INFINITY PHARMACEUTICALS, INC.
Form 10-K
February 23, 2016
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UNITED STATES

SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

FORM 10-K

(Mark One)

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

For the fiscal year ended: December 31, 2015

¨ **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, $.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 x

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 x

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 x 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 x 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. x

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 x	Accelerated filer ¨	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 x

The aggregate market value of voting Common Stock held by non-affiliates of the registrant as of June 30, 2015 was $528,764,262 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 February 16, 2016: 49,339,647

Documents incorporated by reference:

Portions of our definitive proxy statement to be filed with the Securities and Exchange Commission no later than April 29, 2016 in connection with our 2016 annual meeting of stockholders are incorporated by reference into Part III of this Annual Report on Form 10-K.

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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 discovery and development goals and milestones in 2016, our future discovery and 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, potential, will, 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 discovery and clinical 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 discovering, developing and delivering best-in-class medicines to 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. Our most advanced product candidate is duvelisib, also known as IPI-145, an oral, dual-inhibitor of the delta and gamma isoforms of phosphoinositide-3-kinase, or PI3K, which is currently being evaluated for the treatment of hematologic malignancies, or blood cancers. We believe that duvelisib is the only inhibitor of PI3K-delta and gamma being investigated in Phase 3 clinical trials. We are pursuing duvelisib in oncology through a strategic collaboration with AbbVie Inc., or AbbVie. For information regarding our collaboration, please see below under the heading *AbbVie* in the section entitled Strategic Alliances.

Through the efforts of our dedicated discovery research program, during 2016 we expanded our pipeline with the addition of IPI-549, an orally administered, clinical-stage, immuno-oncology product candidate that selectively inhibits the gamma isoform of PI3K. In addition to duvelisib and IPI-549, we are working to generate new product candidates for potential investigation in oncology.

Product Development Pipeline

Historically, our product development programs have arisen from a combination of internally developed programs and strategic licensing arrangements. We focus on targets that have the potential to fundamentally change how disease is treated and where we believe we can use our scientific capabilities to identify differentiated product candidates with well-defined development paths. We seek to leverage what we believe to

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be our innovative approaches to drug discovery and translational medicine and our robust internal capabilities across all of the relevant scientific disciplines, including medicinal chemistry, cell biology, biochemistry, pharmacology and molecular pathology. Our goal is to integrate these disciplines to rapidly identify product candidates and to better understand which populations of patients may benefit most from our product candidates.

The table and descriptions below summarize key information about our product candidates, duvelisib and IPI-549. None of our product candidates are approved for any indication by the United States Food and Drug Administration or any other regulatory agency.

Duvelisib: Dual Inhibitor of PI3K Delta and Gamma

	Indication	Status
Indolent non-Hodgkin Lymphoma		
DYNAMO	Refractory indolent non-Hodgkin lymphoma	Phase 2, open-label, single-arm clinical study Designed with potential to support accelerated approval Primary endpoint: response rate according to the International Working Group, or IWG, criteria Enrollment complete: 129 patients Expect to report topline data in the third quarter of 2016
CONTEMPO	Previously untreated follicular lymphoma	Phase 1b/2 open label, two-arm clinical study Duvelisib plus obinutuzumab or rituximab Targeting approximately 100 patients Primary endpoint: Safety; complete response rate according to IWG criteria Enrollment ongoing Expect to report initial data from this study in the second half of 2016
BRAVURA	Relapsed indolent non-Hodgkin lymphoma	Phase 3, double-blind, placebo-controlled clinical study Duvelisib plus rituximab and bendamustine compared to placebo plus rituximab and bendamustine Targeting approximately 600 patients Primary endpoint: progression-free survival Enrollment ongoing
FRESCO	Relapsed or refractory follicular lymphoma	Phase 2 randomized clinical study Duvelisib in combination with rituximab compared to chemotherapy in combination with rituximab Targeting 230 patients

		Primary endpoint: progression-free survival Enrollment ongoing
DYNAMO+R	Previously treated follicular lymphoma	Phase 3 randomized, placebo-controlled clinical study Duvelisib plus rituximab compared to placebo plus rituximab Study identified for closure

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	Indication	Status
Chronic Lymphocytic Leukemia		
DUO	Relapsed or refractory chronic lymphocytic leukemia	Phase 3, randomized, monotherapy clinical study Duvelisib compared to ofatumumab Primary endpoint: progression-free survival Enrollment complete: 319 patients Expect to report topline data in the second half of 2016
SYNCHRONY	Patients with chronic lymphocytic leukemia whose disease has progressed following treatment with a Bruton s tyrosine kinase inhibitor	Phase 1b open-label clinical study Duvelisib in combination with obinutuzumab Primary endpoint: Safety Targeting approximately 64 patients Enrollment ongoing
Advanced Hematologic Malignancies		
Duvelisib + Venetoclax	Relapsed or refractory indolent or aggressive non-Hodgkin lymphoma, chronic lymphocytic leukemia, or small lymphocytic lymphoma	Phase 1b/2 open label clinical study Duvelisib in combination with venetoclax Targeting approximately 174 patients Initiated, not yet recruiting
IPI-549: PI3K Gamma-Selective Inhibitor		
Solid Tumors	Patients with a range of solid tumors, including melanoma and non-small cell lung cancer	Phase 1 clinical study Includes a dose-escalation phase and an expansion phase, and is designed to evaluate IPI-549 as a monotherapy as well as in combination with an anti-PD-1 antibody therapy Enrollment ongoing

PI3 Kinase Inhibitor Program

The PI3Ks are a family of enzymes involved in multiple cellular functions, including cell proliferation and survival, cell differentiation, cell migration, and immunity. PI3K-delta and PI3K-gamma are two proteins with distinct and mostly non-overlapping roles believed to support the growth and survival of malignant B-cells. Specifically, preclinical data suggest that PI3K-delta signaling can lead to the proliferation of malignant B-cells, and that both PI3K-gamma and PI3K-delta play an important role in the formation and maintenance of the supportive tumor microenvironment.

Duvelisib: Targeting Hematologic Malignancies by Dual Inhibition of PI3K Delta and Gamma Isoforms

We believe that dual inhibition of PI3K-delta and PI3K-gamma may provide multiple opportunities to develop a differentiated therapy for the treatment of certain hematologic malignancies. Our lead product candidate, duvelisib, is an oral, dual inhibitor of PI3K-delta and PI3K-gamma, which we believe is the only dual inhibitor of PI3K-delta and PI3K-gamma being investigated in Phase 3 clinical trials. Duvelisib is an investigational compound, and its safety and efficacy have not yet been evaluated by the FDA or any other health authority.

Hematologic malignancies are cancers of the blood or bone marrow such as non-Hodgkin lymphoma, or NHL, and chronic lymphocytic leukemia, or CLL. It is estimated that there will be approximately 134,650 newly diagnosed cases of NHL in the seven major pharmaceutical markets (United States, France, Germany, Italy,

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Japan, Spain, and United Kingdom) in 2016. The distribution of NHL subtypes differs by country. In the United States and major European countries in 2012, diffuse large B-cell lymphoma, or DLBCL, accounted for 37-43% of NHL cases while CLL accounted for 25-33% and follicular lymphoma for 17-22%. Even with advances in treatment options for these diseases, the clinical outlook for patients still remains poor. A significant proportion of patients relapse following treatment and become refractory to current agents, representing a significant unmet medical need.

To address this need, we are conducting DUETTS (Duvelisib Trials in Hematologic Malignancies), a worldwide clinical investigation of duvelisib in blood cancers initially focusing on lymphoma and CLL. The investigation of duvelisib in our DUETTS trials, discussed below in detail, is supported by data from our Phase 1, open-label, dose-escalation study designed to evaluate the safety, pharmacokinetics and clinical activity of duvelisib in patients with advanced hematologic malignancies. The maximum tolerated dose of duvelisib was defined at 75 mg twice daily, or BID, and we have closed the trial to further enrollment. Data from this study, presented in December 2014 at the Annual Meeting of the American Society for Hematology, or ASH 2014, showed that duvelisib is clinically active in CLL, iNHL, aggressive NHL, or aNHL, and T-cell lymphoma, as well as other hematologic malignancies. We are continuing to evaluate duvelisib in 14 patients with hematologic malignancies across multiple dose levels from 10 mg BID to 75 mg BID with eight patients (57%) continuing to receive 25 mg bid. These 14 remaining patients represent several hematology indications: four patients with iNHL, mantle cell lymphoma, or MCL, or CLL; seven treatment-naïve, high-risk CLL patients, with high-risk defined as patients aged 65 or older or having either of two genetic abnormalities known as a 17p- deletion or a p53 mutation; two patients with cutaneous T-cell lymphoma, or CTCL, or noncutaneous T-cell lymphoma; and one patient with aNHL.

Indolent Non-Hodgkin Lymphoma

As part of the DUETTS program in lymphoma, we are conducting DYNAMO , a Phase 2, open-label, single arm monotherapy study evaluating the safety and efficacy of duvelisib dosed at 25 mg twice daily in 129 patients with iNHL. DYNAMO enrollment criteria include patients with follicular lymphoma, the most common subtype of iNHL, marginal zone lymphoma, and small lymphocytic lymphoma, or SLL, whose disease is refractory to rituximab, a monoclonal antibody treatment, and to either chemotherapy or radioimmunotherapy and who must have progressed within six months of receiving their last therapy. The primary endpoint of the study is response rate according to the International Working Group, or IWG, Criteria. We completed enrollment in DYNAMO in September 2015 and expect to report topline data in the third quarter of 2016.

The DYNAMO study is designed with the potential to support accelerated approval of duvelisib in patients with follicular lymphoma and SLL, assuming we are able to generate positive safety and efficacy data from the study and on the condition that we conduct a confirmatory study. The FDA has granted orphan drug designation to duvelisib for the potential treatment of follicular lymphoma, and has granted fast track designation to the investigation of duvelisib for the treatment of patients with follicular lymphoma who have received at least two prior therapies. The availability of accelerated approval is uncertain, and is dependent on a number of factors including whether duvelisib has demonstrated a meaningful benefit relative to available therapies. For a further discussion of the FDA s accelerated approval pathway, and certain risks related to our ability to seek accelerated approval for duvelisib, see Government Regulation and Product Approvals Review and Approval of Drugs in the United States and Risk Factors Risks Related to Regulatory Approval and Marketing of Our Product Candidates and Other Legal Compliance Matters elsewhere in this report.

The investigation of duvelisib in DYNAMO is supported by preliminary data from our Phase 1, open-label, dose-escalation study designed to evaluate the safety, pharmacokinetics and clinical activity of duvelisib in patients with advanced hematologic malignancies, discussed in more detail below. Data presented at ASH 2014 from our Phase 1 study have demonstrated that duvelisib administered at 25 mg BID is clinically active in patients with iNHL, with a 72% (13 of 18 evaluable patients) overall response rate and a 33% (6 of 18 evaluable

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patients) complete response rate. Among patients with follicular lymphoma, the overall response rate was 69% (9 of 13 evaluable patients), including a 38% complete response rate (5 of 13 evaluable patients). As of the time of ASH 2014, the median progression free survival and median overall survival had not yet been reached, with 69% of patients progression-free and with an 89% overall survival rate at 24 months. Duvelisib was generally well tolerated, and the majority of side effects were low-grade, asymptomatic and transient. The majority of adverse events were Grade 1 or 2, reversible and/or clinically manageable. At the 25 mg BID dose, the most common Grade 3 side effects were an increase in alanine aminotransferase, or ALT, or aspartate aminotransferase, or AST (32%), diarrhea (16%), neutropenia and pneumonia (11% each). Grade 4 neutropenia was 11% (two patients), Grade 4 ALT or AST increase was 5% (one patient) and Grade 4 pneumonia was 5% (one patient).

Additional DUETTS clinical studies in lymphoma include CONTEMPO, BRAVURA, and FRESCO. CONTEMPO is a Phase 1b/2 clinical study of duvelisib in combination with obinutuzumab, a monoclonal antibody treatment, or rituximab in patients with previously untreated follicular lymphoma. We expect to report initial data from CONTEMPO in the second half of 2016. BRAVURA is a Phase 3, double-blind, placebo-controlled study in patients with relapsed iNHL designed to evaluate the safety and efficacy of duvelisib plus rituximab and bendamustine, a chemotherapy, compared to placebo plus rituximab and bendamustine in approximately 600 patients. The primary endpoint is progression-free survival. We requested advice from the FDA to determine if BRAVURA, as designed, can serve as a confirmatory study if DYNAMO supports an accelerated approval. FRESCO is a Phase 2 randomized study in patients with relapsed or refractory follicular lymphoma that is designed to evaluate the safety and efficacy of duvelisib plus rituximab compared to rituximab plus a combination of chemotherapies referred to as CHOP in approximately 230 patients. The chemotherapies included in CHOP are cyclophosphamide, doxorubicin hydrochloride, vincristine sulfate, and prednisone. The primary endpoint of FRESCO is progression-free survival. DYNAMO+R, a Phase 3 randomized, placebo-controlled study evaluating duvelisib dosed at 25 mg BID in combination with rituximab compared to placebo plus rituximab in patients with previously treated follicular lymphoma has been identified for closure and is no longer enrolling patients.

Chronic Lymphocytic Leukemia

As part of the DUETTS investigation in CLL, we are conducting DUO™ and SYNCHRONY. DUO is a randomized, Phase 3 monotherapy study designed to evaluate the safety and efficacy of duvelisib dosed at 25 mg BID compared to ofatumumab, a monoclonal antibody treatment, in 319 patients with relapsed or refractory CLL. The primary endpoint of the study is progression-free survival. Enrollment of DUO was completed in November 2015, and we expect to report topline data in the second half of 2016 if supported by the interim analysis. SYNCHRONY is a Phase 1b trial of duvelisib in combination with obinutuzumab in CLL patients whose disease has progressed following treatment with a Bruton s tyrosine kinase, or BTK, inhibitor. This study is supported by Phase 1 data of duvelisib in six CLL patients previously treated with ibrutinib, a BTK inhibitor, presented at ASH 2014. Early clinical activity was observed, with partial responses in one CLL patient and stable disease in five CLL patients. The safety profile of duvelisib in these patients appeared consistent with the safety profile observed in other patients with advanced hematologic malignancies treated with duvelisib in the Phase 1 study. The FDA and the European Medicines Agency, or EMA, have granted orphan drug designation to duvelisib for the potential treatment of CLL and SLL. The FDA has granted fast track designation to the investigation of duvelisib for the potential treatment of patients with CLL who have received at least one prior therapy.

The investigation of duvelisib in DUO and SYNCHRONY is supported by preliminary data from our Phase 1 study that demonstrated that duvelisib administered at 25 mg BID is clinically active in patients with relapsed or refractory CLL, with a 57% overall response rate (17 of 30 evaluable patients), including one complete response. At the time of ASH 2014, the median progression free survival and median overall survival in the 31 patients who received the 25 mg BID dose had not yet been reached with a median time on treatment of 7.6 months (range: 0.9 months to 34.1 months). The majority of side effects were Grade 1-2, reversible and/or clinically manageable. Across all doses evaluated in the study (N = 55), the most common Grade 3 side effects were pneumonia (24%), neutropenia (18%) and anemia (16%). Grade 4 pneumonia was 2% (one patient), Grade 4 neutropenia was 24% (13 patients) and Grade 4 anemia was 2% (one patient).

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Additional data from our Phase 1 study has demonstrated clinical activity of duvelisib dosed at 25 mg BID in previously untreated patients with CLL, with an 88% overall response rate (15 partial responses out of 17 evaluable patients, with two additional patients exhibiting stable disease) based on International Workshop on Chronic Lymphocytic Leukemia, or iwCLL, criteria. The study included 18 treatment-naïve CLL patients who were high-risk, defined as age 65 or over and/or having certain genetic abnormalities known as 17p deletions or p53 mutations. Data presented at the annual meeting of the American Society of Clinical Oncology, or ASCO, in June 2015, showed that the median time to response was 3.7 months, and the median progression-free survival and median overall survival had not yet been reached. The majority of adverse events were grade 1 or grade 2 and clinically manageable. The most common Grade 3 side effects among the 18 enrolled patients were diarrhea (22%), an increase in ALT and AST (17%), and rash (11%). Five patients (28%) had Grade 4 neutropenia or decreases in neutrophil count. There were no Grade 4 events of diarrhea, increases in ALT or AST or rash. Six patients discontinued treatment due to an adverse event.

Investigating Duvelisib in Combination with Venetoclax

As part of our collaboration, AbbVie has initiated the first clinical study investigating duvelisib in combination with venetoclax, a first-in-class, investigational, selective B-cell lymphoma 2, or BCL-2, inhibitor. This Phase 1b/2 trial is designed to evaluate the safety and activity of duvelisib in combination with venetoclax in approximately 174 patients with relapsed or refractory, iNHL, aNHL, CLL or SLL. Preclinical data for duvelisib presented at ASCO in June 2015 demonstrates synergy with standards-of-care and emerging therapeutics in development for hematologic malignancies, including duvelisib in combination with venetoclax. For information regarding our collaboration with AbbVie, please see below under the heading *AbbVie* in the section entitled Strategic Alliances.

T-Cell Lymphoma, aNHL and Other Lymphomas

Data from our Phase 1 study presented at ASH 2014 and at the 7th Annual T-cell Lymphoma Forum held in January 2015 demonstrates that duvelisib is clinically active in advanced T-cell lymphomas. Treatment with duvelisib in heavily pre-treated patients with relapsed or refractory T-cell lymphoma resulted in an overall response rate of 42% (14 of 33 patients evaluable for response), including two complete responses and twelve partial responses. Among the 15 patients with peripheral T-cell lymphoma, or PTCL, who were evaluable for response, treatment with duvelisib resulted in two complete responses and six partial responses, for an overall response rate of 53%. Among the 18 patients with CTCL evaluable for response, treatment with duvelisib resulted in to six partial responses for an overall response rate of 33%. Stable disease was observed in one patient with PTCL and six patients with CTCL. The Grade 3 side effects in patients with T-cell lymphoma included increases in ALT or AST in 11 patients (31%), rash in six patients (17%) and pneumonia in five patients (14%). Two patients (6%) had Grade 4 ALT or AST increases, and one patient (3%) had Grade 4 pneumonia. The majority of patients (27 of 35) received duvelisib dosed at 75 mg BID.

Duvelisib Global Regulatory Filings

We expect to report topline data from our DYNAMO study in the third quarter of 2016, and if supported by the DYNAMO data, we anticipate that we will submit a New Drug Application, or NDA, in the fourth quarter of 2016 seeking accelerated approval of duvelisib from the FDA for the treatment of follicular lymphoma and SLL. In addition, we expect to conduct a planned interim analysis of data from our DUO study in the second half of 2016. If supported by the interim analysis of data from our DUO study, we expect to report topline data from our DUO study in the second half of 2016 and submit an NDA in the fourth quarter of 2016 seeking regular approval of duvelisib from the FDA for the treatment of certain patients with CLL. Additionally, if supported by an interim analysis of data from the DUO study and data from our DYNAMO study, we expect that AbbVie will submit a Marketing Authorization Application, or MAA, in the fourth quarter of 2016 seeking approval from the EMA to market duvelisib for certain patients with follicular lymphoma and CLL.

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

In 2015, we expanded our pipeline to include IPI-549, an orally administered, selective PI3K-gamma inhibitor that we intend to evaluate as a potential treatment in solid tumors. Preclinical data from studies investigating IPI-549 indicates that IPI-549 has the potential to heighten an anti-cancer response by targeting macrophages in the immune-suppressive tumor microenvironment and may have the potential to treat a broad range of solid tumors. IPI-549 has demonstrated dose-dependent, single-agent, anti-tumor activity in multiple solid tumor models, including mouse models of lung cancer, colon cancer and breast cancer. Additionally, mice treated with IPI-549 in combination with a type of therapy called a checkpoint inhibitor showed greater tumor growth inhibition than treatment with either IPI-549 or the checkpoint inhibitor alone. Preclinical in vivo data also demonstrated that T-cells, a type of cell that plays a role in the human immune system, are required for the anti-tumor activity of IPI-549. These data were presented at CRI-CIMT-EATI-AACR - The Inaugural International Cancer Immunotherapy Conference in September 2015.

Based on our preclinical data generated to date, we have initiated a Phase 1 first-in-human study that 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 a checkpoint inhibitor therapy 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 and melanoma.

