INFINITY PHARMACEUTICALS, INC.
Form 10-K
March 16, 2011
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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, 2010

Or

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

For the transition period from to

Commission file number: 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.)

780 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:

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 ¨ 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 ¨	Accelerated filer x	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, 2010 was $106,868,142 based on the last reported sale price of the registrant s Common Stock on the NASDAQ Global Market on that date.

Number of shares outstanding of the registrant s Common Stock as of February 28, 2011: 26,545,580

Documents incorporated by reference:

Portions of our definitive proxy statement to be filed with the Securities and Exchange Commission no later than May 2, 2011 in connection with our 2011 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

This report contains forward-looking statements regarding our expectations regarding discovery and development milestones in 2011, our future discovery and development efforts, our collaborations, our future operating results and financial position, our business strategy, and other objectives for future operations. You can identify these forward-looking statements by their use of words such as anticipate, believe, estimate, expect, forecast, intend, plan, project, target, will and other words and terms of similar meaning. You also can identify them 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 our actual results to differ materially from those indicated by forward-looking statements. 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 and other regulatory authorities with respect to the development and commercialization of our drug candidates, our ability to obtain, maintain and enforce intellectual property rights for our drug candidates, our dependence on our alliance partners, our ability to obtain any necessary financing to conduct our planned activities, and other risk factors. Please refer to the section entitled Risk Factors in Part I of this report for a description of these risks and uncertainties. Unless required by law, we do not undertake any obligation to publicly update any forward-looking statements.

PART I

Item 1. Business

Overview

We are a drug discovery and development company that is utilizing our strength in small molecule drug technologies to discover and develop medicines for difficult-to-treat diseases. Our discovery program has generated four clinical stage drug candidates spanning programs in the inhibition of the Hedgehog signaling pathway, heat shock protein 90, or Hsp90, chaperone system, and fatty acid amide hydrolase, or FAAH. In July 2010, we also obtained global development and commercialization rights to develop inhibitors of the delta and gamma isoforms of phosphoinositide-3-kinase, or PI3K.

Hedgehog Pathway Inhibitor Program. Our lead product candidate is IPI-926, a novel, potent, oral molecule that inhibits the Hedgehog pathway by binding to the Smoothened receptor, a protein that plays a critical role in the malignant activation of the Hedgehog pathway. We believe that Smoothened inhibition represents a significant opportunity for addressing a number of difficult-to-treat cancers by disrupting malignant activation of the Hedgehog pathway. We are actively enrolling patients in the Phase 2 portion of a Phase 1b/2 clinical trial evaluating IPI-926 in combination with gemcitabine, also known as Gemzar®, in patients with previously untreated, metastatic, pancreatic cancer, and have initiated a Phase 2 clinical trial evaluating IPI-926 as a single agent in patients with metastatic or locally advanced, inoperable chondrosarcoma. We expect to present data from the Phase 1b portion of the pancreatic cancer trial later this year. We are also evaluating IPI-926 in a Phase 1 clinical trial in patients with advanced or metastatic solid tumors, including patients with basal cell carcinoma, or BCC. Preliminary data from this trial were presented at the European Society for Medical Oncology Congress in October 2010 and we expect to present follow-up data at a medical meeting later in 2011. Mundipharma International Corporation Limited, or Mundipharma, has commercialization rights outside of the United States for products arising out of our Hedgehog pathway inhibitor program.

Hsp90 Chaperone Inhibitor Program. Our next most advanced program is directed at Hsp90 which is emerging as a major therapeutic target of interest for the treatment of a broad range of cancers. Inhibition of the Hsp90 chaperone knocks out a critical source of support for cancer cells, leading to tumor growth inhibition and cancer cell death. Thus, Hsp90 chaperone inhibition may represent an important approach to treating certain cancers. Our lead Hsp90 inhibitor, IPI-504, is a novel, small molecule, semi-synthetic analog of the natural product geldanamycin that is delivered as a water-based, intravenous infusion. IPI-504 is currently being

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evaluated in two ongoing clinical trials, both of which are focused on patients with non-small cell lung cancer, or NSCLC. One trial is a Phase 1b trial in combination with docetaxel, also known as Taxotere®, that initially enrolled patients with advanced solid tumors and expanded in 2009 to focus on patients with advanced NSCLC. The second trial is an investigator sponsored trial in NSCLC patients with anaplastic lymphoma kinase, or ALK, gene rearrangements. We anticipate reporting final data from the Phase 1b trial during 2011. We also expect to present data from a completed Phase 2 clinical trial evaluating IPI-504 in combination with Herceptin® (trastuzumab) in patients with HER2-positive metastatic breast cancer at a medical meeting in 2011.

