an aggregate of 1,738,752 shares of our common stock were reserved for issuance upon the exercise of outstanding awards granted under the 2000 Plan. The 2000 Plan was terminated upon approval of the 2010 Plan; therefore, no further grants may be made under the 2000 Plan.

2013 Employee Stock Purchase Plan

Our ESPP permits eligible employees to purchase shares of our common stock at a discount and consists of consecutive, overlapping 24-month offering periods, each consisting of four six-month purchase periods. On the first day of each offering period, each employee who is enrolled in the ESPP will automatically receive an option to purchase up to a whole number of shares of our common stock. The purchase price of each of the shares purchased in a given purchase period will be 85% of the closing price of a share of our common stock on the first day of the offering period or the last day of the purchase period, whichever is lower. We suspended the ESPP program on June 24, 2016. During 2016, 15,860 shares of common stock were purchased for total proceeds of approximately $18,000. During 2015, 124,358 shares of common stock were purchased for total proceeds of $1.0 million. During 2014, 76,572 shares of common stock were purchased for total proceeds of $0.8 million.

Compensation Expense

Total stock-based compensation expense, related to all equity awards, comprised the following:

	Year Ended December 31,		
	2016	2015	2014
	(in thousands)		
Research and development	$6,421	$8,474	$7,502
General and administrative	7,293	6,226	5,086
Total stock-based compensation expense	$13,714	$14,700	$12,588

As of December 31, 2016, we had approximately $5.1 million of total unrecognized compensation cost, net of estimated forfeitures, related to unvested options and restricted stock, which are expected to be recognized over a weighted-average period of 1.7 years.

Restricted Stock

During 2016, our Board of Directors approved grants of 1,792,250 shares of restricted common stock to eligible employees who continue employment with us. The restricted stock was granted pursuant to our 2010 Plan, is subject to forfeiture and will vest based on the achievement of specified performance conditions. The grant date fair value of the restricted stock is based on the closing price of our common stock on each of the grant dates. We recognized $1.2

million of stock compensation expense based on the fair value measured on the date of grant for the year ended December 31, 2016 related to the vested restricted stock.

A summary of our restricted stock activity for the year ended December 31, 2016 is as follows:

	Restricted Stock	Weighted-Average Grant-Date Fair Value
Unvested at January 1, 2016	—	$ —
Granted	1,792,250	1.49
Vested	(751,789)	1.54
Canceled	(243,350)	1.54
Unvested at December 31, 2016	797,111	$ 1.43

Stock Options

Valuation Assumptions

We estimate the fair value of stock options at the date of grant using the Black-Scholes valuation model with the following weighted-average assumptions:

	December 31,		
	2016	2015	2014
Risk-free interest rate	1.8 %	1.5 %	1.7 %
Expected annual dividend yield	—	—	—
Expected stock price volatility	73.0 %	70.8 %	70.9 %
Expected term of options	5.4 years	5.4 years	5.0 years

The valuation assumptions were determined as follows:

- Risk-free interest rate: The yield on zero-coupon U.S. Treasury securities for a period that was commensurate with the expected term of the awards.
- Expected annual dividend yield: The estimate for annual dividends was zero, because we have not historically paid a dividend and do not intend to do so in the foreseeable future.
- Expected stock price volatility: We determined the expected volatility by using our available implied and historical price information.
- Expected term of options: The expected term of the awards represents the period of time that the awards were expected to be outstanding. We used historical data and expectations for the future to estimate employee exercise and post-vest termination behavior.

We stratify employees into two groups to evaluate exercise and post-vesting termination behavior. We estimate forfeitures based upon historical data, adjusted for known trends, and will adjust the estimate of forfeitures if actual forfeitures differ or are expected to differ from such estimates. Subsequent changes in estimated forfeitures are recognized through a cumulative adjustment in the period of change and will also impact the amount of stock-based compensation expense in future periods. As of December 31, 2016, 2015 and 2014, the weighted-average forfeiture rate was estimated to be 24%, 14%, and 14%, respectively.

All options granted to employees during the years ended December 31, 2016, 2015 and 2014 were granted with exercise prices equal to the fair market value of our common stock on the date of grant. We consider the closing price of our common stock as reported on the NASDAQ Global Select Market to be the fair market value.

A summary of our stock option activity for the year ended December 31, 2016 is as follows:

	Stock Options	Weighted-Average Exercise Price	Weighted-Average Remaining Contractual Life (years)	Aggregate Intrinsic Value (in millions)
Outstanding at January 1, 2016	8,265,577	$ 13.73		
Granted	1,617,472	6.14		
Exercised	(67,077)	6.40		