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 to date have been generated under research collaborative agreements including our corporate alliances.

AbbVie

On September 2, 2014, we entered into a collaboration and license agreement with AbbVie, which we refer to as the AbbVie Agreement. Under the AbbVie Agreement, we are collaborating with AbbVie to develop and commercialize products containing duvelisib, which we refer to as Duvelisib Products, in oncology indications. IPI-549 is excluded from the collaboration. Under the terms of the AbbVie Agreement, we have granted to AbbVie licenses under applicable patents, patent applications, know-how and trademarks to develop, commercialize and manufacture Duvelisib Products in oncology indications. These licenses are generally co-exclusive with rights we retain, except that we have granted AbbVie exclusive licenses to commercialize Duvelisib Products outside the United States. We and AbbVie retain the rights to perform our respective obligations and exercise our respective rights under the AbbVie Agreement, and we and AbbVie may each grant sublicenses to affiliates or third parties.

Under the AbbVie Agreement, we and AbbVie have created a governance structure, including committees and working groups to manage the development, manufacturing and commercialization responsibilities for Duvelisib Products. Generally, we and AbbVie must mutually agree on decisions, although in specified circumstances either we or AbbVie would be able to break a deadlock.

We and AbbVie share oversight of development and have each agreed to use diligent efforts, as defined in the AbbVie Agreement, to carry out our development activities under an agreed upon development plan. We have primary responsibility for the conduct of development of Duvelisib Products, unless otherwise agreed, and AbbVie has responsibility for the conduct of certain contemplated combination clinical studies, including those examining duvelisib and venetoclax, which we refer to as the AbbVie Studies. We have the responsibility to manufacture Duvelisib Products until we transition manufacturing responsibility to AbbVie, which we expect to

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occur as promptly as practicable while ensuring continuity of supply. Excluding the AbbVie Studies, we are responsible for all costs to develop and manufacture Duvelisib Products up to a maximum amount of $667 million after which we will share Duvelisib Product development and manufacturing costs equally with AbbVie. The development and manufacturing costs of the AbbVie Studies will be shared equally.

We and AbbVie share operational responsibility and decision making authority for commercialization of Duvelisib Products in the United States. Specifically, we have the primary responsibility for advertising, distribution, and booking sales, and we share certain other commercialization functions with AbbVie. Assuming regulatory approval, we and AbbVie are obligated to each provide half of the sales representative effort to promote Duvelisib Products in the United States. Outside the United States, AbbVie has, with limited exceptions, operational responsibility and decision making authority to commercialize Duvelisib Products. We and AbbVie will share the cost of manufacturing and supply for commercialization of Duvelisib Products in the United States, and AbbVie will bear the cost of manufacturing and supply for commercialization of Duvelisib Products outside the United States.

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 in September 2015. Further, AbbVie has agreed to pay us up to an additional $400 million in potential future milestone payments comprised of $125 million associated with the acceptance by the FDA of the first NDA submission for duvelisib, $75 million associated with the acceptance of the first MAA submission for duvelisib, up to $75 million associated with the achievement of specified regulatory approval milestones, and up to $125 million associated with the achievement of specified commercialization milestones. Under the terms of the AbbVie Agreement, we and AbbVie will equally share commercial profits or losses of Duvelisib Products in the United States, including sharing equally the existing royalty obligations to Mundipharma International Corporation Limited, or Mundipharma, and Purdue Pharmaceutical Products L.P., or 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. For more information about such obligations, refer to the sections below titled Takeda and Mundipharma and Purdue.

Additionally, AbbVie has 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. We are responsible for the existing royalty obligations to Mundipharma and Purdue outside the United States, and AbbVie has agreed to reimburse us for our existing Duvelisib Product milestone payment obligations to Takeda outside the United States. The tiered royalty from AbbVie is subject to a reduction of 4% at each tier if our royalties to Mundipharma and Purdue are reduced according to the terms of our respective agreements with Mundipharma and Purdue. This tiered royalty can further be reduced based on specified factors, including patent expiry, generic entry, and royalties paid to third parties with blocking intellectual property. These royalties are payable on a product-by-product and country-by-country basis until AbbVie ceases selling the product in the country.

Subject to limited exceptions, we have agreed that we and our affiliates will not commercialize, or assist others in commercializing, in oncology indications any product that is a PI3K delta, gamma inhibitor that meets certain agreed-to criteria, other than Duvelisib Products, and AbbVie has agreed to similar restrictions. Registration-directed clinical trials and commercialization of Duvelisib Products for uses outside of oncology indications would require our and AbbVie s mutual consent.

The AbbVie Agreement will remain in effect until all development, manufacturing and commercialization of Duvelisib Products cease, unless terminated earlier. Either we or AbbVie may terminate the AbbVie Agreement if the other party is subject to certain insolvency proceedings or if the other party materially breaches the AbbVie Agreement and the breach remains uncured for a specified period, which may be extended in certain circumstances. However, we may terminate the AbbVie Agreement only on a country-by-country basis in the event AbbVie is not using diligent efforts to obtain regulatory approval or to commercialize Duvelisib Products

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in a country outside the United States. AbbVie may also terminate the AbbVie Agreement for convenience after a specified notice period. In the event there is a material uncured breach by either us or AbbVie of development or commercialization obligations, the non-breaching party may also have the right to assume and conduct such applicable development or commercialization obligations. If AbbVie or any of its affiliates or sublicensees challenges the patents we have licensed to AbbVie, we can terminate the AbbVie Agreement if the challenge is not withdrawn after a specified notice period.

If the AbbVie Agreement is terminated, we would receive all rights to the regulatory filings related to duvelisib upon our request, our license to AbbVie would terminate, and AbbVie would grant us a perpetual, irrevocable license to develop, manufacture and commercialize products containing duvelisib, excluding any compound which is covered by patent rights controlled by AbbVie or its affiliates. This license would be royalty-free, unless the AbbVie Agreement is terminated for material breach, in which case, depending on the breaching party and the timing of the material breach, a royalty rate may be payable by us ranging from a low single-digit percentage to a low double-digit percentage of net sales, and, in some cases, subject to a payment cap.

If the AbbVie Agreement is terminated, we would not be entitled to receive payment for any milestone achieved after notice of termination but before the effective date of termination. Further, if the AbbVie Agreement is terminated, there are certain wind-down obligations to ensure a smooth transition of the responsibilities of the parties including, unless the AbbVie Agreement is terminated by AbbVie for our material breach, the continued conduct of certain development and commercialization activities by AbbVie for a limited transition period and the continued funding by AbbVie of its half of the cost of the AbbVie Studies ongoing at the time of termination, except for those AbbVie Studies that may be transitioned to Infinity following termination.

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, and we paid Intellikine a $13.5 million upfront license fee. In January 2012, Intellikine was acquired by Takeda, acting through its Millennium business unit. We refer to our PI3K inhibitor program licensor as Takeda. In December 2012, we amended and restated our development and license agreement with Takeda.

Under the terms of the amended and restated agreement, we retained worldwide development rights and, in exchange for an agreement to pay Takeda $15 million in installments, we regained commercialization rights for products arising from the agreement for all therapeutic indications, and we are solely responsible for research conducted under the agreement.

We are obligated to pay to Takeda up to $5 million in remaining 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 $450 million in success-based milestone payments for the approval and commercialization of two distinct products, of which one could be a Duvelisib Product and the other could be a product containing IPI-549. In February 2014, we paid Takeda a $10 million milestone payment in connection with the initiation of DUO, our Phase 3 study of duvelisib in patients with relapsed or refractory CLL. 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 million. As a result of our exercise of this option, we are no longer obligated under the amended and restated development and license agreement to pay to Takeda tiered royalties with respect to worldwide net sales in oncology indications of products containing or comprised of duvelisib.

Except for duvelisib products 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

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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 amended and restated 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. Either party may terminate the 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 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 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 agreement also provides for customary reciprocal indemnification obligations of the parties.

Mundipharma and Purdue

On July 17, 2012, we terminated our strategic alliance with Mundipharma and Purdue, and we entered into termination and revised relationship agreements with each of those entities, which we refer to as the 2012 Termination Agreements. The strategic alliance was previously governed by strategic alliance agreements that we entered into with each of Mundipharma and Purdue in November 2008. The strategic alliance agreement with Purdue was focused on the development and commercialization in the United States of products targeting fatty acid amide hydrolase, or FAAH. The strategic alliance agreement with Mundipharma was focused on the development and commercialization outside the United States of all products and product candidates that inhibit or target the Hedgehog pathway, FAAH, PI3K and product candidates arising out of our early discovery projects in all disease fields.

Under the terms of the 2012 Termination Agreements:

All intellectual property rights that we had previously licensed to Mundipharma and Purdue to develop and commercialize products under the previous strategic alliance agreements terminated resulting in the return to us of worldwide rights to all product candidates that had previously been covered by the strategic alliance.

We have no further obligation to provide research and development services to Mundipharma and Purdue as of July 17, 2012.

Mundipharma and Purdue have no further obligation to provide research and development funding to us. Under the strategic alliance, Mundipharma was obligated to reimburse us for research and development expenses we incurred, up to an annual aggregate cap for each strategic alliance program other than FAAH. We did not record a liability for amounts previously funded by Purdue and Mundipharma as this relationship was not considered a financing arrangement.

We are obligated to pay Mundipharma and Purdue a 4% royalty in the aggregate, subject to reduction as described below, on worldwide net sales of products that were covered by the alliance until such time as they have recovered approximately $260 million, representing the research and development funding paid to us for research and development services performed by us through the termination of the strategic alliance. After this cost recovery, our royalty obligations to Mundipharma and Purdue will be reduced to a 1% royalty on net sales in the United States of products that were previously subject to the strategic alliance. All payments are contingent upon the successful commercialization of products that were subject to the alliance, which products require significant further development. As such, there is significant uncertainty about whether any such products will ever be approved or commercialized. If no products are commercialized, no payments will be due by us to Mundipharma and Purdue; therefore, no amounts have been accrued.

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Royalties are payable under these agreements until the later to occur of the last-to-expire of specified patent rights and the expiration of non-patent regulatory exclusivities in a country, provided that if royalties are payable solely on the basis of non-patent regulatory exclusivity, each of the royalty rates is reduced by 50%. In addition, royalties payable under these agreements after Mundipharma and Purdue have recovered all research and development expenses paid to us are subject to reduction on account of third-party royalty payments or patent litigation damages or settlements which might be required to be paid by us if litigation were to arise, with any such reductions capped at 50% of the amounts otherwise payable during the applicable royalty payment period.

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 eight issued or allowed U.S. patents related to our duvelisib program, which expire on various dates between 2029 and 2032, excluding any patent term extension. We have three issued or allowed U.S. patents related to our PI3K gamma program, which expire on various dates between 2033 and 2034, excluding any patent term extension. In addition, we have approximately 275 patents and patent applications pending worldwide related to our PI3K programs. Any patents that may issue from our pending patent applications would expire between 2029 and 2035, excluding any patent term extension. These patents and patent applications disclose compositions of matter, pharmaceutical compositions, methods of use and synthetic methods.

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 protect our proprietary technology and processes, in part, by confidentiality agreements with our employees, consultants, collaborators and contractors.

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.

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

PI3K Inhibitor Program

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

- Gilead Sciences, Inc., or Gilead, has received approval from the FDA of idelalisib for the treatment of people with CLL, SLL, or follicular lymphoma, and which we believe is conducting a Phase 1b clinical trial of acalisib;
- Bayer AG, which we believe is conducting Phase 2 and Phase 3 clinical trials of copanlisib;
- TG Therapeutics, Inc., which we believe is conducting Phase 1, Phase 2, and Phase 3 clinical trials of TGR-1202;
- Novartis, which we believe is conducting a Phase 2 clinical trial of buparlisib;
- Acerta Pharma BV, which we believe is conducting Phase 1 clinical trials of ACP 319;
- Genentech, which we believe is conducting a Phase 1 clinical trial of apitolisib;
- Incyte Corporation, which we believe is conducting a Phase 1 clinical trial of INCB-050465, and which we also believe is conducting a Phase 1 clinical trial of INCB-040093; and
- Rhizen Pharmaceuticals S.A., which we believe is conducting Phase 1 clinical trials of RP-6530.

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

- Pharmacyclics LLC, a wholly-owned subsidiary of AbbVie, through its collaboration with Janssen Biotech, which has received approval from the FDA of ibrutinib, a BTK inhibitor, for the treatment of people with MCL, CLL, or Waldenström s macroglobulinemia, and is conducting multiple late stage clinical studies of ibrutinib in additional hematologic malignancies;
- AbbVie, which we believe is conducting a Phase 3 and multiple Phase 1 and Phase 2 clinical trials of venetoclax, a BCL-2 inhibitor, in hematologic malignancies;

Celgene Corporation, which has received FDA approval of lenalidomide, an immunomodulator, for the treatment of people with multiple myeloma, MCL, and myelodyplastic syndromes, and is conducting late stage clinical studies of lenalidomide in additional hematologic malignancies; we also believe that Celgene is conducting a Phase 1 clinical trial of CC-292, a BTK inhibitor, in patients with CLL;

Acerta Pharma BV, which we believe is conducting a Phase 3 clinical trial of ACP-196, a BTK inhibitor, in patients with CLL;

Incyte Corporation, which has received FDA approval of ruxolitinib, a JAK inhibitor, in patients with intermediate or high-risk myelofibrosis, and which we believe is conducting a Phase 2 clinical trial in CLL;

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Novartis AG, which we believe is conducting a Phase 2 trial of CTL-019, which targets CD-19, in a trial that includes iNHL and CLL and acute lymphocytic leukemia, or ALL, patients;

Novartis AG, which we believe is conducting a Phase 1b trial of BCL-201, a BCL-2 inhibitor, in combination with idelalisib in patients with follicular lymphoma or MCL;

Genentech, which we believe is conducting a Phase 2 trial of polatuzumab vedotin, which targets CD79b ADC, in patients with follicular lymphoma or DLBCL;

MorphoSys, which we believe is conducting Phase 2 clinical trials of MOR208, a B-lymphocyte antigen CD-19 inhibitor, in patients with NHL, CLL, and ALL;

Celgene, which we believe is conducting Phase 1/2 and Phase 1 clinical trials of CC-122, a pleiotropic pathway modifier, in patients with CLL, and NHL;

BeiGene Co., Ltd, which we believe is conducting Phase 1 clinical trials of BGB-3111, a BTK inhibitor, in patients with B-cell malignancies;

Gilead Sciences, Inc./Ono Pharmaceutical Group, which we believe is conducting Phase 1 clinical trials of ONO-4059, a BTK inhibitor, in patients with NHL and CLL; and

Bristol-Myers Squibb Company, Roche Group and its subsidiary Genentech, and AstraZeneca PLC, each of which we believe is conducting clinical trials of anti-PD-1 or anti-PD-L1 antibodies, in patients with hematologic malignancies.

Research and Development

As of February 1, 2016, our research and development group consisted of 164 employees, of whom 34% hold Ph.D. or M.D. degrees and an additional 13% hold other advanced degrees. Our research and development group is focusing on drug discovery, preclinical research, translational medicine, clinical trials and manufacturing technologies. Our research and development expense for the years ended December 31, 2015, 2014 and 2013 was approximately $199.1 million, $143.6 million and $99.8 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. As required by our agreement with AbbVie, we are in the process of transitioning the responsibility to manufacture Duvelisib Products to AbbVie as promptly as is practicable while ensuring continuity of supply. Excluding the AbbVie Studies, we are responsible for all costs to develop and manufacture Duvelisib Products up to a maximum amount of $667 million, after which we will share Duvelisib Product development and manufacturing costs equally with AbbVie. The development and manufacturing costs of the AbbVie Studies will be shared equally. We and AbbVie will share the cost of manufacturing and supply for commercialization of Duvelisib Products in the United States, and AbbVie will bear the cost of manufacturing and supply for commercialization of Duvelisib Products outside the United States. Commercial quantities of any drugs we seek to develop will have to be manufactured in facilities and by processes that comply with the 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

Under the AbbVie Agreement, we and AbbVie share operational responsibility and decision making authority for commercialization of Duvelisib Products in the United States, while AbbVie has, with limited exceptions, operational responsibility and decision making authority to

commercialize Duvelisib Products outside of the United States. We are currently developing the infrastructure and personnel we believe to be necessary to successfully market, sell, and distribute Duvelisib Products in the United States, and we intend for

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such infrastructure to serve as the foundation for the launch of future drug products, subject to receiving marketing approval for those products. Further, we expect AbbVie s established marketing and sales infrastructure, global marketing presence, and history of successful product launches positions duvelisib to best be delivered to patients, subject to receipt of marketing approval by the requisite regulatory bodies.

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. We are currently developing the infrastructure and personnel we believe to be necessary to support an effective compliance program.

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 IND, 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 a new drug application, or 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;

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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

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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. 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

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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, currently exceeding $2.3 million, and the sponsor of an approved NDA is also subject to annual product and establishment user fees, currently exceeding $114,000 per product and $585,000 per establishment. These fees are typically increased annually. 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 specified 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.

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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 is required to 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 and Priority Review 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 fast track designation, breakthrough therapy designation and priority review 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

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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, in 2012, Congress enacted the Food and Drug Administration Safety and Innovation Act, or FDASIA. This law established a new regulatory scheme allowing for expedited review of products designated as breakthrough therapies. 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.

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

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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

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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, 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

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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

As an alternative path to FDA approval for modifications to formulations or uses of products previously approved by the FDA pursuant to an NDA, an applicant may submit an NDA under Section 505(b)(2) of the FDCA. Section 505(b)(2) was enacted as part of the Hatch-Waxman Amendments and permits the filing of an NDA where at least some of the information required for approval comes from studies not conducted by, or for, the applicant. If the 505(b)(2) applicant can establish that reliance on FDA s previous findings of safety and effectiveness is scientifically and legally appropriate, it 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, including clinical trials, to support the change from the previously approved reference drug. The FDA may then approve the new product candidate for all, or some, of the label indications for which the reference drug has been approved, as well as for any new indication sought by the 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 earlier 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.

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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 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 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

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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 United States PTO reviews and approves the application for any patent term extension in consultation with the FDA.

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 Good Clinical Practice, or 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.

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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

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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

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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.

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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

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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 Affordable Care Act, 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.

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By way of example, the United States and state governments continue to propose and pass legislation designed to reduce the cost of healthcare. In March 2010, the United States Congress enacted the Affordable Care Act, which, among other things, includes changes to the coverage and payment for products under government health care programs. Among the provisions of the Affordable Care Act 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. PPACA 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 Affordable Care Act 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.

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There have been, and likely will continue to be, legislative and regulatory proposals at the foreign, federal and state levels directed at broadening the availability of healthcare and containing or lowering the cost of healthcare. Such reforms could have an adverse effect on anticipated revenues from product candidates that we may successfully develop and for which we may obtain marketing approval and may affect overall financial condition and ability to develop product candidates.

Employees

As of February 1, 2016, we had 222 full-time employees, 164 of whom were engaged in research and development and 58 of whom were engaged in general business management, administration and finance. Approximately 46% 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 subsidiary 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 February 1, 2016:

Name	Age	Position
Adelene Q. Perkins	56	President and Chief Executive Officer
Julian Adams, Ph.D.	61	President of Research & Development
William C. Bertrand, Jr., J.D.	51	Executive Vice President, General Counsel
Lawrence E. Bloch, M.D., J.D.	50	Executive Vice President, Chief Financial Officer and Chief Business Officer
Sujay Kango	52	Executive Vice President, Chief Commercial Officer

Adelene Q. Perkins has served as our President and Chief Executive Officer since January 2010, President and Chief Business Officer from October 2008 through December 2009 and as 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

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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.