In parallel with the development of IPI-504, we are pursuing development of IPI-493, a proprietary, orally available inhibitor of Hsp90. IPI-493 has demonstrated anti-tumor activity in multiple preclinical models of human cancer, including NSCLC, breast cancer, colon cancer, and hematological malignancies. We are evaluating IPI-493 in two Phase 1, dose escalation studies to determine the optimal dose and schedule for future development.

In 2011, we anticipate reporting data from our Hsp90 program and announcing a path forward based on data from our ongoing clinical trials and relevant preclinical studies. We have worldwide development and commercialization rights for our Hsp90 chaperone inhibitor program.

PI3K Inhibitor Program. In July 2010, we entered into a development and license agreement with Intellikine, Inc., or Intellikine, under which we obtained global development and commercialization rights to Intellikine s portfolio of inhibitors targeting the delta and/or gamma isoforms of PI3K. We believe that specifically targeting PI3Kdelta and PI3Kgamma may provide multiple opportunities to develop differentiated therapies against inflammatory and autoimmune diseases as well as hematologic cancers. Our lead compound in this program, IPI-145, is an orally-available, small molecule, dual-selective inhibitor of PI3Kdelta and PI3Kgamma. IPI-145 has demonstrated activity in several preclinical models of inflammation. We intend to commence clinical development of IPI-145 in the second half of 2011. Mundipharma has commercialization rights outside of the United States for products arising from our PI3K inhibitor program.

FAAH Inhibitor Program. Finally, we have a program directed toward fatty acid amide hydrolase, or FAAH. It is believed that inhibition of FAAH may enable the body to bolster its own analgesic and anti-inflammatory response, and may have applicability in a broad range of painful or inflammatory conditions. The lead compound in our FAAH program is IPI-940, a novel, orally available inhibitor of FAAH with potential application for the treatment of a broad range of painful or inflammatory diseases. In October 2010, we reported top-line data from a Phase 1 randomized clinical trial of IPI-940 in 48 healthy adult volunteers demonstrating marked FAAH inhibition and increased anandamide levels. In addition, IPI-940 was well tolerated, with no observed dose-limiting toxicities or clinically significant changes in clinical laboratory values, vital signs or electrocardiogram parameters. Additional Phase 1 development of IPI-940 is ongoing.

In October 2010, Mundipharma and its independent associated company Purdue Pharmaceutical Products L.P., or Purdue, exercised their rights to assume worldwide development and commercialization activities for products arising out of the FAAH program and will fund 100% of all subsequent research, development and commercialization expenses. We anticipate completing transition activities for the FAAH program in 2011 to facilitate Phase 2 clinical trials in pain by Purdue.

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 was 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,

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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. Since January 3, 2011, our common stock has traded on the NASDAQ Global Select Market.

Our principal executive offices are located at 780 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 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.

Product Development Pipeline

Our product development programs arise from what we believe to be an innovative approach to drug discovery and translational medicine, and our robust internal capabilities across all of the key scientific disciplines, including medicinal chemistry, cell biology, biochemistry, pharmacology and molecular pathology. More importantly, our goal is to successfully integrate these disciplines to rapidly identify drug candidates and assess their potential utility.

Our four current clinical candidates which have broad potential applicability in the fields of oncology and pain emerged from our internal research efforts. Behind these programs, we have several innovative projects in earlier stages of development, encompassing emerging targets in fields such as cancer metabolism, apoptosis and protein homeostasis. We are drawn to targets that have the potential to represent fundamentally new approaches to how disease is treated, and where we can use our scientific capabilities to identify differentiated drug candidates with clearly-defined development paths. And because discovery doesn t stop when a drug candidate is identified, we also deploy our discovery capabilities to better understand which populations, or subpopulations, of patients may benefit most from our products.

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, inflammatory disease and pain all areas with broad commercial potential. This strategy also ensures that our success is not dependent on any single product or indication, allowing us to optimize our portfolio on several dimensions in response to new data.

We also believe that the ability to deliver innovative new medicines to patients is an essential component of our mission. To this end, we have retained U.S. commercialization rights to all product candidates in our portfolio that are primarily directed to cancer and inflammatory diseases and have a substantial royalty interest in the U.S. commercialization of IPI-940, which is primarily directed to pain.