Julian Adams, Ph.D., has served as our President of Research & Development since October 2007, our Chief Scientific Officer between September 2006 and May 2010, as Chief Scientific Officer of IPI from October 2003 until the merger with DPI in September 2006, as our President between September 2006 and October 2007 and as President of IPI from February 2006 until September 2006. Prior to joining Infinity, Dr. Adams served as Senior Vice President, Drug Discovery and Development at Millennium Pharmaceuticals, Inc. from 1999 to 2001, where he led the development of bortezomib, also known as Velcade®. Dr. Adams served as Senior Vice President, Research and Development at LeukoSite Inc., a private biopharmaceutical company, from July 1999 until its acquisition by Millennium in December 1999. Dr. Adams served as a director and Executive Vice President of Research and Development at ProScript, Inc., a private biopharmaceutical company, from 1994 until its acquisition by LeukoSite in 1999. Prior to joining ProScript, Dr. Adams held a variety of positions with Boehringer Ingelheim, a private pharmaceutical company, and Merck & Co., Inc., a publicly traded pharmaceutical company. Dr. Adams has served as a director of Aileron Therapeutics, Inc., a privately held biopharmaceutical company, between 2011 and 2013, a director of Warp Drive Bio, LLC, since 2013, and a director of the Princess Margaret Cancer Foundation since November 2014. Dr. Adams received a B.S. from McGill University and a Ph.D. from the Massachusetts Institute of Technology in the field of synthetic organic chemistry.

William C. Bertrand, Jr., J.D., has served as Executive Vice President and General Counsel since October 2015. Prior to Infinity, Mr. Bertrand held various roles of increasingly responsibility at Salix Pharmaceuticals, Inc., a subsidiary of Valeant Pharmaceuticals, Inc., a pharmaceutical company, and most recently served as senior vice president, general manager at Salix where he was responsible for its commercial business as well as the transition and integration of Salix into Valeant. From 2001 to 2013, Mr. Bertrand held positions of increasing responsibility at MedImmune, Inc., a pharmaceutical company, serving as its first and only general counsel from 2003 to 2013, prior to and following its sale to AstraZeneca PLC in 2008. Prior to MedImmune, Mr. Bertrand served as associate general counsel at Pharmacia Corporation, a pharmaceutical company. Mr. Bertrand currently serves as a director of Ardelyx, a publicly traded biotechnology company, from October 2015 and has served as a director of Trustwave Holdings, Inc., a privately held information security corporation, from 2011 to August 2015, Inotek Pharmaceuticals, a publicly traded biotechnology company, from 2011 to 2013, BrainCells, Inc., a privately held biotechnology company, from 2008 to 2011, Tech Council of Maryland, a technology and biotechnology trade association, from 2010 to 2013, and Montgomery County Roundtable for Education from 2010 to 2013. He earned a B.S. in Biology from Wayne State University and a J.D. from the University of Wisconsin-Madison.

Lawrence E. Bloch, M.D., J.D., has served as Executive Vice President, Chief Financial Officer and Chief Business Officer since July 2012. 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

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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.

Sujay Kango has served as Executive Vice President and Chief Commercial Officer since April 2015. Prior to joining Infinity, Mr. Kango most recently served from April 2011 to March 2015 as vice president, global marketing, sales operations, and business analytics, at Onyx Pharmaceuticals, an Amgen subsidiary and a pharmaceutical company, where he led the global Onyx proteasome inhibitor franchise, including Kyprolis® and oprozomib and co-chaired the Onyx-Bayer executive committee responsible for oversight of the companies global kinase inhibitor franchise. Prior to Onyx, from January 2006 to March 2011, he held several leadership positions at Merck & Co., a pharmaceutical company, including vice president, hepatitis franchise and vice president, oncology integrated business unit. Prior to Merck, from November 1990 to May 2005, Mr. Kango held various commercial and marketing roles of increasing responsibility at Johnson & Johnson and Schering-Plough, each of which is a pharmaceutical company. Mr. Kango serves as a director of Cancer Care of New Jersey. Mr. Kango earned a B.S. in Microbiology and an M.B.A. from McNeese State University.

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 U.S. Securities and Exchange Commission. 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.

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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, 2015, we had an accumulated deficit of $595.6 million. We expect to continue to spend significant resources to fund the research and development of duvelisib and our other product candidates. 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 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.

Our product candidates are in varying stages of preclinical and 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 one of our product candidates successfully completes clinical trials and receives regulatory approval. We do not expect to generate any revenue from product sales until at least 2017, assuming we are able to file for regulatory approval for duvelisib in 2016 and receive approval in 2017. 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, diversify our pipeline of product candidates or continue our operations and cause a decline in the value of our common stock.

We have no history of commercializing pharmaceutical products, which may make it difficult to evaluate the prospects for our future viability.

To date, our operations have focused on financing and staffing our company, developing our product pipeline and conducting preclinical and clinical research. We have not yet demonstrated an ability to obtain marketing approvals, manufacture a commercial scale product or arrange for a third party to do so on our behalf, or conduct sales and marketing activities necessary for successful product commercialization. Accordingly, you should consider our prospects in light of the costs, uncertainties, delays and difficulties frequently encountered by companies in the early stages of development, especially clinical stage biopharmaceutical companies such as ours. Any predictions you make about our future success or viability may not be as accurate as they could be if we had a history of successfully developing and commercializing pharmaceutical products.

We may encounter unforeseen expenses, difficulties, complications, delays and other known or unknown factors in achieving our business objectives. We are transitioning from a company with a development focus to a company capable of supporting commercial activities. We may not be successful in such a transition.

We expect our financial condition and operating results to continue to fluctuate significantly from quarter to quarter and year to year due to a variety of factors, many of which are beyond our control. Accordingly, you should not rely upon the results of any quarterly or annual periods as indications of future operating performance.

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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 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, and we expect our expenses to increase in connection with seeking and possibly obtaining regulatory approval of any of our product candidates and building our product sales, marketing, manufacturing and distribution capabilities. If we are unable to raise capital when needed or on attractive terms, we would be forced to delay, reduce or eliminate our research and development programs or commercialization efforts.

In the absence of additional funding or business development activities and based on our current operating plans, we believe that our existing cash, cash equivalents and available-for-sale securities at December 31, 2015 will be adequate to satisfy our capital needs through the first quarter of 2017. Until we can generate sufficient levels of cash from operations, which we do not expect to achieve for at least the next two years, if at all, 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, and/or through licensing select programs or partial economic rights that could include payments to us of up-front, royalty and/or milestone payments. Our need to raise additional funds may be accelerated if our research and development or commercialization expenses exceed our current expectation, 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;
- the costs of commercialization activities for any of our product candidates that receive marketing approval, including the costs and timing of establishing product sales, marketing, distribution and manufacturing capabilities, increases, to the extent such costs are not the responsibility of any collaborators;
- the costs of preparing, filing and prosecuting patent applications, maintaining and protecting our intellectual property rights and defending against intellectual property related claims increases;
- the receipt of any potential milestone payments from our strategic collaborator AbbVie Inc., or AbbVie, is delayed beyond our original assumptions;

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.

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

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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 or terminate some or all of our development programs or to scale back, suspend or terminate our business operations.

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

In the near term, we are dependent on the success of our PI3K inhibitor programs including duvelisib and IPI-549. If we are unable to complete the clinical development of, obtain marketing approval for or successfully commercialize these product candidates, either alone or with collaborators, or if we experience significant delays in doing so, our business could be substantially harmed.

We currently have no products approved for sale and are investing a significant portion of our efforts and financial resources in the development of our phosphoinositide-3-kinase, or PI3K, inhibitor programs including duvelisib and IPI-549. Our prospects are substantially dependent on our ability, or that of AbbVie or any future collaborator, to develop, obtain marketing approval for and successfully commercialize product candidates in one or more disease indications.

The success of our PI3K inhibitor programs will depend on several factors, including the following:

- initiation and successful enrollment and completion of clinical trials;
- 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 performance of AbbVie;
- 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;

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- 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 duvelisib, IPI-549, or any other product candidates under our PI3K inhibitor programs, 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.

We may fail to discover and develop additional potential product candidates.

A significant portion of the research that we are conducting involves our PI3K inhibitor programs including duvelisib and IPI-549. We may not be successful in identifying additional compounds that have commercial value or therapeutic utility. Our drug discovery process may fail to yield viable product candidates for clinical development or commercialization for a number of reasons, including:

- potential product candidates may, on further study, be shown to have harmful side effects or other characteristics that indicate that they are unlikely to receive marketing approval and achieve market acceptance;
- competitors may develop alternative therapies that render our potential product candidates non-competitive or less attractive; or
- a potential product candidate may not be capable of being produced at an acceptable cost.

Our research programs to identify new product candidates will require substantial technical, financial and human resources, and we may be unsuccessful in our efforts to identify new product candidates. If we are unable to identify suitable additional compounds for preclinical and clinical development, our ability to develop product candidates and obtain product revenues in future periods could be compromised, which could result in significant harm to our financial position and adversely impact our stock price.

All of our product candidates remain subject to clinical testing and regulatory approval. This process is highly uncertain, and we may never be able to obtain marketing approval for any of our product candidates.

To date, we have not obtained approval from the FDA or any foreign regulatory authority to market or sell any of our product candidates. Our product candidates are 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 duvelisib, our most advanced product candidate, in all phases of clinical development, and we anticipate initiating additional trials of duvelisib in 2016 (see Item 1 - Business above). If any of these trials or other trials of our product candidates are successful, we may need to conduct further clinical trials and will need to apply for regulatory approval before we may market or sell any of our future products. Satisfaction of these and other regulatory requirements is costly, time consuming, uncertain and subject to unanticipated delays. It is possible that none of the product candidates we are developing, or may in the future develop, either alone or with collaborators, will obtain marketing approval. Even if one or more of our product candidates 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

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clinical trials. Conversely, as a result of the same factors, our clinical trials may indicate an apparent positive effect of a product candidate 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 our product candidates, or mistakenly believe that our product candidates are toxic or not well tolerated when that is not in fact the case.

Our product candidates must undergo rigorous clinical trials prior to receipt of regulatory approval. Any problems in these clinical trials could delay or prevent commercialization of our product candidates.

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 our product candidates:

- 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 a product candidate 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 our product candidates, for any of the foregoing reasons, could adversely affect our efforts 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.

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Adverse events or undesirable side effects caused by, or other unexpected properties of, product candidates that we develop may be identified during development and could delay or prevent their marketing approval or limit their use.

Adverse events or undesirable side effects caused by, or other unexpected properties of, any current or future product candidates that we may develop could cause us, any collaborators, an institutional review board or regulatory authorities to interrupt, delay or halt clinical trials of one or more of our product candidates 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 any of our product candidates 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 that product candidate 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 current or future collaborators, experience any of a number of possible unforeseen events in connection with clinical trials of our current or future product candidates that we, or any collaborators, may develop, potential clinical development, marketing approval or commercialization of our product candidates could be delayed or prevented.

We, or any 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 our current or future product candidates that we, or any collaborators, may develop, 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 our product candidates 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 product development programs;
- the number of patients required for clinical trials of our product candidates 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 our product candidates may be greater than we anticipate;
- our third-party contractors or those of any collaborators, including those manufacturing our product candidates 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 our product candidates for various reasons, including a finding that the participants are being exposed to unacceptable health risks, undesirable side effects or other unexpected characteristics of the product candidate;

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

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to unacceptable health risks, undesirable side effects or other unexpected characteristics of the product candidate 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 our product candidates 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 our product candidates. We do not know whether any preclinical tests or 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 our product candidates 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 our product candidates and may harm our business and results of operations. We have designed our DYNAMO study with the potential to support accelerated approval of duvelisib for the treatment of follicular lymphoma and SLL, indications for which Gilead has received accelerated approval to manufacture and market idelalisib. If we experience delays in the conduct of our DYNAMO study, or Gilead is able to complete its confirmatory study and receive full approval to market idelalisib for the treatment of follicular lymphoma or SLL faster than anticipated, our efforts to seek accelerated approval for duvelisib for the treatment of follicular lymphoma or SLL may be materially adversely affected. In addition, many of the factors that lead to clinical trial delays may ultimately lead to the denial of marketing approval of any of our product candidates.

Results of preclinical studies and early clinical trials may not be predictive of results of future late-stage clinical trials.

We have completed a small number of clinical trials for our lead product candidate duvelisib, and we are currently conducting several additional trials for duvelisib and 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 our product candidates warrant marketing approval, the FDA or comparable foreign regulatory authorities may disagree and may not grant marketing approval of our product candidates.

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

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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 our product candidates, the development timeline and regulatory approval and commercialization prospects for our most advanced product candidates, 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.

Additionally, the availability of safe and effective treatments for the relevant disease being studied may impact patient enrollment in our clinical trials. For example, AbbVie has received approval to manufacture and market ibrutinib, a BTK inhibitor for the treatment of chronic lymphocytic leukemia, or CLL, an indication for which we are currently evaluating duvelisib in our DUO and SYNCHRONY clinical trials, and Gilead has received accelerated approval to manufacture and market idelalisib for the treatment of follicular lymphoma and SLL, indications for which we are currently evaluating duvelisib.

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 efforts 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.

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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 our current or future product candidates that we, or any collaborators, may develop.

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 our product candidates or may conclude after review of our data that our application is insufficient to obtain marketing approval of our product candidates. If the FDA does not accept or approve our NDAs for any of our product candidates, 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 our product candidates 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 our product candidates, which could significantly harm our business.

Even if any product candidates that we, or any collaborators, may develop receive 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 collaborator, to market the product, and we could become subject to costly and damaging product liability claims.

Even if we receive regulatory approval for any of our product candidates, we will have tested them 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 our products for a longer period of time, the product candidate might be less effective than indicated by our clinical trials. Furthermore, new risks and side effects associated with our products 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 our product (including a black box warning or a contraindication) or the manner in which it is administered, reformulate our product or make changes and obtain new approvals for our and our suppliers manufacturing facilities. We also might have to withdraw or recall our products from the marketplace, and regulators might seize our products. We might be subject to fines, injunctions, or the imposition of civil or criminal penalties. Any safety concerns with respect to a product may also result in a significant drop in the potential sales of that product, 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 any product candidates that we, or any collaborators, may develop receive 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 any of our product candidates obtains regulatory approval, that product 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;

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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 the product is designated under physician treatment guidelines as a first, second or third line therapy;

changes in the standard of care for the targeted indications for the product;

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 any of our approved drugs fails to achieve market acceptance, we would not be able to generate significant revenue from those drugs, which may adversely impact our ability to become profitable.

Even if we receive regulatory approvals for marketing our product candidates, 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 of our product candidates, the manufacturing, marketing and sale of these drugs will be subject to continuing regulation, including compliance with quality systems regulations, 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 our 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. We plan to build focused capabilities to commercialize development programs for certain indications where we believe that the medical specialists for the indications are sufficiently concentrated to allow us to effectively promote the product with a targeted sales team. The development of sales, marketing and distribution capabilities will require substantial resources, will 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

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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 plan 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.

In certain indications, we plan to seek to enter into collaborations that we believe may contribute to our ability to advance development and ultimately commercialize our product candidates. We also intend to seek to enter into collaborations where we believe that realizing the full commercial value of our development programs will require access to broader geographic markets or the pursuit of broader patient populations or indications. Under our collaboration and license agreement with AbbVie, which we refer to as the AbbVie Agreement, for example, we and AbbVie are obligated to each provide half of the sales representative effort to promote products containing duvelisib, which we refer to as Duvelisib Products, in the United States. Outside the United States, AbbVie has, with limited exceptions, operational responsibility and decision making authority to commercialize Duvelisib Products. We and AbbVie will share the cost of manufacturing and supply for commercialization of Duvelisib Products in the United States, and AbbVie will bear the cost of manufacturing and supply for commercialization of Duvelisib Products outside the United States.

As a result of entering into arrangements such as the AbbVie Agreement 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 ours less attractive or obsolete.

In building our product development pipeline, we have intentionally pursued targets with applicability across multiple therapeutic areas and indications. This approach gives us several product opportunities in oncology diseases, which 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. Moreover, there are a number of large pharmaceutical companies currently marketing and selling products in this segment including Bristol-Myers Squibb Company; the Roche Group and its subsidiary Genentech; Novartis AG; Pfizer, Inc.; and Johnson & Johnson. In addition to currently approved drugs, there are a significant number of drugs that are currently under development and may become available in the future for the treatment of various forms of cancer.

Duvelisib is a dual inhibitor of the delta and gamma isoforms of PI3K. We are aware of a number of companies developing product candidates or selling products directed to isoforms of PI3K. Specifically, we believe that Gilead Sciences, Inc., or Gilead; Incyte Corporation; Acerta Pharma BV; and TG Therapeutics, Inc. are conducting clinical trials of drugs that target the delta isoform of PI3K. We also believe that Rhizen Pharmaceuticals S.A. is conducting clinical trials of a drug that targets both the delta and gamma isoforms of

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PI3K. We also believe that SignalRx Pharmaceuticals is conducting a clinical trial of a drug that targets the delta, gamma, and alpha isoforms of PI3K, and that Novartis AG, Bayer, and Genentech are each conducting clinical trials of drugs that target the delta, gamma, alpha, and beta isoforms of PI3K.

Additionally, many companies are developing product candidates or selling products directed to disease targets such as Bruton s tyrosine kinase (or BTK), B-cell lymphoma 2 (or BCL-2), Janus Kinase (or JAK), B-lymphocyte antigen CD-19, and programmed death 1/ligand 1 (or PD-1/PD-L1), Cluster of Differentiation 79B antibody-drug conjugate (or CD79B ADC), and pleiotropic pathways in the fields of hematology-oncology, including in the specific diseases for which we are currently developing duvelisib, or for which we may develop duvelisib in the future, including: AbbVie; Pharmacyclics LLC, a wholly-owned subsidiary of AbbVie; BeiGene Co., Ltd; Janssen Biotech through its collaboration with AbbVie; Celgene Corporation; a joint collaboration between Gilead and Ono Pharmaceutical Group under their exclusive license agreement; Acerta Pharma BV; Incyte Corporation; MorphoSys AG; Novartis AG; Roche Group and its subsidiary Genentech; Bristol-Myers Squibb Company; and AstraZeneca PLC.

Many of our competitors have:

- significantly greater financial, technical and human resources than we have, and may be better equipped to discover, develop, manufacture and commercialize product candidates than we are;
- more experience in preclinical testing and clinical trials, obtaining regulatory approvals and manufacturing and marketing products than we do; and/or
- product candidates that are in later-stage clinical development than our own product candidates, or have been approved by the FDA, such as ibrutinib, a BTK inhibitor being developed and commercialized by AbbVie for the treatment of people with mantle cell lymphoma or CLL, and idelalisib, a compound targeting the delta isoform of PI3K, being developed and commercialized by Gilead for the treatment of people with CLL, follicular B-cell non-Hodgkin lymphoma, or small lymphocytic lymphoma.

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 our own product candidates. These competitive products may have superior safety or efficacy, have more attractive pharmacologic properties, or may be manufactured less expensively than our future products. 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 our future products 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 any product candidate that we, or they, develop, 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 our product candidates will depend substantially, both domestically and abroad, on the extent to which the costs of our product candidates 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 our product candidates. Even if coverage is provided, the approved reimbursement amount may not be high enough to allow us, or any

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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 one or more product candidates, even if our product candidates obtain 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 any of our product candidates will depend in part on the extent to which coverage and adequate reimbursement for these products 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 our product candidates profitably. These payors may not view our products, if any, 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 our products, if any, 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 products, which could result in lower than anticipated product revenues. If the prices for our products, if any, 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 any of our product candidates for which we, or any future collaborator, obtain marketing approval could significantly harm our operating results, our ability to raise capital needed to commercialize products and our overall financial condition.

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If the FDA or comparable foreign regulatory authorities approve generic versions of any of our products that receive marketing approval, or such authorities do not grant our products appropriate periods of data exclusivity before approving generic versions of our products, the sales of our products 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 any of our product candidates 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 our product candidates in clinical trials. We currently have clinical trial insurance and will seek to obtain product liability insurance prior to the commercial launch of any of our product candidates. 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 our product candidates or future products, 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 our future products, or expand our business.

Risks Related to Our Dependence on Third Parties

If our strategic alliance with AbbVie, or any future alliance we may enter into, is unsuccessful, our operations may be negatively impacted.

We have a strategic collaboration with AbbVie to research, develop and jointly commercialize products containing or comprised of duvelisib, which we refer to as Duvelisib Products, in oncology indications. We refer to this agreement as the AbbVie Agreement. Pursuant to the AbbVie Agreement, AbbVie has committed to

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providing substantial funding, as well as significant capabilities in development, manufacturing, marketing and sales. However, we may not be able to maintain our alliance with AbbVie or any future collaborator if, for example, development or approval of duvelisib or other product candidates is delayed or sales of Duvelisib Products or other products are disappointing. Further, AbbVie may be the only alliance we are able to successfully execute, making us overly dependent on the success of duvelisib in oncology indications and therefore particularly vulnerable if duvelisib or the alliance with AbbVie fails, as discussed in the next risk factor.

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.

The success of a strategic alliance, whether with AbbVie or any future 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 our product candidates 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 product candidate through clinical development, regulatory approval and commercialization; or
- cannot obtain the necessary regulatory approvals.
- delays clinical trials, provides insufficient funding for a clinical trial program, stops a clinical trial or abandons a product candidate, repeats or conducts new clinical trials or requires a new formulation of a product candidate for clinical testing;
- independently develops, or develops with third parties, products that compete directly or indirectly with our product candidates;
- 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 breach or terminate its arrangements with us 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, if AbbVie were to terminate our

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strategic collaboration, we would not be entitled to receive payment for any milestone that is not achieved prior to AbbVie s delivery to us of a termination notice, and AbbVie has limited obligations to continue the conduct and funding of ongoing development and commercialization activities.

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. For example, in May 2015, AbbVie acquired Pharmacyclics, Inc., or Pharmacyclics, a competitor of ours that had received approval to manufacture and market ibrutinib for the treatment of CLL and is developing ibrutinib in follicular lymphoma, which are indications for which we are developing duvelisib. As part of our collaboration, we and AbbVie must agree on the development and commercialization strategy for Duvelisib Products, which could lead to difficulties as a result of competing priorities or conflicts of interest related to the development and potential commercialization of duvelisib in competition with ibrutinib. Any difficulties we encounter may have an adverse effect on the development and commercialization of duvelisib and, consequently, our business.

As is the case with our strategic collaboration with AbbVie, 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. Under the AbbVie Agreement, for instance, we have granted AbbVie exclusive licenses to commercialize Duvelisib Products outside the United States.

If AbbVie or any future collaborator fails to develop or effectively commercialize our product or development candidates, we may not be able to develop and commercialize that product candidate independently, and our financial condition and operations would be negatively impacted.

We might seek to establish additional 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.

We might seek one or more collaborators for the development and commercialization of one or more of our product candidates. 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 product candidates from foreign regulatory authorities, we might enter into strategic relationships with international biotechnology or pharmaceutical companies for the commercialization of such product candidates 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 our product candidate 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 the product candidate, 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 our product candidate. If we elect to increase our expenditures to fund development or commercialization activities on our own, we may need to obtain additional capital, which may not be available to us on acceptable terms or at all. If we do not have sufficient funds, we may not be able to further develop our product candidates or bring them to market and generate product revenue.

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Such 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 specified product candidates. In the AbbVie Agreement, for example, we and AbbVie have agreed, subject to limited exceptions, that we will not commercialize, or assist others in commercializing, in oncology indications certain PI3K delta, gamma inhibitors, and AbbVie has agreed to similar restrictions.

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 the product candidate for which we are seeking to collaborate, reduce or delay its development program or one or more of our other development programs, 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 efforts to obtain regulatory approval for and to commercialize our product candidates may 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 efforts to obtain regulatory approval for and to commercialize our product candidates may be delayed.

We currently rely on third-party manufacturers to produce our preclinical and clinical drug supplies, and we intend to rely upon third-party manufacturers to produce commercial supplies of any approved product candidates.

Our product candidates require precise, high quality manufacturing. The third-party manufacturers on which we rely may not be able to comply with the FDA s current good manufacturing practices, or 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 our product candidates 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 our product candidates, delays, suspension or withdrawal of

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approvals, license revocation, seizures or recalls of product candidates or products, operating restrictions and/or criminal prosecution, any of which could significantly and adversely affect supply of our product candidates 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 our product candidates 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, our product candidates have been manufactured for preclinical testing and clinical trials primarily by third-party manufacturers. If the FDA or other regulatory agencies approve any of our product candidates for commercial sale, we expect that we would continue to rely, at least initially, on third-party manufacturers to produce commercial quantities of our approved product candidates. These manufacturers may not be able to successfully increase the manufacturing capacity for any approved product candidates 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 a product candidate, 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.

We may not be able to successfully transition responsibilities for the manufacturing of Duvelisib Products to AbbVie.

We may be unsuccessful in transferring the responsibility to manufacture Duvelisib Products to AbbVie. The transition process may be more complicated, time consuming and expensive than originally intended, which may negatively affect the supply of Duvelisib Products. Should the strategic collaboration with AbbVie terminate, the process of transitioning manufacturing back to us may be time consuming and expensive, and we may become unable to maintain an adequate supply of Duvelisib Products worldwide.

We currently have limited marketing, sales and distribution experience and capabilities and are dependent upon AbbVie to commercialize Duvelisib Products outside the United States.

We and AbbVie share the obligations to commercialize Duvelisib Products in oncology in the United States, and AbbVie has the sole obligation to commercialize Duvelisib Products in oncology outside the United States. To successfully commercialize Duvelisib Products, we will need to, and we intend to, establish adequate marketing, sales and distribution capabilities for commercialization in the United States. Failure to establish these capabilities, whether due to insufficient resources or some other cause, will limit or potentially halt our ability to successfully commercialize any product candidates, thereby adversely affecting our financial results. Even if we do develop such capabilities, we will compete with other companies that have more experienced and well-funded marketing, sales and distribution operations.

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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 our product candidates.

We currently have rights to certain intellectual property, through licenses from third parties, to develop duvelisib, IPI-549 and other product candidates under our PI3K inhibitor programs. We may decide to license additional third-party technology that we deem necessary or useful for our business. 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 any of our product candidates 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 our product candidates 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 the affected product candidate, 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 or 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 duvelisib and IPI-549. 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 any product 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 the product candidate 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, we could lose our license rights under that agreement, including rights to duvelisib.

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

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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 our product candidates.

We own or hold exclusive licenses to a number of U.S. and foreign patents and patent applications directed to our product candidates. Our success depends on our ability to obtain patent protection both in the United States and in other countries for our product candidates, their methods of manufacture and their methods of use. Our ability to protect our product candidates 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 PTO, 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 our products. The laws of some foreign jurisdictions do not protect intellectual property rights to the same extent as in the United States. Many

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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

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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 our product candidates.

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 PTO 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, our product candidates or their therapeutic use. In the event that a third party has also filed a U.S. patent application relating to our product candidates or a similar invention, we may have to participate in interference or derivation proceedings declared by the PTO 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 our product candidates.

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 our product candidates. 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 product candidates, even when we are aware of third-party patents that may be relevant to such product candidates, 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 our products.

While we are not currently aware of any litigation or third-party claims of intellectual property infringement related to our product candidates, 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 the infringing product candidates or approved products;

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.

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If any of the foregoing were to occur, we may be unable to commercialize the affected products, 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

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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 PTO 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 Our Product Candidates and Other Legal Compliance Matters

Even if we complete the necessary preclinical studies and clinical trials, the marketing approval process is expensive, time-consuming and uncertain and may prevent us from obtaining approvals for the commercialization of some or all of our product candidates. 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 our product candidates, and our ability to generate revenue will be materially impaired.

Our product candidates and the activities associated with their development and commercialization, including their design, testing, manufacture, safety, efficacy, recordkeeping, 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 a product candidate will prevent us from commercializing the product candidate. We and our collaborators have not received approval to market any of our product candidates 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. Our product candidates 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

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interpretations of the data obtained from preclinical and clinical testing could delay, limit or prevent marketing approval of a product candidate. 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 our product candidates, the commercial prospects for our product candidates may be harmed and our ability to generate revenues will be materially impaired.

Failure to obtain marketing approval in foreign jurisdictions would prevent our product candidates 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 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 our products in any market.

Although we have received fast track designation by the FDA for duvelisib for a certain indication, that designation may not actually lead to a faster development or regulatory review or approval process and it does not ensure that we will receive marketing approval.

The FDA has designated as a fast track development program both the investigation of duvelisib for treatment of patients with follicular lymphoma who have received at least two prior therapies and the investigation of duvelisib for the treatment of patients with CLL who have received at least one prior therapy. Any drug sponsor may apply for such designation if their product candidate is intended for the treatment of a serious or life-threatening disease or condition and the product candidate demonstrates the potential to address an unmet medical need. The FDA has broad discretion whether or not to grant fast track designation. Although duvelisib has received such designation this may not actually result in a faster development process, review or approval compared to standard FDA procedures. The FDA may withdraw fast track designation if it believes that the clinical development program does not continue to meet the criteria for fast track designation.

We may not qualify for accelerated approval or expedited review for any of our product candidates, and qualification for such programs does not guarantee we will be able to develop or market our product more quickly.

Some of our product candidates may be eligible for the FDA s programs that are designed to facilitate the development and expedite the review of certain drugs such as the FDA s accelerated approval program, but we cannot provide any assurance that any of our product candidates will qualify for one or more of these programs. Even if a product candidate qualifies for one or more of these programs, the FDA may later decide that the product candidate no longer meets the conditions for qualification. For example, the DYNAMO study is designed with the potential to support accelerated approval of duvelisib for treatment of patients with follicular lymphoma or small lymphocytic lymphoma, or SLL. The availability of accelerated approval is dependent on a number of factors including whether we generate positive safety and efficacy data from the study and duvelisib has demonstrated a meaningful benefit over available therapies. In addition, even after receiving accelerated

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approval, companies are required to conduct studies to confirm the anticipated clinical benefit of a drug, known as confirmatory trials. If the confirmatory trial shows that the drug actually provides a clinical benefit, then the FDA grants regular approval for the drug. If the confirmatory trial does not show that the drug provides clinical benefit, FDA has regulatory procedures in place that could lead to removing the drug from the market. We cannot guarantee that duvelisib will qualify for accelerated approval or, even if it receives accelerated approval, that we would successfully complete a confirmatory study. In particular, we are aware that Gilead has received accelerated approval for idelalisib, its product, to treat follicular lymphoma and SLL. Idelalisib is currently approved by the FDA for CLL. If Gilead is able to complete its confirmatory study and receive full approval to market idelalisib for the treatment of follicular lymphoma or SLL faster than anticipated, our efforts to seek accelerated approval for duvelisib for the treatment of follicular lymphoma or SLL may be materially adversely affected. Moreover, even if we are able to receive accelerated approval for duvelisib the FDA may upon review of data from our confirmatory study later decide that duvelisib no longer meets the conditions for approval resulting in revocation of approval.

Even if we or our collaborators obtain marketing approvals for our product candidates, the terms of approvals and ongoing regulation of our products may limit how we manufacture and market our products, 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 any of our product candidates for which we or they obtain marketing approval. 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, which include requirements relating to quality control and quality assurance as well as the corresponding maintenance of records and documentation and reporting requirements. We, our contract manufacturers, any collaborators and their contract manufacturers could be subject to periodic unannounced inspections by the FDA to monitor and ensure compliance with cGMPs.

Accordingly, assuming we, or any of our collaborators, receive marketing approval for one or more of our product candidates, 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.

Any product candidate for which we or our collaborators obtain marketing approval 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 our product candidates, when and if any of them are 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.

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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 a product candidate 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.

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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;

- 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, with data collection beginning in August 2013; 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

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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 our other product candidates and affect the prices 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 our other product candidates, 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 and Education Affordability Reconciliation Act, or collectively the PPACA. Among the provisions of the PPACA of potential importance to our business and our product candidates 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;
- 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;

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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 PPACA 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. 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 regulatory approval is obtained.

We expect that the PPACA, 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 in additional downward pressure on the price that we receive for any approved product. Any reduction in reimbursement from Medicare or other government programs may result in a similar reduction in payments from private payors. The implementation of cost containment measures or other healthcare reforms may prevent us from being able to generate revenue, attain profitability, or commercialize our products. 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.

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.

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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.

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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 attract and 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.

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Recruiting and 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. 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 encounter difficulties in managing organizational change, which could adversely affect our operations.

As of February 1, 2016, we had 222 full-time employees. We expect to experience significant growth in the number of our employees and the scope of our operations, particularly in the areas of drug manufacturing, regulatory affairs and sales, marketing and distribution. To manage these growth activities, we must continue to implement and improve our managerial, operational and financial systems, expand our facilities and continue to recruit and train additional qualified personnel. Our management may need to devote a significant amount of its attention to managing these growth activities. Due to limited experience with commercialization including sales and marketing, we may not be able to effectively manage the expansion of our operations, retain key employees, or identify, recruit and train additional qualified personnel. Our inability to manage the expansion of our operations effectively may result in weaknesses in our infrastructure, give rise to operational mistakes, loss of business opportunities, loss of employees and reduced productivity among remaining employees. Our expected growth could also require significant capital expenditures and may divert financial resources from other projects, such as the development of additional product candidates. If we are unable to effectively manage our expected growth, our expenses may increase more than expected, our ability to generate revenues could be reduced and we may not be able to implement our business strategy, including the successful commercialization of our product candidates.

Under the AbbVie Agreement, we and AbbVie have created a governance structure, including committees and working groups to manage the development, manufacturing and commercialization responsibilities for the Duvelisib Products. Generally, we and AbbVie must mutually agree on decisions, although in specified circumstances either we or AbbVie would be able to break a deadlock. Any future alliance may also require implementation of a similarly complex governing structure. We may not be able to implement improvements in an efficient or timely manner or to maintain our corporate culture during periods of organizational change. If we do not meet these challenges, we may be unable to take advantage of market opportunities, execute our business strategies or respond to competitive pressures, which in turn may give rise to inefficiencies that would increase our losses or delay our programs.

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 business, product, product candidate or technology 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

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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 our product candidates;
- the results of preclinical studies and planned clinical trials of our discovery-stage programs;
- product portfolio decisions resulting in the delay or termination of our product development programs;
- future sales of, and the trading volume in, our common stock;
- 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 collaboration and license agreement with AbbVie, or our amended and restated development and license agreement with Takeda;
- the results and timing of regulatory reviews relating to the approval of our product candidates;
- 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 any of our product candidates, if approved, to achieve commercial success;

the results of clinical trials conducted by others on drugs that would compete with our product candidates;

the regulatory approval of drugs that would compete with our product candidates;

issues in manufacturing our product candidates or any approved products;

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;

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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.

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, 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, 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.

As of December 31, 2015, we had cumulative federal and state net operating loss carryforwards of $371.1 million and $250.9 million, respectively, each of which if not utilized will expire at various dates through 2035. In addition, we have cumulative federal and state tax credit carryforwards of $33.3 million and $10.2 million, respectively, available to reduce federal and state income taxes which expire through 2035 and 2030, respectively. 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

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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 February 16, 2016, stockholders holding 5% or more of our common stock, as well as our executive officers, directors, and their respective affiliates, owned in the aggregate approximately 53% 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.

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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, 2015, we had $245 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

As of February 1, 2016, under two lease agreements, we leased an aggregate of approximately 116,000 square feet of laboratory and office space among three buildings located at 780, 784 and 790 Memorial Drive in Cambridge, Massachusetts. On September 25, 2014, we entered into a new lease covering 61,000 square feet of office space located at 784 Memorial Drive. On November 6, 2014, we entered into a lease extension covering 54,861 square feet of laboratory and office space at 780 and 790 Memorial Drive. Each lease expires on March 31, 2025, and each 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.

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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. Prior to January 3, 2011, our common stock was traded on the NASDAQ Global Market. 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.

	2015		2014	
	High	Low	High	Low
First quarter	$ 17.42	$ 13.66	$ 16.70	$ 11.30
Second quarter	15.44	10.23	13.25	8.40
Third quarter	11.13	7.56	16.93	8.80
Fourth quarter	10.85	7.19	18.25	11.90

Holders

As of February 1, 2016, there were 52 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, 2010 through December 31, 2015 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, 2010, and that all dividends were reinvested. No cash dividends have been declared or paid on our common stock.

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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.

Comparison of 5-Year Cumulative Total Return

among Infinity Pharmaceuticals, Inc.,

the NASDAQ Biotechnology Index,

and NASDAQ Stock Market (U.S.) Index

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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,				
	2015	2014	2013	2012	2011
Statement of Operations Data:					
Collaboration revenue	$ 109,066	$ 164,995	$	$ 47,114	$ 92,773
Operating expenses:					
Research and development	199,109	143,633	99,760	118,595	108,582
General and administrative	37,065	29,285	27,916	27,882	22,719
Total operating expenses	236,174	172,918	127,676	146,477	131,301
Gain on termination of Purdue entities alliance				46,555	
Loss from operations	(127,108)	(7,923)	(127,676)	(52,808)	(38,528)
Interest income (expense), net	(933)	(9,310)	896	(1,349)	(1,514)
Income from Massachusetts tax incentive award				193	
Loss before income taxes	(128,041)	(17,233)	(126,780)	(53,964)	(40,042)
Income tax	(335)	(183)			
Net loss	$ (128,376)	$ (17,416)	$ (126,780)	$ (53,964)	$ (40,042)
Basic and diluted loss per common share	$ (2.62)	$ (0.36)	$ (2.64)	$ (1.70)	$ (1.50)
Basic and diluted weighted average number of common shares outstanding	49,083,479	48,561,653	47,936,001	31,711,264	26,620,278

	As of December 31,				
	2015	2014	2013	2012	2011
Selected Balance Sheet Data:					
Cash, cash equivalents and available-for-sale securities, including long-term	$ 245,231	$ 333,245	$ 214,468	$ 326,635	$ 115,937
Working capital	184,641	289,691	202,735	311,086	88,995
Total assets	288,821	369,144	230,710	335,660	124,490
Long-term debt due to Purdue entities, net of debt discount(1)					37,553
Due to Takeda, less current portion(2)			6,456	6,252	
Construction liability(3)		15,456			
Financing obligation(4)	20,007				
Accumulated deficit	(595,588)	(467,212)	(449,796)	(323,016)	(269,052)
Total stockholders equity	98,557	209,472	201,275	310,205	15,433

(1) In November 2011, we borrowed $50 million under a line of credit agreement with Purdue and its independent associated entity, Purdue Pharma L.P., or PPLP. We reduced the long-term debt on our balance sheet with a debt discount. On September 7, 2012, upon completion of the sale and issuance of common stock to PPLP under the 2012 securities purchase agreement, the line of credit agreement with PPLP terminated in its entirety.

(2) 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

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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.

(3) 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 12 of the consolidated financial statements.

(4) 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 a prohibited form of continuing involvement. As of December 31, 2015, we held building and building improvements of approximately $23.6 million and a financing obligation of approximately $20 million. See note 12 of the consolidated financial statements.

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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 a clinical-stage biopharmaceutical company dedicated to discovering, developing and delivering best-in-class medicines to patients with difficult-to-treat diseases. Our most advanced product candidate is duvelisib, also known as IPI-145, an oral, dual inhibitor of the delta and gamma isoforms of phosphoinositide-3-kinase, or PI3K, which we are investigating in hematologic malignancies. In addition, we are developing IPI-549, an orally administered, clinical-stage, immuno-oncology product candidate that selectively inhibits the gamma isoform of PI3K and is currently being evaluated in solid tumors in a Phase 1 trial. Duvelisib and IPI-549 are investigational drug candidates and their safety and efficacy have not yet been evaluated by the U.S. Food and Drug Administration, or FDA, or any other health authority.

Duvelisib is being investigated in multiple late-stage clinical trials under our DUETTS (**Duve**lisib **T**rials in Hema**t**ologic Malignancie**s**) program, a worldwide investigation of duvelisib in blood cancers in collaboration with AbbVie Inc., or AbbVie. We expect to report topline data from our DYNAMO study in the third quarter of 2016, and if supported by the DYNAMO data, we anticipate that we will submit a New Drug Application, or NDA, in the fourth quarter of 2016 seeking accelerated approval of duvelisib from the FDA for the treatment of follicular lymphoma and small lymphocytic lymphoma. In addition, we expect to conduct a planned interim analysis of data from our DUO study in the second half of 2016. If supported by the interim analysis of data from our DUO study, we expect to report topline data from our DUO study in the second half of 2016 and submit an NDA in the fourth quarter of 2016 seeking regular approval from the FDA of duvelisib for the treatment of certain patients with CLL. Further, if supported by an interim analysis of data from the DUO study and data from our DYNAMO study, we expect that AbbVie will submit a Marketing Authorization Application, or MAA, in the fourth quarter of 2016 seeking approval from the European Medicines Agency, or EMA, to market duvelisib for certain patients with follicular lymphoma and CLL.

IPI-549, a selective PI3K-gamma inhibitor, is currently being evaluated in a Phase 1, first-in-human study that 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 a checkpoint inhibitor therapy 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 and melanoma.