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Our product development programs as of February 28, 2011 are illustrated in the following chart:

During 2011, we expect to advance our product development pipeline by achieving the following program milestones:

Hedgehog Pathway Inhibitor Program

- Continuing enrollment in the Phase 2 portion of the Phase 1b/2 clinical trial evaluating IPI-926 in combination with gemcitabine in patients with pancreatic cancer and the Phase 2 clinical trial evaluating IPI-926 as a single agent in patients with chondrosarcoma
- Presenting data from the Phase 1b portion of the pancreatic cancer trial
- Beginning additional clinical development
- Initiating a broad investigator-sponsored clinical trial program

Hsp90 Chaperone Inhibitor Program

- Presenting Phase 1 data of IPI-504 in combination with docetaxel in patients with solid tumors, including an expansion cohort in patients with non-small cell lung cancer
- Announcing a path forward for our Hsp90 program

PI3K Inhibitor Program

- Beginning a Phase 1 clinical trial in the second half of 2011

FAAH Inhibitor Program

- Completing transition activities to facilitate Phase 2 trials in pain by Purdue

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Discovery Program

Expanding our pipeline by naming a new development candidate

Hedgehog Pathway Inhibitor Program

The Hedgehog pathway represents a new way of understanding and potentially attacking the progression and reoccurrence of a broad range of cancers. The Hedgehog pathway is normally active during embryonic development and regulates tissue and organ formation. Malignant activation of the Hedgehog pathway is believed to be responsible for a broad range of cancers through three distinct mechanisms:

Targeting the tumor microenvironment: In certain cancers, such as pancreatic cancer, the tumor cells signal to stromal cells in the microenvironment, which provides support for tumor growth and survival. Inhibition of the Hedgehog pathway may deplete the stroma, increase the vascularity of the tumor, and render the tumor more accessible to chemotherapy.

Targeting residual disease: In some cancers, such as NSCLC, prostate cancer and ovarian cancer, the Hedgehog pathway may signal to tumor progenitor cells. These tumor progenitor cells may be responsible for tumor regrowth following tumor regression or tumor debulking with chemotherapy or targeted agents. Inhibition of the Hedgehog pathway in these cancers may delay tumor regrowth.

Targeting the tumor cell: In some cancers, such as BCC, and some meduloblastomas, genetic mutation is responsible for malignant activation of the Hedgehog pathway. In these cancers, inhibition of the Hedgehog pathway may result in tumor cell death and tumor regression.

We are developing IPI-926, a novel, potent, oral molecule that inhibits the Hedgehog pathway by binding to the Smoothened receptor, a protein that plays a critical role in the malignant activation of the Hedgehog pathway. We believe that Smoothened inhibition represents a significant opportunity for addressing a number of difficult-to-treat cancers by disrupting malignant activation of the Hedgehog pathway. When systemically administered in multiple preclinical animal models representing a wide variety of cancers, IPI-926 has demonstrated significant anti-tumor activity and attractive pharmacologic properties such as oral bioavailability, long plasma half-life and duration of action, and dose-dependent inhibition of tumor growth.

We are actively enrolling patients in the Phase 2 portion of a Phase 1b/2 trial evaluating IPI-926 in combination with gemcitabine in patients with previously untreated, metastatic, pancreatic cancer. Pancreatic cancer is the fourth leading cause of cancer death in the United States, and it is estimated that more than 40,000 people are diagnosed with pancreatic cancer in the United States annually. Notoriously difficult-to-treat, pancreatic cancer has the highest mortality rate of all major cancers. The one-year relative survival rate for pancreatic cancer is 20 percent and the five-year relative survival rate is just five percent. The average life expectancy for patients with metastatic disease is three to six months. Unfortunately, pancreatic cancer is one of the few cancers for which the survival rate has not improved substantially over nearly 40 years.

The Phase 2 portion of the trial is a multi-center, randomized, double-blind, study that will compare treatment with IPI-926 in combination with gemcitabine to treatment with placebo and gemcitabine. The primary endpoint is overall survival. Secondary endpoints include progression free survival, time to progression, and overall response rate. The trial is expected to enroll approximately 120 patients. The Phase 2 portion of the trial follows the successful completion of Phase 1b portion of the trial, which evaluated once-daily oral administration of IPI-926 at escalating doses in combination with weekly intravenous administration of gemcitabine and established 160 mg/m^2 as the dose of IPI-926 that will be used in the Phase 2 portion of the ongoing trial. We expect to present data from the Phase 1b portion of the trial later in 2011.

We have also initiated a Phase 2 clinical trial evaluating IPI-926 as a single agent in patients with metastatic or locally advanced, inoperable chondrosarcoma. Chondrosarcoma is a rare, life-threatening bone cancer. In the United States, chondrosarcoma accounts for approximately one-third of the 2,000 cases of primary bone cancer

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diagnosed each year. The most common locations for chondrosarcoma tumors are the bones of the extremities and the pelvis. Chondrosarcoma predominantly affects middle-aged and older adults, usually occurring in patients over 40 years old, with the incidence gradually increasing up to age 75. As chondrosarcomas are largely resistant to chemotherapy and radiotherapy, the standard therapeutic strategy is surgery. For patients with metastatic disease or with locally advanced tumors who are not candidates for surgery, no treatment has been shown to be effective and there is no established standard of care.