We have primarily incurred operating losses since inception. Our net loss was $128.4 million, $17.4 million and $126.8 million for the years ended December 31, 2015, 2014 and 2013, respectively. As of December 31, 2015, we had an accumulated deficit of $595.6 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. We do not expect to generate any revenue from product sales until at least 2017, assuming we are able to file for regulatory approval for duvelisib in 2016 and receive approval in 2017.

We expect to continue to spend significant resources to fund the research, development, and potential commercialization of duvelisib and our other product candidates, and we expect to incur significant operating losses for the foreseeable future. While we may have net income in some periods as the result of non-recurring revenue from our collaboration with AbbVie, we expect to incur substantial operating losses over the next several

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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.

As of December 31, 2015, we had approximately $245 million in cash, cash equivalents and available-for-sale securities. We will need substantial additional funds to support our planned operations. While subject to the achievement of specified milestones, we intend to rely on proceeds from our collaboration with AbbVie together with our existing cash, cash equivalents and available-for-sale securities to fund our operations. Details regarding our collaboration with AbbVie can be found in this Form 10-K in Part I, Item 1 under the heading entitled *AbbVie*. Such proceeds may not be realized in the time frames we anticipate, or at all, and we expect that we will also be required to fund our operations in part through the sale of debt or equity securities, through debt facility arrangements, or through collaboration arrangements related to our other programs that could include up-front, royalty, or milestone payments. 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 through the first quarter of 2017.

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 discovery and development company. Our research and development expense to date has primarily consisted 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;

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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 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. Interest expense is related to the amortization of the loan commitment asset recognized under our Facility Agreement with Deerfield and the financing obligation related to the 784 Memorial Drive lease (see note 12).

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 are 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 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,

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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, and in the period the sales occur. We have not recognized any royalty revenue to date.

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, 2015, 2014 and 2013, in thousands, together with the change in each item as a percentage.

	2015	% Change	2014	% Change	2013
Collaboration revenue	$ 109,066	(34)%	$ 164,995		$
Research and development expense:					
Programs	(146,609)	14%	(128,633)	29%	(99,760)
Takeda payments	(52,500)	250%	(15,000)		
Total research and development expense	(199,109)	39%	(143,633)	44%	(99,760)
General and administrative expense	(37,065)	27%	(29,285)	5%	(27,916)
Interest expense	(1,368)	(86)%	(9,649)		
Investment and other income	435	28%	339	(62)%	896
Income tax	(335)	83%	(183)		

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Revenue

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 are being recognized using the proportionate performance method as services are provided over the estimated service period of approximately five years. We have 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. We have recorded the remaining amount of $24.5 million and $85.5 million as short-term and long-term deferred revenue, respectively, as of December 31, 2014.

The development, regulatory and commercialization milestones represent non-refundable amounts that would be paid by AbbVie to us if certain milestones are achieved in the future. We have elected to apply the milestones method of revenue recognition to these milestones. We have determined that all remaining milestones, if achieved, are substantive as they relate solely to past performance, are commensurate with estimated enhancement of value associated with the achievement of each milestone as a result of our performance, which are reasonable relative to other deliverables and terms of the arrangement and are unrelated to the delivery of any further elements under the arrangement.

We did not recognize revenue during the year ended December 31, 2013 as our strategic alliance with Mundipharma International Corporation Limited, or Mundipharma, and Purdue Pharmaceutical Products L.P., or Purdue, terminated in 2012, and our AbbVie strategic alliance commenced in 2014.

We expect to continue to recognize revenue related to development and committee services we perform under our collaboration agreement with AbbVie in 2016. We also expect to accrue in 2016 the next two anticipated milestones of $125 million associated with the acceptance by the FDA of the first NDA submission for duvelisib and $75 million associated with the acceptance by the EMA of the first MAA submission for duvelisib.

Research and Development Expense

Research and development expenses represented approximately 84% of our total operating expenses for the year ended December 31, 2015, 83% of our total operating expenses for the year ended December 31, 2014, and 78% of our total operating expenses for the year ended December 31, 2013.

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;

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$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.

The increase in research and development expense for the year ended December 31, 2014 compared to the year ended December 31, 2013 was primarily attributable to:

$28.0 million increase in clinical development expenses related to duvelisib;

$10.0 million milestone payment to Takeda for the initiation of DUO, our first phase 3 study with a PI3K inhibitor, and $5.0 million option fee payment to Takeda in connection with the 2014 amendment of our development and license agreement with Takeda; and

$9.2 million increase in compensation expense primarily due to an increase in contingent cash compensation and hiring of additional personnel.

These increases were partially offset by a decrease of $5.8 million in clinical development expenses due to the conclusion of our development of our Hsp90 inhibitor program.

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, 2015, 2014 and 2013, and from January 1, 2006 through December 31, 2015, we estimate that we incurred the following expenses by program:

Program	Year Ended December 31, 2015	Year Ended December 31, 2014	Year Ended December 31, 2013	January 1, 2006 to December 31, 2015
			(in millions)	
PI3K Inhibitor(1)	$ 189.6	$ 120.8	$ 71.7	$ 472.4
Hsp90 inhibitor	0.1	1.6	12.1	137.8
Hedgehog pathway inhibitor		0.1	1.2	164.1

(1) 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 programs to increase as we continue clinical development of duvelisib and 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 discovery and 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.

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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 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;
- the cost of establishing clinical supplies of any product candidates; 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, 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.

The increase in general and administrative expense for the year ended December 31, 2014 as compared to the year ended December 31, 2013 was primarily attributable to an increase of $1.5 million in compensation expense, primarily due to an increase in contingent cash compensation.

Interest Expense

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 Deerfield, which terminated in February 2015.

The increase in interest expense for the year ended December 31, 2014 as compared to the year ended December 31, 2013 was primarily attributable to the amortization of the loan commitment asset recognized under our Facility Agreement with Deerfield. In addition, in connection with the amendment of the Deerfield facility agreement on September 22, 2014, we reduced the loan commitment asset by 50% resulting in an additional expense of $1.8 million during 2014.

Investment and Other Income

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.

Investment and other income decreased in the year ended December 31, 2014 as compared to the year ended December 31, 2013 primarily as a result of lower yields. In addition, during the year ended December 31, 2013, we received a non-recurring cash distribution from one of our insurance carriers.

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Income Tax

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 at least the next year, 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, 2015, is less than six months. Because our product candidates are in various stages of clinical and preclinical development and the outcome of these efforts is uncertain, we cannot estimate the actual amounts necessary to successfully complete the development and commercialization of our product candidates or whether, or when, we may achieve profitability.

Our significant capital resources are as follows:

	December 31, 2015	December 31, 2014
	(in thousands)	
Cash, cash equivalents and available-for-sale securities	$ 245,231	$ 333,245
Working capital	184,641	289,691

	Year Ended December 31,		
	2015	2014	2013
	(in thousands)		
Cash (used in) provided by:			
Operating activities	$ (83,653)	$ 117,715	$ (113,907)
Takeda payments (included in operating activities above)	(59,167)	(21,667)	
Investing activities	(37,903)	117,853	606
Capital expenditures (included in investing activities above)	(6,426)	(1,362)	(1,754)
Financing activities	2,321	3,723	5,673

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, 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.

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 DYNAMO in September 2015. Further, AbbVie has agreed to pay us up to an additional $400 million in potential future milestone payments comprised of $125 million associated with the acceptance by the FDA of the first NDA

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submission for duvelisib, $75 million associated with the acceptance of the first MAA submission for duvelisib, up to $75 million associated with the achievement of specified regulatory approval milestones, and up to $125 million associated with the achievement of specified commercialization milestones.

On February 24, 2014, we entered into a Facility Agreement with Deerfield. The draw period has expired without our having drawn down on the Facility Agreement. During the year ended December 31, 2015, we paid a $1.5 million fee to Deerfield related to not drawing down any amount under the Facility Agreement.

Our investing activities for the years ended December 31, 2015, 2014 and 2013 included purchases and proceeds from maturities and sales of available-for-sale securities and purchases of property and equipment. Our investing activities for the year ended December 31, 2015 included $121.5 million in purchases of available-for-sale securities and proceeds of $89.5 million from maturities of available-for-sale securities. Capital expenditures for the year ended December 31, 2015 of $6.4 million primarily consisted of building and leasehold improvements. We recognized an additional $5.1 million in leasehold improvements which were paid for by our landlord.

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.

Our financing activities for the year ended December 31, 2013 included $5.3 million of proceeds from issuances of common stock from stock option exercises related to stock incentive plans and $0.4 million of proceeds from issuances of common stock related to our employee stock purchase plan.

We will need substantial additional funds to support our planned operations. AbbVie has paid us a $130 million enrollment milestone payment during the year ended December 31, 2015 and a $275 million upfront payment during the year ended December 31, 2014. In addition, AbbVie has agreed to pay us up to an aggregate of $400 million in milestone payments associated with the achievement of specified regulatory and commercialization events. We expect to accrue in 2016 the next two anticipated milestones of $125 million associated with the acceptance by the FDA of the first NDA submission for duvelisib and $75 million associated with the acceptance of the first MAA submission for duvelisib. In the absence of additional funding or business development activities, we believe that our existing cash, cash equivalents and marketable securities will be adequate to satisfy our capital needs through the first quarter of 2017. We have not included any of the $400 million of potential future AbbVie 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, which we do not expect to achieve for at least the next two years, 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

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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. Under our agreement with AbbVie, we have received $405 million in research and development funding to date.

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.

Contractual Obligations

As of December 31, 2015, we had the following contractual obligations, excluding contingent milestone payments:

		Payments Due by Period (in thousands)					
Contractual Obligations	**Total**	**2016**	**2017**	**2018**	**2019**	**2020**	

							2021 and beyond
784 facility	$ 19,952	$ 1,873	$ 2,044	$ 2,044	$ 2,044	$ 2,227	$ 9,720
780/790 facility	34,127	3,153	3,468	3,514	3,839	3,839	16,314
Software contract obligations	910	715	195				
Total contractual cash obligations	$ 54,989	$ 5,741	$ 5,707	$ 5,558	$ 5,883	$ 6,066	$ 26,034

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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 above. We are obligated to pay to Takeda up to $5 million in remaining success-based milestones for the development of a second product candidate, and up to $450 million in success-based milestones for the approval and commercialization of two distinct products. Because the achievement of these milestones had not occurred as of December 31, 2015, 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, 2015 and 2014, the accompanying consolidated balance sheet reflects the building and accumulated construction costs of approximately $23.0 million and $16.0 million, respectively, a financing obligation of approximately $20.0 million at December 31, 2015 and a construction liability of approximately $15.5 million at December 31, 2014 (see note 12 of the financial statements). In November 2014, we entered into an operating lease amendment with ARE-770/784/790 Memorial Drive, LLC for 54,861 square feet of leased premises at 780 and 790 Memorial Drive, Cambridge, Massachusetts.

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

In May 2014, the Financial Accounting Standards Board, or FASB, issued Accounting Standard Update, or ASU, No. 2014-09, *Revenue from Contracts with Customers*, 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. 2014-09 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. We are currently evaluating the method of adoption and the potential impact that ASU No. 2014-09 may have on our financial position and results of operations.

In August 2014, the FASB issued ASU No. 2014-15, *Disclosure of Uncertainties about an Entity s Ability to Continue as a Going Concern,* which provides guidance on determining when and how to disclose going

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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 interim and annual periods beginning after December 15, 2016, with early adoption permitted. The adoption of this guidance would not result in additional disclosure in our financial statements as of December 31, 2015. See note 2 for additional information on our existing cash, cash equivalents and available-for-sale securities. We will continue to evaluate the potential impact that ASU No. 2014-15 may have.

In November 2015, the FASB issued ASU No. 2015-17, *Income Taxes Balance Sheet Classification of Deferred Taxes,* which requires that deferred tax assets and liabilities be classified as noncurrent rather than being separated into current and noncurrent. ASU No. 2015-17 is effective for interim and annual periods beginning after December 15, 2016, with early adoption available. We early adopted ASU 2015-17 as of October 1, 2015 on a prospective basis and did not retrospectively adjust prior periods.

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 approximate $0.4 million decrease in the fair value of our investments as of December 31, 2015, as compared to an approximately $0.1 million decrease as of December 31, 2014. 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.

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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, 2015 and 2014, 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, 2015. 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, 2015 and 2014, and the consolidated results of its operations and its cash flows for each of the three years in the period ended December 31, 2015, 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, 2015, 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 February 23, 2016 expressed an unqualified opinion thereon.

/s/ Ernst & Young LLP

Boston, Massachusetts

February 23, 2016

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INFINITY PHARMACEUTICALS, INC.

Consolidated Balance Sheets

(in thousands, except share and per share amounts)

	December 31, 2015	December 31, 2014
Assets		
Current assets:		
Cash and cash equivalents	$ 188,170	$ 307,405
Available-for-sale securities	57,061	25,321
Loan commitment asset, net (note 10)		647
Prepaid expenses and other current assets	9,466	11,195
Total current assets	254,697	344,568
Property and equipment, net	28,240	18,970
Long-term available-for-sale securities		519
Restricted cash	1,681	1,680
Long-term receivable (note 12)	1,821	3,006
Other assets	2,382	401
Total assets	$ 288,821	$ 369,144
Liabilities and stockholders equity		
Current liabilities:		
Accounts payable	$ 9,628	$ 5,947
Accrued expenses	24,604	17,768
Due to Takeda		6,667
Deferred revenue, current	35,408	24,495
Financing obligation, current (note 12)	416	
Total current liabilities	70,056	54,877
Deferred revenue, less current portion	95,531	85,510
Deferred rent, less current portion (note 12)	4,632	3,375
Financing obligation, less current portion (note 12)	19,591	
Construction liability (note 12)		15,456
Other liabilities	454	454
Total liabilities	190,264	159,672
Commitments and contingencies (note 12)		
Stockholders equity:		
Preferred Stock, $.001 par value; 1,000,000 shares authorized, no shares issued and outstanding at December 31, 2015 and 2014		
Common Stock, $.001 par value; 100,000,000 shares authorized, 49,305,136 and 48,878,828 shares issued and outstanding at December 31, 2015 and December 31, 2014, respectively	49	49
Additional paid-in capital	694,051	676,521
Accumulated deficit	(595,588)	(467,212)
Accumulated other comprehensive income	45	114
Total stockholders equity	98,557	209,472
Total liabilities and stockholders equity	$ 288,821	$ 369,144

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

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INFINITY PHARMACEUTICALS, INC.

Consolidated Statements of Operations and Comprehensive Loss

(in thousands, except share and per share amounts)

	Years Ended December 31,		
	2015	2014	2013
Collaboration revenue	$ 109,066	$ 164,995	$
Operating expenses:			
Research and development	199,109	143,633	99,760
General and administrative	37,065	29,285	27,916
Total operating expenses	236,174	172,918	127,676
Loss from operations	(127,108)	(7,923)	(127,676)
Other income (expense):			
Interest expense	(1,368)	(9,649)	
Investment and other income	435	339	896
Total other income (expense)	(933)	(9,310)	896
Loss before income taxes	(128,041)	(17,233)	(126,780)
Income tax	(335)	(183)	
Net loss	$ (128,376)	$ (17,416)	$ (126,780)
Basic and diluted loss per common share	$ (2.62)	$ (0.36)	$ (2.64)
Basic and diluted weighted average number of common shares outstanding	49,083,479	48,561,653	47,936,001
Other comprehensive income (loss):			
Net unrealized holding gains (losses) on available-for-sale securities arising during the period	$ (69)	$ (42)	$ 22
Comprehensive loss	$ (128,445)	$ (17,458)	$ (126,758)

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

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INFINITY PHARMACEUTICALS, INC.

Consolidated Statements of Cash Flows

(in thousands)

	Years Ended December 31,		
	2015	**2014**	**2013**
Operating activities			
Net loss	$ (128,376)	$ (17,416)	$ (126,780)
Adjustments to reconcile net loss to net cash provided by (used in) operating activities:			
Depreciation	2,292	1,773	1,823
Stock-based compensation, including 401(k) match	14,700	12,588	12,155
Non-cash interest expense on amount Due to Takeda		211	415
Amortization of loan commitment asset	647	9,649	
Net amortization of premium/discount on available-for-sale securities	272	1,257	2,201
Other, net	(162)	83	(2)
Changes in operating assets and liabilities:			
Prepaid expenses and other assets	933	(494)	(7,284)
Accounts payable, accrued expenses and other liabilities	10,517	6,815	3,565
Due to Takeda	(6,667)	(6,667)	
Deferred revenue	20,934	110,005	
Deferred rent	1,257	(89)	
Net cash provided by (used in) operating activities	(83,653)	117,715	(113,907)
Investing activities			
Purchases of property and equipment	(6,426)	(1,362)	(1,754)
Purchases of available-for-sale securities	(121,456)	(21,789)	(249,764)
Proceeds from maturities of available-for-sale securities	89,515	141,004	251,093
Proceeds from sales of available-for-sale securities	464		1,031
Net cash provided by (used in) investing activities	(37,903)	117,853	606
Financing activities			
Proceeds from issuances of common stock related to stock incentive plans	1,866	3,881	5,299
Proceeds from issuances of common stock related to employee stock purchase plan	964	836	374
Payments on construction liability	(273)		
Payments on financing obligation	(236)		
Restricted cash		(548)	
Deferred transaction costs		(446)	
Net cash provided by financing activities	2,321	3,723	5,673
Net increase (decrease) in cash and cash equivalents	(119,235)	239,291	(107,628)
Cash and cash equivalents at beginning of period	307,405	68,114	175,742
Cash and cash equivalents at end of period	$ 188,170	$ 307,405	$ 68,114
Supplemental cash flow information			
Cash paid for interest	$ 721	$	$
Cash paid for income taxes	$ 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	$
Reclass 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.

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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, 2012	47,499,257	$ 48	$ 633,039	$ (323,016)	$ 134	$ 310,205
Exercise of stock options	634,420		5,299			5,299
Exercise of warrants	32,248					
Stock-based compensation expense			11,495			11,495
401(k) plan match issued in common stock	30,010		660			660
Issuance of common stock related to employee stock purchase plan	31,903		374			374
Unrealized gain on marketable securities					22	22
Net loss				(126,780)		(126,780)
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

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

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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, 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.

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INFINITY PHARMACEUTICALS, INC.

Notes to Consolidated Financial Statements

1. Organization

Infinity Pharmaceuticals, Inc. is an innovative biopharmaceutical company dedicated to discovering, developing and delivering 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, 2015 and 2014 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 interest and investment 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).

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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, 2015 will be adequate to satisfy our capital needs based on planned levels of spending through the first quarter of 2017. We have not included any of the future potential $400 million of AbbVie milestone payments in this forecast (see note 13). 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 discovery and 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 and 2015.

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. When placed into service, these assets are depreciated over the lease term to a residual value approximately equal to the remaining financing obligation at the end of the financing term. 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

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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 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.

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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, and 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, 2015 and 2014.

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

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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,		
	2015	2014	2013
Stock options	8,265,577	6,577,296	6,083,318
Warrants	1,000,000	1,000,000	

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, 2015, 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 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, and recognize the expense over the requisite service period on a straight-line basis. 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. 2014-09, *Revenue from Contracts with Customers*, which supersedes all existing revenue recognition requirements, including most industry-specific guidance. The new standard requires a company to recognize

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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. 2014-09 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. We are currently evaluating the method of adoption and the potential impact that ASU No. 2014-09 may have on our financial position and results of operations.

In August 2014, the FASB issued ASU No. 2014-15, *Disclosure of Uncertainties about an Entity s Ability to Continue as a Going Concern,* 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 interim and annual periods beginning after December 15, 2016, with early adoption permitted. The adoption of this guidance would not result in additional disclosure in our financial statements as of December 31, 2015. See note 2 for additional information on our existing cash, cash equivalents and available-for-sale securities. We will continue to evaluate the potential impact that ASU No. 2014-15 may have.

In November 2015, the FASB issued ASU No. 2015-17, *Income Taxes Balance Sheet Classification of Deferred Taxes,* which requires that deferred tax assets and liabilities be classified as noncurrent rather than being separated into current and noncurrent. ASU No. 2015-17 is effective for interim and annual periods beginning after December 15, 2016, with early adoption available. We early adopted ASU 2015-17 as of October 1, 2015 on a prospective basis and did not retrospectively adjust prior periods.