Our Phase 2 clinical trial is designed to compare the safety and efficacy of IPI-926 to matching placebo in patients with metastatic or locally advanced, inoperable chondrosarcoma. The primary endpoint of the trial is progression-free survival. Secondary endpoints include time to progression, overall survival, overall response rate and response duration. Patients in the placebo treatment arm who experience disease progression will have the option to cross over and receive IPI-926 in an open-label arm of the trial. We have received orphan drug designation from the U.S. Food and Drug Administration, or FDA, for IPI-926 for the treatment of chondrosarcoma.

We are also evaluating IPI-926 in a Phase 1 clinical trial in patients with advanced or metastatic solid tumors, including patients with BCC. Preliminary data from this trial were presented at the European Society for Medical Oncology Congress in October 2010. At the time of the data presentation, 60 patients had been enrolled, including 24 patients with BCC. In the BCC cohort, 17 patients were enrolled who were naïve to treatment with a Hedgehog pathway inhibitor. At that time, four clinical partial responses had been observed in this group of patients. Only one patient with BCC naïve to treatment with a Hedgehog pathway inhibitor had discontinued from the trial due to progression of disease, and this patient was on trial for more than 18 months. The patients who have remained on study are continuing to be followed, and we expect to present follow-up data on these patients at a medical meeting later in 2011. In addition, among patients with non-BCC solid tumors enrolled in the trial, three patients had stable disease that was durable for at least six months. IPI-926 was generally well tolerated in this trial, with the most common adverse events observed being Grade 1 and 2 fatigue and nausea. Pharmacokinetic data also confirmed the potential for once daily dosing.

Mundipharma International Corporation Limited, or Mundipharma, has commercialization rights outside of the United States for products arising out of our Hedgehog pathway inhibitor program.

Hsp90 Chaperone Inhibitor Program

Hsp90 is emerging as a major therapeutic target of interest for the treatment of a broad range of cancers. Proteins are the essential building blocks and machines of the human body, and in order for proteins to function properly they must be stable and properly folded. The chaperone system of proteins, of which Hsp90 is a member, serves to maintain the structure and activity of specific proteins within the cell. The proteins chaperoned by Hsp90 are known as its client proteins, and include cancer-causing forms of ALK, BCR-ABL, mutant EGFR, mutant FLT3 and HER2. Inhibition of the Hsp90 chaperone knocks out a critical source of support for cancer cells, leading to tumor growth inhibition and cancer cell death. Thus, Hsp90 chaperone inhibition may represent an important approach to treating certain cancers.

We are developing two drug candidates in our Hsp90 chaperone inhibitor program: IPI-504 (retaspimycin hydrochloride), an intravenously-administered small molecule, and IPI-493, which is administered orally. We are conducting various clinical and preclinical studies of IPI-504 and IPI-493. These studies are focused on establishing a dose and schedule of administration that optimizes safety and efficacy of these candidates, and identifying patient populations, or subpopulations, most likely to benefit from Hsp90 chaperone inhibition.

IPI-504. Our lead Hsp90 inhibitor, IPI-504 (retaspimycin hydrochloride), is a novel, small molecule, semi-synthetic analog of the natural product geldanamycin that is delivered as a water-based, intravenous infusion. IPI-504 has also been shown in preclinical studies to inhibit Hsp90 potently and selectively, thereby inhibiting cancer cell growth. In addition, preclinical studies suggest that IPI-504 preferentially targets and accumulates in

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tumor tissues. For these reasons, we believe that IPI-504 has broad potential for the treatment of patients with a wide variety of solid and hematological tumors, including cancers that are resistant to other drugs.

We have two ongoing clinical trials evaluating IPI-504, both of which are focused on patients with NSCLC. Lung cancer is the leading cause of cancer death in the United States for both men and women and an estimated 222,520 new cases were expected in 2010. NSCLC is the most common form of lung cancer, accounting for about 85% of all lung cancers, and has a five year survival rate of just 17%.

We are continuing to evaluate patients in a Phase 1b clinical trial of IPI-504 in combination with docetaxel, also known as Taxotere®. The trial initially enrolled patients with advanced solid tumors, and expanded in late 2009 to focus on patients with advanced NSCLC. Preliminary data from the trial presented during the 2009 American Society of Clinical Oncology, or ASCO, Annual Meeting show that, to date, the combination regimen has been generally well tolerated in patients with a variety of solid tumor malignancies. Pharmacokinetic data showed no effect of IPI-504 on the clearance of docetaxel from the body. Data reported also show evidence of anti-tumor activity, with one partial response in a patient with metastatic pancreatic cancer refractory to gemcitabine, and six additional patients who experienced stable disease for at least three months. We anticipate reporting final data from this trial during 2011.