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, 2015, an aggregate of 5,929,155 shares of our common stock were reserved for issuance upon the exercise of outstanding awards, and up to 3,278,358 shares of common stock may be issued pursuant to awards granted under the 2010 Plan.

2000 Stock Incentive Plan

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, 2015, an aggregate of 2,316,686 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.

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2001 Stock Incentive Plan

In connection with the merger between Discovery Partners International, Inc., or DPI, and Infinity Pharmaceuticals, Inc., or IPI, in 2006, which we refer to as the DPI merger, we assumed awards that were granted under the Infinity Pharmaceuticals, Inc. Pre-Merger Stock Incentive Plan, or the 2001 Plan. The 2001 Plan provided for the grant of incentive stock options, nonstatutory stock options and restricted stock awards. Under the 2001 Plan, stock awards were granted to IPI s employees, officers, directors and consultants. Incentive stock options were granted at a price not less than fair value of the common stock on the date of grant. The board of directors of IPI determined the vesting of the awards. As of December 31, 2015, an aggregate of 19,736 shares of our common stock were reserved for issuance upon the exercise of outstanding assumed awards. The 2001 Plan was not assumed by us following the DPI merger; therefore, no further grants may be made under the 2001 Plan.

2013 Employee Stock Purchase Plan

Our 2013 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. 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. During 2013, 31,903 shares of common stock were purchased for total proceeds of $0.4 million.

Compensation Expense

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

	Year Ended December 31,		
	2015	2014	2013
		(in thousands)	
Research and development	$ 8,474	$ 7,502	$ 6,213
General and administrative	6,226	5,086	5,942
Total stock-based compensation expense	$ 14,700	$ 12,588	$ 12,155

As of December 31, 2015, we had approximately $19.4 million of total unrecognized compensation cost, net of estimated forfeitures, related to unvested options and awards under our ESPP, which are expected to be recognized over a weighted-average period of 2.3 years.

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:

	Year Ended December 31,		
	2015	2014	2013
Risk-free interest rate	1.5%	1.7%	1.1%
Expected annual dividend yield			
Expected stock price volatility	70.8%	70.9%	64.6%
Expected term of options	5.4 years	5.0 years	5.4 years

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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, 2015, 2014 and 2013, the weighted-average forfeiture rate was estimated to be 14%, 14%, and 13%, respectively.

All options granted to employees during the years ended December 31, 2015, 2014 and 2013 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, 2015 is as follows:

	Stock Options	Weighted-Average Exercise Price	Weighted-Average Remaining Contractual Life (years)	Aggregate Intrinsic Value (in millions)
Outstanding at January 1, 2015	6,577,296	$ 13.76		
Granted	2,570,841	14.07		
Exercised	(225,578)	14.51		
Forfeited	(656,982)	17.26		
Outstanding at December 31, 2015	8,265,577	$ 13.73	6.0	$ 2.3
Vested or expected to vest at December 31, 2015	7,847,146	$ 13.71	5.8	$ 2.3
Exercisable at December 31, 2015	5,648,016	$ 13.02	4.8	$ 2.3

The weighted-average fair value per share of options granted during the years ended December 31, 2015, 2014 and 2013 was $8.48, $7.45 and $18.07, respectively.

The aggregate intrinsic value of options outstanding at December 31, 2015 was calculated based on the positive difference between the closing fair market value of our common stock on December 31, 2015 and the exercise price of the underlying options. The aggregate intrinsic value of options exercised during the years ended December 31, 2015, 2014 and 2013 was $1.5 million, $4.0 million and $16.0 million, respectively. The

total cash received from employees and non-employees as a result of stock option exercises during the year ended December 31, 2015 was $1.8 million.

No related income tax benefits were recorded during the years ended December 31, 2015, 2014 or 2013.

We settle employee stock option exercises with newly issued shares of our common stock.

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During the year ended December 31, 2014, two members of our board of directors retired, and we extended these directors rights to exercise their vested stock options for an additional six-month period. In addition, one employee whose employment terminated received an accelerated vesting of his unvested options. In connection with these modifications, we recognized an additional $0.4 million of stock-based compensation expense during the year ended December 31, 2014.

Employee Stock Purchase Plan

The weighted-average fair value of each purchase right granted during the year ended December 31, 2015, 2014 and 2013 was $4.24, $5.66 and $8.68, respectively. For the years ended December 31, 2015, 2014 and 2013, the fair values were estimated using the Black-Scholes valuation model using the following weighted-average assumptions:

	Year Ended December 31,		
	2015	2014	2013
Risk-free interest rate	0.4%	0.3%	0.3%
Expected annual dividend yield			
Expected stock price volatility	60.3%	66.7%	91.5%
Expected term of options	1.25 years	1.25 years	1.25 years

4. Cash, Cash Equivalents and Available-for-Sale Securities

The following is a summary of cash, cash equivalents and available-for-sale securities:

	December 31, 2015			
	Cost	Gross Unrealized Gains	Gross Unrealized Losses	Estimated Fair Value
		(in thousands)		
Cash and cash equivalents due in 90 days or less	$ 188,170	$	$	$ 188,170
Available-for-sale securities:				
Corporate obligations due in one year or less	46,049	52	(4)	46,097
Asset-backed securities due in one year or less	10,967		(3)	10,964
Total available-for-sale securities	57,016	52	(7)	57,061
Total cash, cash equivalents and available-for-sale securities	$ 245,186	$ 52	$ (7)	$ 245,231

	December 31, 2014			
	Cost	Gross Unrealized Gains	Gross Unrealized Losses	Estimated Fair Value
		(in thousands)		
Cash and cash equivalents due in 90 days or less	$ 307,405	$	$	$ 307,405
Available-for-sale securities:				
Corporate obligations due in one year or less	21,324	6	(1)	21,329
Mortgage-backed securities due after ten years	412	107		519
U.S. government-sponsored enterprise obligations due in one year or less	3,990	2		3,992
Total available-for-sale securities	25,726	115	(1)	25,840

Total cash, cash equivalents and available-for-sale securities	$ 333,131	$ 115	$ (1)	$ 333,245

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We held six debt securities at December 31, 2015 that had been in an unrealized loss position for less than twelve months. The fair value of these securities was $25.1 million. We evaluated our securities for other-than-temporary impairments based on quantitative and qualitative factors. We considered the decline in market value for these six securities to be primarily attributable to current economic and market conditions. It is not more likely than not that we will be required to sell these securities, and we do not intend to sell these securities before the recovery of their amortized cost bases. Based on our analysis, we do not consider these investments to be other-than-temporarily impaired as of December 31, 2015.

As of December 31, 2015, we held eight securities in financial institutions and other corporate debt securities located in Japan, Sweden, Germany, Australia, the United Kingdom and France with a fair value of $52.8 million. These securities are short term in nature and are all scheduled to mature within twelve months. There were no material unrealized losses incurred by these securities.

We had no material realized gains or losses on our available-for-sale securities for the years ended December 31, 2015, 2014 and 2013. There were no other-than-temporary impairments recognized for the years ended December 31, 2015, 2014 and 2013.

5. Fair Value

We use a valuation hierarchy for disclosure of the inputs used to measure fair value. This hierarchy prioritizes the inputs into three broad levels. Level 1 inputs, which we consider the highest level inputs, are quoted prices (unadjusted) in active markets for identical assets or liabilities. Level 2 inputs are quoted prices for similar assets and liabilities in active markets or inputs that are observable for the asset or liability, either directly or indirectly through market corroboration, for substantially the full term of the financial instrument. Level 3 inputs are unobservable inputs based on our own assumptions used to measure assets and liabilities at fair value. The classification of a financial asset or liability within the hierarchy is determined based on the lowest level input that is significant to the fair value measurement. For our fixed income securities, we reference pricing data supplied by our custodial agent and nationally known pricing vendors, using a variety of daily data sources, largely readily-available market data and broker quotes. We validate the prices provided by our third-party pricing services by reviewing their pricing methods and obtaining market values from other pricing sources. After completing our validation procedures, we did not adjust or override any fair value measurements provided by our pricing services as of December 31, 2015 and 2014.

The following table provides the assets carried at fair value measured on a recurring basis as of December 31, 2015:

	Level 1	Level 2
	(in thousands)	
Assets:		
Cash and cash equivalents	$ 139,196	$ 48,974
Corporate obligations (including commercial paper)		46,097
Asset-backed securities		10,964
Total	$ 139,196	$ 106,035

The fair value of the available-for-sale securities and cash and cash equivalents (including asset types listed below with maturities of three months or less at the time of purchase) is based on the following inputs:

Corporate Obligations:

Commercial paper: calculations by custodian based on the three month Treasury bill published on last business day of the month.

Other: benchmark yields, reported trades, broker/dealer quotes, issuer spreads, two-sided markets, benchmark securities, bids, offers and reference data.

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Mortgage-backed securities: benchmark yields, reported trades, broker/dealer quotes, issuer spreads, two-sided markets, benchmark securities, bids, offers and reference data, new issue data, monthly payment information and collateral performance.

U.S. government-sponsored enterprise obligations: benchmark yields, reported trades, broker/dealer quotes, issuer spreads, two-sided markets, benchmark securities, bids, offers and reference data.

The carrying amounts reflected in the consolidated balance sheets for unbilled accounts receivable, prepaid expenses and other current assets, other assets, accounts payable and accrued expenses approximate their fair value due to their short term maturities.

There have been no changes to the valuation methods during the year ended December 31, 2015. We evaluate transfers between levels at the end of each reporting period. There were no transfers of assets or liabilities between Level 1 and Level 2 during the year ended December 31, 2015. We had no available-for-sale securities that were classified as Level 3 at any point during the year ended December 31, 2015.

6. Prepaid expenses and other current assets

Prepaid expenses and other current assets consist of the following:

	December 31,	
	2015	2014
	(in thousands)	
Prepaid comparator drug	$	$ 5,085
Prepaid expenses	6,898	4,124
Other current assets	1,383	322
Short-term receivable (note 12)	1,185	
Value-added tax		1,664
Total prepaid expenses and other current assets	$ 9,466	$ 11,195

7. Property and Equipment

Property and equipment consist of the following:

	December 31,	
	2015	2014
	(in thousands)	
Laboratory equipment	$ 12,190	$ 12,615
Computer equipment and software	5,704	5,550
Furniture and fixtures	2,136	720
Construction in process		16,004
Building and building improvements	23,586	
Leasehold improvements	5,533	5,041
	49,149	39,930
Less accumulated depreciation	(20,909)	(20,960)
	$ 28,240	$ 18,970

During the year ended December 31, 2015, $2.3 million of fully depreciated assets were retired.

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

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of the building during the construction period. The construction was substantially complete, and the Leased Premises were 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. As of December 31, 2015, we recognized the building as building and building improvements of $14.7 million on our consolidated balance sheet (see note 12). As of December 31, 2014, we recognized the building as construction in process of $14.7 million on our consolidated balance sheet (see note 12).

During the year ended December 31, 2013, we capitalized approximately $0.4 million of costs associated with internally developed software. Depreciation expense associated with this software was $0.1 million, $0.1 million and $49,000 during 2015, 2014 and 2013, respectively.

8. Restricted Cash

We held $1.7 million in restricted cash as of December 31, 2015 and December 31, 2014. The balances are held on deposit with a bank to collateralize standby letters of credit in the name of our facility lessors in accordance with our facility lease agreements.

9. Other assets

Other assets consist of the following:

	December 31,	
	2015	2014
	(in thousands)	
Value-added tax	$ 2,034	$
Long term prepaid expenses	284	373
Other assets	64	28
Total other assets	$ 2,382	$ 401

10. Debt Facility Agreement

On February 24, 2014, we entered into a facility agreement with affiliates of Deerfield Management Company, L.P., or Deerfield, pursuant to which Deerfield agreed to loan us up to $100 million, subject to the terms and conditions set forth in the facility agreement. On September 22, 2014, we amended the facility agreement with Deerfield to reduce the maximum principal amount that we may draw down to $50 million. We refer to the facility agreement with Deerfield, as amended, as the Facility Agreement. Under the terms of the Facility Agreement, we had the right to draw down on the Facility Agreement in $25 million minimum disbursements, which we refer to as the Loan Commitment, at any time during a pre-specified draw period. The draw period expired without our having drawn down on the Facility Agreement.

On February 25, 2015, we paid a $1.5 million fee to Deerfield representing 3% of the total amount not drawn under the amended facility. In connection with the execution of the original facility agreement in February 2014, we issued to Deerfield warrants to purchase an aggregate of 1,000,000 shares of common stock at an exercise price of $13.83 per share. The warrants have dividend rights to the same extent as if the warrants were exercised into shares of common stock. The warrants expire on the seventh anniversary of their issuance and contain certain limitations that prevent the holder from acquiring shares upon exercise of a warrant that would result in the number of shares beneficially owned by the holder exceeding 9.985% of the total number of shares of common stock then issued and outstanding.

Our total cost of securing the Loan Commitment was $11.8 million and is comprised of $8.4 million representing the fair value of the 1,000,000 warrants issued on February 24, 2014; $3.0 million representing the original facility fee; and $0.4 million of transaction costs. As a result of the amendment of the Facility

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Agreement, the original facility fee was reduced by 50%, or $1.5 million, and we recorded a corresponding decrease in the loan commitment asset. In addition, since our borrowing capacity was reduced by 50%, the remaining loan commitment asset outstanding as of September 22, 2014 was also reduced by 50% resulting in an additional expense of $1.8 million during the year ended December 31, 2014. The total fair value is considered a Loan Commitment Asset which was classified as a current asset on the December 31, 2014 consolidated balance sheet. This amount is considered a fee to secure the Loan Commitment and was being amortized to interest expense on a straight line basis over the draw period. We recorded $0.6 million and $9.6 million of interest expense associated with the amortization and write-off of the loan commitment asset pursuant to the modification of the facility for the year ended December 31, 2015 and 2014, respectively.

11. Accrued Expenses

Accrued expenses consisted of the following:

	December 31,	
	2015	2014
	(in thousands)	
Accrued compensation and benefits	$ 8,732	$ 7,353
Accrued drug manufacturing costs	3,494	1,280
Accrued clinical studies	8,531	5,134
Accrued preclinical studies	400	543
Facility fee		1,500
Deferred rent, current	261	
Other	3,186	1,958
Total accrued expenses	$ 24,604	$ 17,768

12. Commitments and Contingencies

We lease our office and laboratory space under two separate lease agreements with BHX, LLC, as trustee of 784 Realty Trust for space at 784 Memorial Drive, and ARE-770/784/790 Memorial Drive, LLC for space at 780 and 790 Memorial Drive.

784 Memorial Drive Lease Arrangement

On September 25, 2014, we entered into a lease agreement, or the Lease, with BHX, LLC, as trustee of 784 Realty Trust, or the Landlord, for the lease of office space at 784 Memorial Drive, Cambridge, Massachusetts. The term of the Lease commenced on November 1, 2014, the Commencement Date, and expires on March 31, 2025, the Expiration Date. Pursuant to the Lease, on the Commencement Date we agreed to lease 61,000 square feet of the leased premises, which represents the entire building, the Leased Premises.

From the Commencement Date until March 31, 2015, the total base rent of the Lease was zero dollars per month. From April 1, 2015 through March 31, 2020, the total base rent of the Lease is $170,292 per month. From April 1, 2020 until the Expiration Date, the total base rent of the Lease will be $190,625 per month. In addition to the base rent, we are also responsible for our share of the operating expenses, utility costs and real estate taxes, in accordance with the terms of the Lease. Pursuant to the terms of the Lease, we provided a security deposit in the form of a letter of credit in the initial amount of $1.0 million, which may be reduced by up to $750,000 over time in accordance with the terms of the Lease. The letter of credit plus the associated bank fee of $30,000 has been included in our accompanying consolidated balance sheets as restricted cash. The Landlord agreed to pay up to $5,856,100 for certain updates and repairs to be made to the Leased Premises. We have two consecutive rights to extend the term of the Lease for five years under each extension, provided that we provide notice to the Landlord no earlier than 18 months or later than 12 months prior to expiration of the Lease. The base rent for each extension term shall be equal to 95% of the then fair market base rent per square foot for the premises. The Lease

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contains customary provisions allowing the Landlord to terminate the lease if we fail to remedy a default of any of our obligations under the Lease within specified time periods or upon our bankruptcy or insolvency.

Upon signing the lease agreement, we paid the first month s rent for April 2015 in the amount of $170,292, which was recorded as a prepaid expense on the accompanying consolidated balance sheet at December 31, 2014.

Upon the Commencement Date, building construction was initiated to suit our future needs. We were responsible for the construction project, including having responsibility to pay for a portion of the structural elements of the building and bearing the risk of cost overruns. Therefore, we were deemed for accounting purposes to be the owner of the building during the construction period. Accordingly, we determined the fair value of the building as of November 1, 2014 through an independent appraisal and recorded the building as an asset on our consolidated balance sheet, together with a corresponding construction liability, in November 2014 when the lease and construction commenced. On our consolidated balance sheet, we recorded project construction costs as an asset during the construction period and reflected an increase in the construction financing obligation for the amount of Landlord incentives received. 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 construction liability was reclassified to a financing obligation as such transaction did not qualify for sale-leaseback accounting due to our continuing involvement with the property in the form of non-recourse financing to the lessor as well as our obligation to pay for all costs in excess of the specified Landlord allowances. Depreciation on the building and building improvements commenced in June 2015 and will be recorded over the initial term of the lease using a residual value equal to the financing obligation at the end of the lease term, which approximates the net book value using the estimated useful lives of the respective assets. Interest expense is recorded on a monthly basis using an estimated incremental borrowing rate based on comparable 10 year secured financings and commenced in June 2015 when the building was placed into service. In April and May 2015, the construction financing obligation was reduced by that portion of the lease payment allocated to the construction financing obligation principal. Commencing in June 2015, the financing obligation is reduced on a monthly basis by that portion of the lease payment allocated to the financing obligation principal.

At December 31, 2015 and 2014, the accompanying consolidated balance sheet reflects the building and accumulated construction costs of approximately $23.0 million and $16.0 million, respectively, a financing obligation of approximately $20.0 million at December 31, 2015 and a construction liability of approximately $15.5 million at December 31, 2014.

We divide our future lease payments into a portion that is allocated to the financing obligation and a portion that is allocated to the land on which the building is located. The portion of the lease obligation allocated to the land is treated for accounting purposes as an operating lease commencing in November 2014 and recorded on a straight-line basis over the initial lease term. Rent expense pertaining to the land was approximately $0.4 million and $0.1 million for the twelve months ended December 31, 2015 and 2014, respectively.

In November 2015 we subleased approximately 12,000 square feet of the Leased Premises to two tenants with initial terms ending in July 2017 and October 2017, respectively. We also granted each tenant an option to extend the term for one year. For the year ending December 31, 2015 sublease income of approximately $0.1 million is included in other income in our consolidated statements of operations and comprehensive loss and is not offset against rent expense because, for accounting purposes, we are considered the owner of the building. Minimum future sublease income under these noncancelable subleases is approximately $0.7 million and $0.5 million in 2016 and 2017, respectively.

780/790 Memorial Drive Lease Arrangement

On November 6, 2014, we entered into a Seventh Amendment to Lease, the Lease Amendment, by and between us and ARE-770/784/790 Memorial Drive, LLC, the landlord, which amends the original lease

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agreement dated July 2, 2002, as amended to date, or the Original Lease. We refer to the Original Lease together with the Lease Amendment as the Memorial Drive Lease. We refer to the area rented under the Memorial Drive Lease as the Premises.

Under the Lease Amendment: (i) the Premises consist of 54,861 square feet, of which 51,000 square feet are located at 780 Memorial Drive, or the 780 Premises, and the remaining 3,861 square feet are located at 790 Memorial Drive, or the 790 Premises; effective February 1, 2016 we surrendered 13,159 square feet of the previously leased 17,020 square feet at the 790 Premises; (ii) we have extended the base term of the Memorial Drive Lease through March 31, 2025; and (iii) we have two separate five-year options to extend the term of the Memorial Drive Lease to 2035 on the same terms and conditions (other than with respect to base rent). The Memorial Drive Lease provides that we shall continue to pay the base rent as provided in the Original Lease until January 31, 2016. The base rent shall then increase to $69.00 per square foot of the Premises on February 1, 2016 and again to $70.00 per square foot of the Premises on February 1, 2018. The Memorial Drive Lease provides that no base rent for the Premises shall be due (i) for the period commencing on February 1, 2015 through July 31, 2015, (ii) for the period commencing on February 1, 2016 through February 29, 2016, (iii) for the period commencing on February 1, 2017 through February 28, 2017, and (iv) for the period commencing on February 1, 2018 through February 28, 2018. We also received allowances of $3.0 million for the design and construction of tenant improvements. The total of these allowances of $3.0 million has been reflected on our consolidated balance sheets as a receivable, with a corresponding amount included in deferred rent liability. Of this $3.0 million, approximately $1.2 million has been classified as a current asset and represents the estimated improvements that will be performed during 2016. The deferred rent is being amortized to rent expense over the term of the lease. Pursuant to the terms of the Lease Amendment, the security deposit in the form of a letter of credit has been reduced from $1.1 million to $0.6 million. The deposit has been included in our accompanying condensed consolidated balance sheets as restricted cash.

We have determined that the proposed improvements on the 780 Premises generally consist of normal tenant improvements and that we will not be deemed for accounting purposes to be the owner of the building during the construction period.

Future minimum payments, excluding operating costs and taxes, under the two lease agreements described above are as follows:

	784 Facility	780/790 Facility
	(in thousands)	
Years Ending December 31:		
2016	$ 1,873	$ 3,153
2017	2,044	3,468
2018	2,044	3,514
2019	2,044	3,839
2020	2,227	3,839
2021 and beyond	9,720	16,314
Total minimum lease payments	$ 19,952	$ 34,127

Rent expense of $4.6 million, $4.7 million and $4.7 million, before considering sublease income, was incurred during the years ended December 31, 2015, 2014 and 2013, respectively. Deferred rent is being amortized to rent expense over the life of the lease. During the years ended December 31, 2015, 2014 and 2013, we subleased a portion of our facility space at 790 Memorial Drive for total sublease income of $0.6 million, $0.2 million and $0.2 million, respectively. We record sublease payments that we receive on the sublease at 790 Memorial Drive as an offset to rent expense in our consolidated statements of operations and comprehensive loss. The sublease expires in January 2016. Future minimum sublease income under the existing sublease is expected to be $0.1 million for the year ended December 31, 2016.

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13. Collaborations

AbbVie

On September 2, 2014, we entered into a collaboration and license agreement with AbbVie, which we refer to as the AbbVie Agreement. Under the AbbVie Agreement, we are collaborating with AbbVie to develop and commercialize products containing duvelisib, an oral, dual inhibitor of the delta and gamma isoforms of phosphoinositide-3-kinase, or PI3K, which we refer to as Duvelisib Products, in oncology indications. IPI-549 is excluded from the collaboration. Under the terms of the AbbVie Agreement, we have granted to AbbVie licenses under applicable patents, patent applications, know-how and trademarks to develop, commercialize and manufacture Duvelisib Products in oncology indications. These licenses are generally co-exclusive with rights we retain, except that we have granted AbbVie exclusive licenses to commercialize Duvelisib Products outside the United States. We and AbbVie retain the rights to perform our respective obligations and exercise our respective rights under the AbbVie Agreement, and we and AbbVie may each grant sublicenses to affiliates or third parties.

Under the AbbVie Agreement, we and AbbVie have created a governance structure, including committees and working groups to manage the development, manufacturing and commercialization responsibilities for Duvelisib Products. Generally, we and AbbVie must mutually agree on decisions, although in specified circumstances either we or AbbVie would be able to break a deadlock.

We and AbbVie share oversight of development and have each agreed to use diligent efforts, as defined in the AbbVie Agreement, to carry out our development activities under an agreed upon development plan. We have primary responsibility for the conduct of development of Duvelisib Products, unless otherwise agreed, and AbbVie has responsibility for the conduct of certain contemplated combination clinical studies, including those examining duvelisib and venetoclax, which we refer to as the AbbVie Studies. The development and manufacturing costs for the AbbVie Studies are shared equally. During the year ended December 31, 2015, we recognized an expense of $1.2 million in research and development expense related to our share of the AbbVie Studies cost.

We have the responsibility to manufacture Duvelisib Products until we transition manufacturing responsibility to AbbVie. Excluding the AbbVie Studies, we are responsible for all costs to develop and manufacture Duvelisib Products up to a maximum amount of $667 million after which we will share Duvelisib Product development and manufacturing costs equally with AbbVie. During the year ended December 31, 2015, we recognized an expense of $8.0 million in research and development expense related to costs incurred by AbbVie for other than the AbbVie Studies.

We and AbbVie share operational responsibility and decision making authority for commercialization of Duvelisib Products in the United States. Specifically, we have the primary responsibility for advertising, distribution, and booking sales, and we share certain other commercialization functions with AbbVie. Assuming regulatory approval, we and AbbVie are obligated to each provide half of the sales representative effort to promote Duvelisib Products in the United States. Outside the United States, AbbVie has, with limited exceptions, operational responsibility and decision making authority to commercialize Duvelisib Products. We and AbbVie will share the cost of manufacturing and supply for commercialization of Duvelisib Products in the United States, and AbbVie will bear the cost of manufacturing and supply for commercialization of Duvelisib Products outside the United States. Prior to commercialization and regulatory approval, we will recognize the cost of manufacturing as a component of research and development and the cost of commercialization as a component of general and administrative expenses. Subsequent to regulatory approval and commercial launch, the cost of manufacturing will be recorded as cost of goods sold. During the years ended December 31, 2015 and 2014, we accounted for AbbVie s share of the costs as a reduction of the related expense. We recognized a credit of $0.8 million in research and development expense related to these costs during the year ended December 31, 2015. During the year ended December 31, 2015 and December 31, 2014, we recognized credits of $2.0 million and $0.1 million, respectively, in general and administrative expense related to these costs.

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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™ in September 2015. DYNAMO is a Phase 2, open-label, single-arm monotherapy study evaluating the safety and efficacy of duvelisib dosed at 25 mg twice daily, or BID, in approximately 120 patients with indolent non-Hodgkin lymphoma, or iNHL, including follicular lymphoma, marginal zone lymphoma and small lymphocytic lymphoma, whose disease is refractory to rituximab and to either chemotherapy or radioimmunotherapy. Further, AbbVie has agreed to pay us up to an additional $400 million in potential future milestone payments comprised of $125 million associated with the acceptance by the FDA of the first NDA submission for duvelisib, $75 million associated with the acceptance of the first MAA submission for duvelisib, up to $75 million associated with the achievement of specified regulatory approval milestones, and up to $125 million associated with the achievement of specified commercialization milestones.

Under the terms of the AbbVie Agreement, we and AbbVie will equally share commercial profits or losses of Duvelisib Products in the United States, including sharing equally the existing royalty obligations to Mundipharma International Corporation Limited, or Mundipharma, and Purdue Pharmaceutical Products L.P., or 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.

Additionally, AbbVie has 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. We are responsible for the existing royalty obligations to Mundipharma and Purdue outside the United States, and AbbVie has agreed to reimburse us for our existing Duvelisib Product milestone payment obligations to Takeda outside the United States. The tiered royalty from AbbVie is subject to a reduction of 4% at each tier if our royalties to Mundipharma and Purdue are reduced according to the terms of our respective agreements with Mundipharma and Purdue. This tiered royalty can further be reduced based on specified factors, including patent expiry, generic entry, and royalties paid to third parties with blocking intellectual property. These royalties are payable on a product-by-product and country-by-country basis until AbbVie ceases selling the product in the country.

We have evaluated the deliverables within the AbbVie Agreement to determine whether or not they provide value on a stand-alone basis. Based on our evaluation, we determined that there are three deliverables: the license, the development services and the committee services. Each deliverable provides value on a stand-alone basis and represents a separate unit of accounting. We determined the best estimate of selling price for each unit of accounting using a discounted cash-flow model. The valuation for each deliverable involves significant estimates and assumptions, including but not limited to, expected market opportunity, assumed royalty rates, pricing objectives, clinical trial timelines, likelihood of success and projected costs. The resulting estimate of selling prices for the license and development services consider the benefits that have been retained by us.

Of the $275 million upfront payment received during the year ended December 31, 2014, $159.1 million was allocated to the license, $115.6 million to the development services and $0.3 million to committee services based on the allocation of best estimate of selling price on a relative basis. We determined the best estimate of selling prices for the license unit of accounting based on estimates and assumptions resulting in an expected future cash flow which was discounted based on an estimated weighted average cost of capital of 11.5%. We determined the best estimate of selling prices for development and committee services based on the nature of the services to be performed and estimates of the associated efforts and third-party rates for similar services using a discount rate of 8% for development services and 11.5% for committee services. We recognized license revenue upon execution of the arrangement. Revenue related to development services and committee services is being recognized using the proportionate performance method as services are provided over the estimated service period of approximately five years. We have determined that the clinical development milestone achieved on September 30, 2015 was not substantive based on risk and effort involved and have applied the proportionate performance method to recognizing the related revenue. Of the $130 million milestone achieved, $75.2 million

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was allocated to the license, $54.7 million to the development services and $0.1 million to committee services based on the same allocation of best estimate of selling price on a relative basis as determined at the inception of the arrangement. Upon achievement of the milestone on September 30, 2015, we recognized the $75.2 million allocated to the license as revenue and $9.8 million of revenue related to the development and committee services performed from the inception of the AbbVie Agreement through September 30, 2015. During the year ended December 31, 2015 and December 31, 2014, we recognized $109 million and $165 million, respectively, of revenue related to the license and development and committee services. We have 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.

The regulatory and commercialization milestones represent non-refundable amounts that would be paid by AbbVie to us if certain milestones are achieved in the future. We have elected to apply the milestones method of revenue recognition to all remaining milestones. We have determined that all remaining milestones, if achieved, are substantive because (i) they relate solely to past performance, (ii) are commensurate with estimated enhancement of value associated with the achievement of each milestone as a result of our performance, which are reasonable relative to other deliverables and terms of the arrangement, and (iii) are unrelated to the delivery of any further elements under the arrangement.

Subject to limited exceptions, we have agreed that we and our affiliates will not commercialize, or assist others in commercializing, in oncology indications any product that is a PI3K delta, gamma inhibitor that meets certain agreed-to criteria, other than Duvelisib Products, and AbbVie has agreed to similar restrictions. Registration-directed clinical trials and commercialization of Duvelisib Products for uses outside of oncology indications would require our and AbbVie s mutual consent.

The AbbVie Agreement will remain in effect until all development, manufacturing and commercialization of Duvelisib Products cease, unless terminated earlier. Either we or AbbVie may terminate the AbbVie Agreement if the other party is subject to certain insolvency proceedings or if the other party materially breaches the AbbVie Agreement and the breach remains uncured for a specified period, which may be extended in certain circumstances. However, we may terminate the AbbVie Agreement only on a country-by-country basis in the event AbbVie is not using diligent efforts to obtain regulatory approval or to commercialize Duvelisib Products in a country outside the United States. AbbVie may also terminate the AbbVie Agreement for convenience after a specified notice period. In the event there is a material uncured breach by either us or AbbVie of development or commercialization obligations, the non-breaching party may also have the right to assume and conduct such applicable development or commercialization obligations. If AbbVie or any of its affiliates or sublicensees challenges the patents we have licensed to AbbVie, we can terminate the AbbVie Agreement if the challenge is not withdrawn after a specified notice period.

If the AbbVie Agreement is terminated, we would receive all rights to the regulatory filings related to duvelisib upon our request, our license to AbbVie would terminate, and AbbVie would grant us a perpetual, irrevocable license to develop, manufacture and commercialize products containing duvelisib, excluding any compound which is covered by patent rights controlled by AbbVie or its affiliates. This license would be royalty-free, unless the AbbVie Agreement is terminated for material breach, in which case, depending on the breaching party and the timing of the material breach, a royalty rate may be payable by us ranging from a low single-digit percentage to a low double-digit percentage of net sales, and, in some cases, subject to a payment cap.

If the AbbVie Agreement is terminated, we would not be entitled to receive payment for any milestone achieved after notice of termination but before the effective date of termination. Further, if the AbbVie Agreement is terminated, there are certain wind-down obligations to ensure a smooth transition of the responsibilities of the parties including, unless the AbbVie Agreement is terminated by AbbVie for our material breach, the continued conduct of certain development and commercialization activities by AbbVie for a limited

transition period and the continued funding by AbbVie of its half of the cost of the AbbVie Studies ongoing at the time of termination, except for those AbbVie Studies that may be transitioned to Infinity following termination.

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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, and we paid Intellikine a $13.5 million upfront license fee. In January 2012, Intellikine was acquired by Takeda, acting through its Millennium business unit. We refer to our PI3K inhibitor program licensor as Takeda. In December 2012, we amended and restated our development and license agreement with Takeda.

Under the terms of the amended and restated agreement, we retained worldwide development rights and, in exchange for an agreement to pay Takeda $15 million in installments, we regained commercialization rights for products arising from the agreement for all therapeutic indications and we are solely responsible for research conducted under the agreement. During the year ended December 31, 2012, we paid $1.7 million of the $15 million, and we recorded the $15 million release payment at its fair value of $14.4 million in research and development expenses. During the year ended December 31, 2014, we paid to Takeda the second installment of $6.7 million. During the year ended December 31, 2015, we paid to Takeda the final installment of $6.7 million.

We are obligated to pay to Takeda up to $5 million in remaining 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 $450 million in success-based milestone payments for the approval and commercialization of two distinct products, of which one could be a Duvelisib Product and the other could be a product containing IPI-549. In February 2014, we paid Takeda a $10 million milestone payment in connection with the initiation of DUO. DUO is a randomized, Phase 3 monotherapy study designed to evaluate the safety and efficacy of duvelisib dosed at 25 mg BID compared to ofatumumab, a monoclonal antibody therapy, in approximately 300 patients with relapsed or refractory chronic lymphocytic leukemia. We recognized the $10 million payment as research and development expense during the year ended December 31, 2014.

On March 31, 2015, we paid to Takeda a $52.5 million fee to exercise an option that we purchased from them in July 2014 for a one-time upfront payment of $5 million. As a result of our exercise of this option, we are no longer obligated under the amended and restated development and license agreement to pay to Takeda the tiered 7% to 11% royalty with respect to worldwide net sales in oncology indications of products containing or comprised of duvelisib. We recognized the $5 million upfront payment and the $52.5 million exercise payment as research and development expense during the year ended December 31, 2014 and December 31, 2015, respectively, as there is no alternative future use beyond the existing research and development activities.

For sales of duvelisib products other than 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 amended and restated 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. Either party may terminate the 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 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 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 agreement also provides for customary reciprocal indemnification obligations of the parties.

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14. Income Taxes

Our income tax expense of $0.3 million and $0.2 million for the years ended December 31, 2015 and 2014, respectively, consisted primarily of current U.S. federal taxes. We had no income tax expense or benefit for the year ended December 31, 2013.

Our income tax expense for the years ended December 31, 2015, 2014 and 2013 differed from the expected U.S. federal statutory income tax expense as set forth below:

	Year Ended December 31,		
	2015	2014	2013
	(in thousands)		
Expected federal tax expense (benefit)	$ (43,534)	$ (5,872)	$ (43,105)
Permanent differences	2,263	3,537	2,681
State taxes, net of the deferred federal benefit	(6,762)	(912)	(6,694)
Tax credit carryforwards	(2,735)	(9,510)	(11,534)
Adjustments to deferred tax assets and deferred tax liabilities	(1,267)	776	129
Alternative minimum tax	321	183	
Other	29	79	62
Change in valuation allowance	52,020	11,902	58,461
Income tax expense	$ 335	$ 183	$

The significant components of our deferred tax assets are as follows:

	Year Ended December 31,	
	2015	2014
	(in thousands)	
Deferred tax assets:		
Net operating loss carryforwards	$ 128,851	$ 133,180
Tax credit carryforwards	40,014	37,278
Deferred revenue	34,924	
Intangible assets	34,710	16,250
Accrued expenses	3,003	2,666
Stock-based compensation	12,172	10,031
Other	(794)	1,428
Valuation allowance	(252,880)	(200,833)
Net deferred tax assets	$	$

We have recorded a valuation allowance against our deferred tax assets in each of the years ended December 31, 2015, 2014 and 2013 because management believes that it is more likely than not that these assets will not be realized. The valuation allowance increased by approximately $52.0 million during the year ended December 31, 2015 primarily as a result of unbenefited deferred tax assets such as deferred revenue and intangible assets. The valuation allowance increased by approximately $12.0 million during the year ended December 31, 2014 primarily as a result of increases in unbenefited deferred tax assets such as tax credits and intangible assets. The valuation allowance increased by approximately $59.1 million during the year ended December 31, 2013 primarily as a result of increases in unbenefited deferred tax assets such as tax losses and credits.

Subject to the limitations described below, at December 31, 2015, we have cumulative net operating loss carryforwards of approximately $371.1 million and $250.9 million available to reduce federal and state taxable income, which expire through 2035, and have begun to expire and will continue to expire through 2035,

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respectively. In addition, we have cumulative federal and state tax credit carryforwards of $33.3 million and $10.2 million, respectively, available to reduce federal and state income taxes which expire through 2035 and 2030, respectively. The net operating loss carryforwards include approximately $31.1 million of deductions related to the exercise of stock options. This amount represents an excess tax benefit and has not been included in the gross deferred tax asset reflected for net operating losses nor the cumulative net operating loss carryforward disclosures above. Additionally, our net operating loss carryforwards and tax credit carryforwards are limited as a result of certain ownership changes, as defined under Sections 382 and 383 of the Internal Revenue Code. This limits the annual amount of these tax attributes that can be utilized to offset future taxable income or tax liabilities. The amount of the annual limitation is determined based on our value immediately prior to an ownership change. Subsequent ownership changes may affect the limitation in future years. The net operating losses and tax credit carryforwards that have and will expire unused in the future as a result of Section 382 and 383 limitations have been excluded from the amounts disclosed above.

At December 31, 2015 and 2014, we had no unrecognized tax benefits. As of December 31, 2015, 2014 and 2013, we had no accrued interest or penalties related to uncertain tax positions and no amounts have been recognized in our consolidated statements of operations. We will recognize interest and penalties related to uncertain tax positions in income tax expense.

We file income tax returns in the U.S. federal, Massachusetts, and other state jurisdictions. The statute of limitations for assessment by the Internal Revenue Service, or IRS, and state tax authorities is closed for tax years prior to 2012, although carryforward attributes that were generated prior to tax year 2012 may still be adjusted upon examination by the IRS or state tax authorities if they either have been or will be used in a future period.

15. Stockholders Equity

Warrants

In July 2002, IPI issued warrants to purchase shares of convertible preferred stock, which subsequently in the DPI merger became warrants to purchase shares of common stock in the DPI merger, in conjunction with the entry into our facility lease. All of these outstanding warrants were exercised in January 2013 at $13.35 per share.

In connection with the execution of the original facility agreement in February 2014, we issued to Deerfield warrants to purchase an aggregate of 1,000,000 shares of common stock at an exercise price of $13.83 per share. See note 10 for additional details related to the facility agreement.

16. Defined Contribution Benefit Plan

We sponsor a 401(k) retirement plan in which substantially all of our full-time employees are eligible to participate. Participants may contribute a percentage of their annual compensation to this plan, subject to statutory limitations. During the years ended December 31, 2015, 2014 and 2013, we matched 50% of the first 6% of participant contributions with shares of our common stock. Our matching contributions during the year ended December 31, 2015, 2014 and 2013 were $0.9 million, $0.7 million and $0.7 million, respectively.