Data from a Phase 2 clinical trial of IPI-504 administered as a single agent in patients with NSCLC were reported during the ASCO Annual Meeting and published in the *Journal of Clinical Oncology* in 2010. The trial was designed to evaluate the safety, tolerability, and anti-tumor activity of IPI-504 in patients with Stage IIIb/IV NSCLC whose tumors have relapsed or become refractory to prior treatment with a tyrosine kinase inhibitor. A total of 76 patients were enrolled and stratified by their EGFR mutation status. A subset of patients also underwent EGFR, KRAS and BRAF genotyping analysis, as well as a fluorescent in situ hybridization assay to detect ALK gene rearrangements. The results of the Phase 2 trial show an objective response rate of seven percent in the overall study population: ten percent in patients who were EGFR wild-type, four percent in those with EGFR mutations, and twelve percent among KRAS wild-type patients. Among the patients with ALK rearrangements, there was a 67 percent response rate, with two of three patients experiencing partial responses and the third patient experiencing a 24 percent disease reduction, all three of whom received IPI-504 for at least six months. IPI-504 was generally well-tolerated in this trial. Most adverse events were Grade 1 or Grade 2. The most commonly reported adverse events (regardless of relationship to drug) were fatigue, nausea, diarrhea, vomiting and cough. Validation of these findings is ongoing in an investigator-sponsored trial at Massachusetts General Hospital by Dr. Lecia Sequist, the principal investigator of the Phase 2 trial.

In 2010, we also completed an interim review of data from the first cohort of patients enrolled in a Phase 2 clinical trial evaluating IPI-504 in combination with Herceptin® (trastuzumab) in patients with HER2-positive metastatic breast cancer. This review showed that IPI-504 was well-tolerated when administered at 300 mg/m^2 once weekly in combination with trastuzumab in this heavily pre-treated patient population. Clinical activity was also observed at this dose and schedule, but it was insufficient to satisfy our rigorous stage gate for continuation of this trial. While we believe that the insufficient clinical activity in this trial was the result of IPI-504 being administered at a less than optimal dose in this combination, we do not intend to continue development of IPI-504 in breast cancer in light of the evolving therapeutic landscape. We expect to present data from this clinical trial at a medical meeting in 2011.

IPI-493. In parallel with the development of IPI-504, we are pursuing development of IPI-493, a proprietary, orally available inhibitor of Hsp90. IPI-493 has demonstrated anti-tumor activity in multiple preclinical models of human cancer, including NSCLC, breast cancer, colon cancer, and hematological malignancies. IPI-493 has also demonstrated favorable pharmaceutical properties, including potent inhibition of Hsp90, selectivity for cancer cells over normal cells and high oral bioavailability. We are evaluating IPI-493 in two Phase 1, dose escalation studies to determine the optimal dose and schedule for future development. One study is designed to assess the safety, tolerability, pharmacokinetic parameters and pharmacodynamic markers of biological activity of IPI-493 in patients with advanced hematologic malignancies. The second study is being conducted in patients with advanced solid tumors.

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In 2011, we anticipate reporting data from our Hsp90 program and announcing a path forward based on data from our ongoing clinical trials and relevant preclinical studies.

We have worldwide development and commercialization rights for our Hsp90 chaperone inhibitor program, which includes IPI-504 and IPI-493, subject to the payment of a single-digit royalty on net sales to our former partner, MedImmune, Inc., an affiliate of AstraZeneca plc.

PI3K Inhibitor Program

In July 2010, we entered into a development and license agreement with Intellikine under which we obtained global development and commercialization rights to Intellikine s portfolio of inhibitors targeting the delta and/or gamma isoforms of PI3K. The PI3Ks are a family of enzymes involved in cellular functions, including cell proliferation and survival, cell differentiation, intracellular trafficking and immunity. The delta and gamma isoforms of PI3K are restricted to immune system cells. Therefore, specifically targeting PI3Kdelta and PI3Kgamma may provide multiple opportunities to develop differentiated therapies against inflammatory and autoimmune diseases as well as hematologic cancers.

Our lead compound in this program, IPI-145, is an orally-available, small molecule, dual-selective inhibitor of PI3Kdelta and PI3Kgamma. IPI-145 has demonstrated activity in several preclinical models of inflammation. We intend to commence clinical development of IPI-145 in the second half of 2011. Mundipharma has commercialization rights outside the United States for products arising from our PI3K inhibitor program.

FAAH Inhibitor Program

FAAH plays a role in the endocannabinoid system, which is made up of a group of enzymes and receptors shown to play an important role in modulating painful and inflammatory conditions affecting the central nervous system and the body as a whole. In response to painful stimuli or inflammation, the endocannabanoid system is activated and endocannabinoids are produced. Many endocannabinoids are fatty acid amides, or FAAs, which produce the body s own powerful analgesic and anti-inflammatory responses. FAAH breaks down FAAs, rendering the beneficial effects of FAAs short-lived. It is believed that inhibition of FAAH may enable the body to bolster its own analgesic and anti-inflammatory response, and have applicability in a broad range of painful or inflammatory conditions.

IPI-940, a novel, orally available inhibitor of FAAH with potential application for the treatment of a broad range of painful or inflammatory conditions. In October 2010, we reported top-line data from a Phase 1 randomized clinical trial of IPI-940 in 48 healthy adult volunteers. The study assessed the pharmacokinetics, pharmacodynamics, safety and tolerability of IPI-940 following single oral administration at escalating dose levels. In the study, administration of IPI-940 resulted in marked FAAH inhibition and increased anandamide levels. In addition, IPI-940 was well tolerated, with no observed dose-limiting toxicities or clinically significant changes in clinical laboratory values, vital signs or electrocardiogram parameters. Additional Phase 1 development of IPI-940 is ongoing.

In October 2010, Mundipharma and Purdue exercised their rights to assume worldwide development and commercialization activities for products arising out of the FAAH program and will fund 100% of all subsequent research, development and commercialization expenses. In 2011, we anticipate completing transition activities to facilitate Phase 2 clinical trials in pain by Purdue.

Strategic Alliances

Since our inception, strategic alliances have been integral to our growth. These alliances have provided access to breakthrough science, significant research support and funding, and innovative drug development

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programs, all intended to help us realize the full potential of our product pipeline while at the same time allowing us to retaining significant downstream value in our programs through commercialization rights and royalties. Since our inception, all of our revenue has been derived from our strategic alliances, and all of our revenue during 2009 and 2010 was derived from our alliance with Purdue and Mundipharma.

Purdue and Mundipharma. In November 2008, we entered into strategic alliance agreements with each of Purdue and Mundipharma to develop and commercialize pharmaceutical products. The alliance currently includes product candidates that inhibit or target the Hedgehog pathway, FAAH, PI3K, and product candidates arising out of all our discovery projects in all disease fields that are conducted during a prescribed funded discovery period . In December 2010, Mundipharma exercised an option to extend the duration of the funded discovery period through December 31, 2012 and Mundipharma has the option to extend this period for an additional year. Our Hsp90 program is expressly excluded from the alliance. The agreement with Purdue is focused on the development and U.S. commercialization of products targeting FAAH. The agreement with Mundipharma is focused on the development and commercialization outside of the United States of all products and product candidates covered by the alliance, including those targeting FAAH. Following entry into the strategic alliance agreements in November 2008, we consider Mundipharma, Purdue and associated entities to be related parties for financial reporting purposes because of their equity ownership in our company.

Under the strategic alliance agreements, we have responsibility and decision-making authority for the performance of early discovery projects and the development of all product candidates on a worldwide basis. There are no joint steering or similar committees for the alliance. In October 2010, Mundipharma and Purdue exercised their rights to assume worldwide development and commercialization activities for products arising out of the FAAH program and will fund 100% of all subsequent research, development and commercialization expenses. For the remaining programs included in the alliance, Mundipharma is obligated to pay 100% of our contractually budgeted amounts for research and development expenses incurred by us until the later of December 31, 2013 and the commencement of the first Phase 3 clinical trial of such product candidate, which we refer to as the transition date . The contractually budgeted amount for the period between November 19, 2008 and December 31, 2009 was $50 million and the contractually budgeted amounts for the year ended December 31, 2010 was $65 million. The contractually budgeted amounts for 2011 and 2012 are $85 million and $110 million, respectively. Any activities we conduct related to the transition of the FAAH program to Purdue and Mundipharma will be reimbursed in addition to the contractually budgeted amount. For the remaining programs in the alliance, we have the right to exceed the contractually budgeted amount at our own expense, which we did in 2010 due primarily to the license of our PI3K inhibitor program, and which we expect to be the case in 2011 on account of enhanced clinical trial activities for IPI-926 and the commencement of clinical development of IPI-145. After the transition date for each product candidate, we will share with Mundipharma all research and development costs for such product candidate equally. We are recognizing revenue for reimbursed research and development services we perform for Mundipharma and Purdue. We recognized $67.0 million, $46.5 million and $2.7 million in such revenue in the years ended December 31, 2010, 2009 and 2008, respectively.