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17. Quarterly Financial Information (unaudited)

	Quarter Ended March 31, 2015	Quarter Ended June 30, 2015	Quarter Ended September 30, 2015	Quarter Ended December 31, 2015
	(in thousands, except shares and per share amounts)			
Collaboration revenue	$ 4,363	$ 4,880	$ 90,743	$ 9,080
Operating expenses:				
Research and development	88,428	34,062	37,729	38,890
General and administrative	8,550	9,410	9,754	9,351
Total operating expenses	96,978	43,472	47,483	48,241
Income (loss) from operations	(92,615)	(38,592)	43,260	(39,161)
Other income (expenses):				
Interest expense	(647)	(99)	(311)	(311)
Interest and investment income (loss)	(40)	263	75	137
Total other income (expense)	(687)	164	(236)	(174)
Income (loss) before income taxes	(93,302)	(38,428)	43,024	(39,335)
Income tax			(480)	145
Net income (loss)	$ (93,302)	$ (38,428)	$ 42,544	$ (39,190)
Income (loss) per common share:				
Basic	$ (1.91)	$ (0.78)	$ 0.85	$ (0.80)
Diluted	$ (1.91)	$ (0.78)	$ 0.84	$ (0.80)
Weighted average number of common shares outstanding:				
Basic	48,939,383	49,076,031	49,188,443	49,227,905
Diluted	48,939,383	49,076,031	49,764,910	49,227,905

	Quarter Ended March 31, 2014	Quarter Ended June 30, 2014	Quarter Ended September 30, 2014	Quarter Ended December 31, 2014
	(in thousands, except shares and per share amounts)			
Collaboration revenue	$	$	$ 160,639	$ 4,356
Operating expenses:				
Research and development	34,491	28,165	44,895	36,082
General and administrative	6,804	7,057	8,042	7,382
Total operating expenses	41,295	35,222	52,937	43,464
Income (loss) from operations	(41,295)	(35,222)	107,702	(39,108)
Other income (expenses):				
Interest expense	(1,139)	(2,938)	(4,537)	(1,035)
Interest and investment income (loss)	168	136	52	(17)

Total other income (expense)	(971)	(2,802)	(4,485)	(1,052)
Income (loss) before income taxes	(42,266)	(38,024)	103,217	(40,160)
Income tax				(183)
Net income (loss)	$ (42,266)	$ (38,024)	$ 103,217	$ (40,343)
Income (loss) per common share:				
Basic	$ (0.87)	$ (0.78)	$ 2.08	$ (0.83)
Diluted	$ (0.87)	$ (0.78)	$ 2.03	$ (0.83)
Weighted average number of common shares outstanding:				
Basic	48,348,767	48,543,853	48,632,888	48,788,917
Diluted	48,348,767	48,543,853	49,735,303	48,788,917

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Item 9. Changes in and Disagreements with Accountants on Accounting and Financial Disclosure

There have been no disagreements with our independent accountants on accounting and financial disclosure matters.

Item 9A. Controls and Procedures

Disclosure Controls and Procedures

Our management, with the participation of our principal executive officer and principal financial officer, evaluated the effectiveness of our disclosure controls and procedures (as defined in Rules 13a-15(e) and 15d-15(e) under the Securities Exchange Act of 1934, as amended, or the Exchange Act) as of December 31, 2015. In designing and evaluating our disclosure controls and procedures, management recognized that any controls and procedures, no matter how well designed and operated, can provide only reasonable assurance of achieving their objectives, and our management necessarily applied its judgment in evaluating the cost-benefit relationship of possible controls and procedures. Based on this evaluation, our principal executive officer and principal financial officer concluded that as of December 31, 2015, our disclosure controls and procedures were (1) designed to ensure that material information relating to us is made known to our management including our principal executive officer and principal financial officer by others, particularly during the period in which this report was prepared and (2) effective, in that they provide reasonable assurance that information required to be disclosed by us in the reports we file or submit under the Exchange Act is recorded, processed, summarized and reported within the time periods specified in the SEC s rules and forms.

Management s report on our internal control over financial reporting (as defined in Rules 13a-15(f) and 15d-15(f) under the Exchange Act) appears below.

No change in our internal control over financial reporting occurred during the fiscal quarter ended December 31, 2015 that has materially affected, or is reasonably likely to materially affect, our internal control over financial reporting.

Internal Control Over Financial Reporting

(a) Management s Report on Internal Control Over Financial Reporting

Our management is responsible for establishing and maintaining adequate internal control over financial reporting. Internal control over financial reporting is defined in Rules 13a-15(f) and 15d-15(f) promulgated under the Exchange Act as a process designed by, or under the supervision of, our principal executive and principal financial officer and effected by our board of directors, management and other personnel, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles and includes those policies and procedures that:

- Pertain to the maintenance of records that in reasonable detail accurately and fairly reflect the transactions and dispositions of the assets of the company;

- Provide reasonable assurance that transactions are recorded as necessary to permit preparation of financial statements in accordance with generally accepted accounting principles, and that receipts and expenditures of the company are being made only in accordance with authorizations of management and directors of the company; and

- Provide reasonable assurance regarding prevention or timely detection of unauthorized acquisition, use or disposition of the company s assets that could have a material effect on the financial statements.

Because of its inherent limitations, internal control over financial reporting may not prevent or detect misstatements. Therefore, even those systems determined to be effective can provide only reasonable assurance

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with respect to financial statement preparation and presentation. Projections of any evaluation of effectiveness to future periods are subject to the risk that controls may become inadequate because of changes in conditions, or that the degree of compliance with the policies or procedures may deteriorate.

Our management assessed the effectiveness of our internal control over financial reporting as of December 31, 2015. In making this assessment, management used the criteria set forth by the Committee of Sponsoring Organizations of the Treadway Commission, or COSO, in *Internal Control Integrated Framework (2013)*. Based on its assessment, management believes that, as of December 31, 2015, our internal control over financial reporting is effective based on those criteria.

Our independent registered public accounting firm has issued an attestation report of our internal control over financial reporting. This report appears below.

(b) Report of Independent Registered Public Accounting Firm

The Board of Directors and Stockholders of

Infinity Pharmaceuticals, Inc.

We have audited Infinity Pharmaceuticals, Inc. s internal control over financial reporting as of December 31, 2015, based on criteria established in Internal Control Integrated Framework issued by the Committee of Sponsoring Organizations of the Treadway Commission (2013 framework) (the COSO criteria). Infinity Pharmaceuticals, Inc. s management is responsible for maintaining effective internal control over financial reporting, and for its assessment of the effectiveness of internal control over financial reporting included in the accompanying Management s Report on Internal Control Over Financial Reporting. Our responsibility is to express an opinion on the company s internal control over financial reporting based on our audit.

We conducted our audit 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 effective internal control over financial reporting was maintained in all material respects. Our audit included obtaining an understanding of internal control over financial reporting, assessing the risk that a material weakness exists, testing and evaluating the design and operating effectiveness of internal control based on the assessed risk, and performing such other procedures as we considered necessary in the circumstances. We believe that our audit provides a reasonable basis for our opinion.

A company s internal control over financial reporting is a process designed to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles. A company s internal control over financial reporting includes those policies and procedures that (1) pertain to the maintenance of records that, in reasonable detail, accurately and fairly reflect the transactions and dispositions of the assets of the company; (2) provide reasonable assurance that transactions are recorded as necessary to permit preparation of financial statements in accordance with generally accepted accounting principles, and that receipts and expenditures of the company are being made only in accordance with authorizations of management and directors of the company; and (3) provide reasonable assurance regarding prevention or timely detection of unauthorized acquisition, use, or disposition of the company s assets that could have a material effect on the financial statements.

Because of its inherent limitations, internal control over financial reporting may not prevent or detect misstatements. Also, projections of any evaluation of effectiveness to future periods are subject to the risk that controls may become inadequate because of changes in conditions, or that the degree of compliance with the policies or procedures may deteriorate.

In our opinion, Infinity Pharmaceuticals, Inc. maintained, in all material respects, effective internal control over financial reporting as of December 31, 2015, based on the COSO criteria.

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We also have audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States), the consolidated balance sheets of Infinity Pharmaceuticals, Inc. as of December 31, 2015 and 2014, 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, 2015 of Infinity Pharmaceuticals, Inc. and our report dated February 23, 2016 expressed an unqualified opinion thereon.

/s/ ERNST & YOUNG LLP

Boston, Massachusetts

February 23, 2016

(c) Changes in Internal Control Over Financial Reporting

No change in our internal control over financial reporting (as defined in Rules 13a-15(f) and 15d-15(f) under the Exchange Act) occurred during the fiscal year ended December 31, 2015 that has materially affected, or is reasonably likely to materially affect, our internal control over financial reporting.

Item 9B. Other Information

Not applicable.

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PART III

Item 10. Directors, Executive Officers and Corporate Governance

The sections titled Proposal 1 Election of Directors, Board and Committee Meetings, Section 16(a) Beneficial Ownership Reporting Compliance and Corporate Governance Guidelines; Code of Conduct and Ethics appearing in the definitive proxy statement we will file in connection with our Annual Meeting of Stockholders to be held on June 17, 2016 are incorporated herein by reference. The information required by this item relating to executive officers may be found in Part I, Item 1 of this report under the heading Business Executive Officers.

Item 11. Executive Compensation

The section titled Compensation of Executive Officers appearing in the definitive proxy statement we will file in connection with our Annual Meeting of Stockholders to be held on June 17, 2016 is incorporated herein by reference.

Item 12. Security Ownership of Certain Beneficial Owners and Management and Related Stockholder Matters

The sections titled Stock Ownership of Certain Beneficial Owners and Management and Securities Authorized for Issuance under Equity Compensation Plans appearing in the definitive proxy statement we will file in connection with our Annual Meeting of Stockholders to be held on June 17, 2016 are incorporated herein by reference.

Item 13. Certain Relationships and Related Transactions, and Director Independence

The sections titled Transactions with Related Persons, Policies and Procedures for Related Persons Transactions, and Determination of Independence appearing in the definitive proxy statement we will file in connection with our Annual Meeting of Stockholders to be held on June 17, 2016 are incorporated herein by reference.

Item 14. Principal Accounting Fees and Services

The section titled Audit Fees appearing in the definitive proxy statement we will file in connection with our Annual Meeting of Stockholders to be held on June 17, 2016 is incorporated herein by reference.

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PART IV

Item 15. Exhibits, Financial Statement Schedules

(a)(1) Financial Statements

The financial statements listed below are filed as a part of this Annual Report on Form 10-K.

(a)(2) Financial Statement Schedules

Financial statement schedules have been omitted because of the absence of conditions under which they are required or because the required information, where material, is shown in the financial statements or notes thereto.

(a)(3) Exhibits

The Exhibits listed in the Exhibit Index are filed as a part of this Annual Report on Form 10-K.

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SIGNATURES

Pursuant to the requirements of Section 13 or 15(d) of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned, thereunto duly authorized.

INFINITY PHARMACEUTICALS, INC.

Date: February 23, 2016

By: /s/ Adelene Q. Perkins
Adelene Q. Perkins

President & Chief Executive Officer

(Principal Executive Officer)

Pursuant to the requirements of the Securities Exchange Act of 1934, this report has been signed below by the following persons on behalf of the registrant and in the capacities and on the dates indicated.

Signature	Title	Date
/s/ Adelene Q. Perkins **Adelene Q. Perkins**	President, Chief Executive Officer; Chair of the Board of Directors *(Principal Executive Officer)*	February 23, 2016
/s/ Lawrence E. Bloch, M.D., J.D. **Lawrence E. Bloch, M.D., J.D.**	Executive Vice President, Chief Financial Officer and Chief Business Officer; Treasurer *(Principal Financial Officer, Principal Accounting Officer)*	February 23, 2016
/s/ José Baselga, M.D., Ph.D. **José Baselga, M.D., Ph.D.**	Director	February 18, 2016
/s/ Jeffrey Berkowitz, J.D. **Jeffrey Berkowitz, J.D.**	Director	February 17, 2016
/s/ Anthony B. Evnin, Ph.D. **Anthony B. Evnin, Ph.D.**	Director	February 23, 2016
/s/ Gwen A. Fyfe, M.D. **Gwen A. Fyfe, M.D.**	Director	February 19, 2016
/s/ Eric S. Lander, Ph.D. **Eric S. Lander, Ph.D.**	Director	February 16, 2016
/s/ Norman C. Selby **Norman C. Selby**	Director	February 23, 2016

/s/ Ian F. Smith **Ian F. Smith**	Director	February 18, 2016
/s/ Michael C. Venuti, Ph.D. **Michael C. Venuti, Ph.D.**	Director	February 23, 2016

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EXHIBIT INDEX

		Incorporated by Reference			
Exhibit No.	**Description**	**Form**	**SEC Filing date**	**Exhibit Number**	**Filed with this 10-K**
3.1	Restated Certificate of Incorporation of the Registrant.	10-Q	8/9/07	3.1	
3.2	Amended and Restated Bylaws of the Registrant.	8-K	03/17/09	3.1	
4.1	Form of Common Stock Certificate.	10-K	3/14/08	4.1	
Collaboration Agreements					
10.1	Collaboration and License Agreement, dated as of September 2, 2014, between Infinity Pharmaceuticals, Inc. and AbbVie Inc.	10-Q	11/10/2014	10.2	
10.2	Amended and Restated Development and License Agreement, dated as of December 24, 2012, by and between the Registrant and Intellikine, LLC.	10-K	3/5/13	10.4	
10.3	Amendment to Amended and Restated Development and License Agreement, dated as of dated July 29, 2014, by and between Infinity Pharmaceuticals, Inc. and Intellikine LLC.	10-Q	11/10/2014	10.1	
10.4	Termination and Revised Relationship Agreement, dated as of July 17, 2012, between the Registrant and Mundipharma International Corporation Limited.	8-K	07/19/12	10.2	
10.5	Termination and Revised Relationship Agreement, dated as of July 17, 2012, between the Registrant and Purdue Pharmaceutical Products L.P.	8-K	7/19/12	10.3	
Financing Agreements					
10.6	Facility Agreement dated February 24, 2014 between Infinity Pharmaceuticals, Inc. and Deerfield Private Design Fund II, L.P., Deerfield Private Design International II, L.P., Deerfield Partners, L.P., and Deerfield International Master Fund, L.P. (collectively, the Deerfield Entities).	10-Q	05/06/2014	10.1	
10.7	First Amendment to Facility Agreement, dated as of September 22, 2014, between Infinity Pharmaceuticals, Inc. and Deerfield Private Design Fund II, L.P., Deerfield Private Design International II, L.P., Deerfield Partners, L.P., and Deerfield International Master Fund, L.P.	10-Q	11/10/2014	10.3	
10.8	Form of Warrant to Purchase Common Stock of Infinity Pharmaceuticals, Inc., issued to the Deerfield Entities, together with a schedule of holders and amounts (issued February 24, 2014).	10-Q	05/06/2014	10.2	
Leases					
10.9	Lease Agreement, dated as of September 25, 2014, between Infinity Pharmaceuticals, Inc. and BHX, LLC, as trustee of 784 Realty Trust.	10-Q	11/10/2014	10.4	

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Exhibit No.	Description	Incorporated by Reference			Filed with this 10-K
		Form	SEC Filing date	Exhibit Number	
10.10	Lease Agreement dated July 2, 2002 between IDI and ARE-770/784/790 Memorial Drive LLC (the Lease), as amended by First Amendment to Lease dated March 25, 2003, Second Amendment to Lease dated April 30, 2003, Third Amendment to Lease dated October 30, 2003 and Fourth Amendment to Lease dated December 15, 2003.	8-K	9/18/06	10.36	
10.11	Fifth Amendment to Lease dated July 8, 2011 between the Registrant and ARE-770/784/790 Memorial Drive LLC.	10-Q	8/9/11	10.1	
10.12	Sixth Amendment to Lease dated July 8, 2012 between the Registrant and ARE-770/784/790 Memorial Drive LLC.	10-Q	8/7/12	10.2	
10.13	Seventh Amendment to Lease, dated as of November 6, 2014, between Infinity Pharmaceuticals, Inc. and ARE-770/784/790 Memorial Drive, LLC.	10-Q	11/10/2014	10.5	
Equity Plans					
10.14*	Pre-Merger Stock Incentive Plan.	8-K	9/18/06	10.18	
10.15*	Form of Incentive Stock Agreement entered into with each of the officers identified on the schedule thereto.	8-K	9/18/06	10.25	
10.16*	Form of Nonstatutory Stock Option Agreement entered into with each of the officers identified on the schedule thereto.	8-K	9/18/06	10.27	
10.17*	2000 Stock Incentive Plan.	S-1	5/9/2000	10.59	
10.18*	Amendment No. 1 to 2000 Stock Incentive Plan; Amendment No. 2 to 2000 Stock Incentive Plan; Amendment No. 3 to 2000 Stock Incentive Plan.	8-K	9/18/06	10.32	
10.19*	Amendment No. 4 to 2000 Stock Incentive Plan.	10-Q	8/9/07	10.1	
10.20*	Amendment No. 5 to 2000 Stock Incentive Plan.	S-8	5/23/08	99.4	
10.21*	Form of Incentive Stock Option Agreement under 2000 Stock Incentive Plan.	8-K	9/18/06	10.33	
10.22*	Form of Nonstatutory Stock Option Agreement under 2000 Stock Incentive Plan.	8-K	9/18/06	10.34	
10.23*	2010 Stock Incentive Plan.	8-K	5/28/10	10.1	
10.24*	Form of Incentive Stock Option Agreement under 2010 Stock Incentive Plan.	8-K	5/28/10	10.2	
10.25*	Form of Nonstatutory Stock Option Agreement under 2010 Stock Incentive Plan.	8-K	5/28/10	10.3	
10.26*	Amendment No. 1 to 2010 Stock Incentive Plan.	8-K	12/14/10	99.2	
10.27*	Amendment No. 2 to 2010 Stock Incentive Plan.	8-K	5/18/12	99.1	
10.28*	Amendment No. 3 to 2010 Stock Incentive Plan.	8-K	6/13/13	10.1	
10.29*	Amendment No. 4 to 2010 Stock Incentive Plan.	8-K	6/13/13	10.1	

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		Incorporated by Reference			
Exhibit No.	Description	Form	SEC Filing date	Exhibit Number	Filed with this 10-K
10.30*	Amendment No. 5 to 2010 Stock Incentive Plan.	8-K	6/16/15	10.1	
10.31*	2013 Employee Stock Purchase Plan, as amended.	8-K	6/13/13	99.1	
Agreements With Executive Officers					
10.32*	Offer Letter between the Registrant and William C. Bertrand, Jr., dated October 1, 2015.				X
10.33*	Offer Letter between the Registrant and Sujay Kango, dated February 24, 2015.				X
10.34*	Offer Letter between the Registrant and David A. Roth, M.D., dated August 15, 2013.				X
10.35*	Separation Agreement between the Registrant and David A. Roth, dated October 1, 2015.				X
10.36*	Offer Letter between the Registrant and Lawrence E. Bloch, M.D., J.D. dated May 15, 2012.	8-K	7/25/12	10.1	
10.37*	Offer Letter between IDI and Julian Adams dated as of August 19, 2003.	8-K	9/18/06	10.10	
10.38*	Amendment to Offer Letter between IDI and Julian Adams dated as of October 25, 2007.	8-K	10/30/07	99.4	
10.39*	Offer Letter between IDI and Adelene Perkins dated as of February 6, 2002.	8-K	9/18/06	10.11	
10.40*	Amendment to Offer Letter between IDI and Adelene Perkins dated as of October 25, 2007.	8-K	10/30/07	99.5	
10.41*	Infinity Pharmaceuticals, Inc. Executive Severance Benefits Plan effective February 6, 2013.	8-K	2/12/13	10.1	
Subsidiaries					
21.1	Subsidiaries of the Registrant. Filed herewith.				X
Consent					
23.1	Consent of Ernst & Young LLP, Independent Registered Public Accounting Firm. Filed herewith.				X
Certifications					
31.1	Certification of principal executive officer pursuant to Rule 13a-14(a)/15d-14(a) of the Securities Exchange Act of 1934, as amended. Filed herewith.				X
31.2	Certification of principal financial officer pursuant to Rule 13a-14(a)/15d-14(a) of the Securities Exchange Act of 1934, as amended. Filed herewith.				X
32.1	Statement of principal executive officer pursuant to 18 U.S.C. §1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002. Filed herewith.				X

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		Incorporated by Reference			
Exhibit No.	Description	Form	SEC Filing date	Exhibit Number	Filed with this 10-K
32.2	Statement of principal financial officer pursuant to 18 U.S.C. §1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002. Filed herewith.				X
101	The following materials from the Registrant s Annual Report on Form 10-K for the year ended December 31, 2015, formatted in XBRL (eXtensible Business Reporting Language): (i) the Consolidated Balance Sheets, (ii) the Consolidated Statements of Operations and Comprehensive Loss, (iii) the Consolidated Statements of Cash Flows, (iv) the Consolidated Statements of Stockholders Equity, and (v) Notes to Consolidated Financial Statements.				X

* Indicates management contract or compensatory plan
Confidential treatment has been requested and/or granted as to certain portions, which portions have been filed separately with the Securities and Exchange Commission.