In December 2010, we amended our strategic alliance agreement with Mundipharma. Under the original agreement Mundipharma had the right to opt out of any early discovery project or any preclinical or clinical development program on an annual basis in November of each year. In the event of an opt-out decision, Mundipharma would continue to provide funding for, in the aggregate, 100% of our contractually budgeted research and development expenses for all programs included in the alliance for the calendar year following the date of such opt out. Under the amendment, these time-based decisions have been modified to become event-based for the Hedgehog program only. Mundipharma will continue to have time-based annual opt-out rights in November of each year for the other programs in the alliance.

Under the amendment, Mundipharma s next funding commitment for the Hedgehog program must be made by the 30th day following the outcome of an end-of-Phase 2 meeting with the FDA pertaining to the ongoing clinical trial of IPI-926 in patients with pancreatic cancer (or, if the end-of-Phase 2 meeting is not held by

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November 1, 2013, then by November 30, 2013). Mundipharma is obligated to fully fund the Hedgehog program until it is required to make this further commitment. If Mundipharma elects to opt-out of continued development funding at this time, then Mundipharma would be obligated to make an immediate payment of $23.65 million to us, which we can use on any research or development program in the alliance. In addition, Mundipharma would be obligated to reimburse us for up to $23.65 million of additional expenses incurred during 2013 that are associated with the completion of Phase 2 clinical trials of IPI-926 that are ongoing at the time of the opt-out, so that aggregate residual funding could total $47.3 million. If Mundipharma elects to continue participation in the Hedgehog program when it makes its next commitment, Mundipharma would thereafter have the annual November opt-out right, and one-year residual funding obligation, contained in the original agreement.

In addition, we and Mundipharma each have the right to opt out of continued development of a product candidate after it has reached the transition date, with a one year tail funding obligation for 50% of post-transition date research and development expenses for the product candidate. If a party exercises its right to opt out of the development of a product or product candidate after the transition date, the other party may elect to continue the development and assume responsibility for the worldwide commercialization of such product or product candidate, subject to the payment of a royalty.

Except as set forth above with respect to FAAH products and opt-out products, we will have the right and responsibility to market and sell products arising from the alliance in the United States and Mundipharma will have the right and responsibility to market and sell products arising from the alliance outside of the United States. Other than pursuant to the strategic alliance agreements, neither we, Purdue nor Mundipharma may develop, manufacture or commercialize products that arise out of the research program or products that are directed to the same target or pathway as a product included in the research program, unless and until a party terminates its rights with respect to such products.

If we in-license any product or product candidate during the funded discovery period for which GLP (Good Laboratory Practice) toxicology studies have been initiated and commercialization rights outside of the United States are available for grant by us to Mundipharma, Mundipharma will have the option to include such in-licensed product or product candidate in the alliance by paying us a prescribed percentage of the up-front license fee or other acquisition cost, which percentage could be up to 60% of such fee or cost, in order for Mundipharma to obtain commercialization rights for such in-licensed product or product candidate in all countries outside of the United States, and by funding research and development costs in the same manner as products or product candidates arising out of our internal discovery programs. The agreement with Mundipharma provides for the agreed-upon research and development budgets to be updated to reflect the inclusion of any in-licensed products or product candidates. There will be no royalties paid between the parties on in-licensed candidates. If we in-license any product or product candidate during the funded discovery period for which GLP toxicology studies have not been initiated, as we did with our PI3K program in 2010, such products are automatically included in the alliance as having arisen out of our internal discovery projects within the then-existing contractually budgeted amounts.

Except with respect to products that have been in-licensed by us, for which no royalties will be payable between the parties, we are obligated to pay Mundipharma a 5% royalty on net sales of the commercialized products until such time as Mundipharma has recovered all research and development expenses paid to us under the research program prior to the applicable transition date. After such cost recovery, we are obligated to pay a tiered, 1% to 3% royalty on U.S. net sales of those products. For products in which Mundipharma has opted-out of development prior to the transition date, we are obligated to pay royalties of 1% to 5% of worldwide net sales as a function of the stage of development of the applicable product candidate at the time of opt-out. For products in which either party has opted-out of development following the transition date, the commercializing party is obligated to pay the other party a 5% royalty on net sales. Mundipharma is obligated to pay us a tiered, 10% to 20% royalty on annual net sales outside of the United States of each product arising out of the alliance, and Purdue is obligated to pay us a tiered, 10% to 20% royalty on annual net sales of FAAH products in the United States. Royalties are payable until the later to occur of the last-to-expire of specified patent rights and the

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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 rates above is reduced by one-half. In addition, all royalties payable under the strategic alliance agreements, whether by us, Purdue or Mundipharma, are subject to reduction on account of third party royalty payments or patent litigation damages or settlements, with any such reductions capped at 50% of the amounts otherwise payable during the applicable royalty payment period. Each of the strategic alliance agreements expire when the parties thereto have no further obligations to each other thereunder. Either party may terminate the strategic alliance agreement to which it is a party on 60 days prior written notice if the other party materially breaches the agreement and fails to cure such breach within the 60-day notice period. The agreements may also be terminated by Purdue or Mundipharma in the event of a change in control of Infinity or in the event that, during the funded research period, either Adelene Q. Perkins or Julian Adams is no longer a full-time executive of Infinity. Upon termination of either strategic alliance agreement by us or either Purdue or Mundipharma, either party to the other strategic alliance agreement may terminate that agreement.

In connection with the entry into the strategic alliance agreements, we also entered into a securities purchase agreement and line of credit agreement with Purdue and its independent associated company, Purdue Pharma L.P., or PPLP. In March 2009, Purdue assigned its interest under the line of credit agreement to PPLP. Under the securities purchase agreement we issued and sold an aggregate of six million shares of our common stock, plus warrants to purchase up to an aggregate of six million shares of our common stock at exercise prices ranging from $15 to $40 per share, for aggregate proceeds of $75 million. As of December 31, 2010, none of these warrants have been exercised, and warrants to purchase up to five million shares of our common stock remain exercisable.

The line of credit agreement provides for the borrowing by us of one or more unsecured loans up to an aggregate maximum principal amount of $50 million. The loans may be drawn by us during the three-year period that began on April 1, 2009. The loans, which may be used by us for any proper corporate purpose, mature on April 1, 2019, which we refer to as the maturity date, and will be subordinate to any senior indebtedness that we may incur. Borrowings made under the line of credit agreement will bear interest, payable on the maturity date, at a fluctuating rate set at the prime rate on the business day prior to the funding of each loan and will be reset on the last business day of each month ending thereafter. Interest will be compounded on each successive three-month anniversary of the funding of each loan. Outstanding loans may be prepaid without penalty or premium prior to the maturity date. Amounts borrowed under the credit agreement, once borrowed, may not be borrowed again. We have certain rights to repay outstanding amounts under the line of credit agreement in shares of our common stock.

Intellikine. In July 2010, we entered a development and license agreement with Intellikine under which we obtained rights to discover, develop and commercialize pharmaceutical products targeting the delta and/or gamma isoforms of PI3K, including IPI-145. We paid Intellikine a $13.5 million upfront license fee. The entirety of this fee is included as research and development expense in the year ended December 31, 2010, although $8.5 million of this fee was paid in January 2011. In addition, we provide financial support for research activities that may be conducted by Intellikine under a two year research program to identify additional novel delta, gamma and dual delta/gamma-specific inhibitors of PI3K for future development. We are recognizing these costs as research and development expense as they are incurred. We may extend the research program for an additional year upon written notice to Intellikine at least 180 days prior to the last day of the initial two-year research term. We are also obligated to pay up to $25 million in success-based milestones for the development of two distinct product candidates, and up to $450 million in success-based milestones for the approval and commercialization of two distinct products. In addition, we are obligated to pay Intellikine tiered royalties ranging from single digits to low teens upon successful commercialization of products licensed to us, which are payable 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, subject to reduction in certain circumstances.

Under the agreement, we obtained rights to direct all development and commercialization activities worldwide for products arising from the agreement for all therapeutic indications. Mundipharma, under the terms

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of its strategic alliance agreement with us, has commercialization rights outside the United States for products arising out of our PI3K inhibitor program. For a product directed primarily to an oncology indication, Intellikine will have the option, at the end of Phase 2 clinical development and upon payment of an option fee, to convert its royalty interest in U.S. sales into the right to share in 50% of profits and losses on U.S. development and commercialization, and to participate in up to 30% of the detailing effort for these products in the United States.

Intellikine may terminate its participation rights in any oncology product with 12 months prior written notice to us, after which Intellikine s participation rights would revert back to the original milestone- and royalty-based payment structure, provided that Intellikine would not be entitled to receive royalty payments for net sales occurring prior to the termination date and certain specified milestone payments.

Other than pursuant to the agreement, neither we nor Intellikine may research, develop or commercialize products directed to the PI3K delta and/or gamma isoforms which meet certain selectivity criteria.

The agreement expires when the parties have no further obligations to each other thereunder, 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. Additionally, Intellikine 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 provided after the end of the research term.

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.

In the United States, we have 18 issued or allowed patents related to our clinical-stage programs expiring on various dates between 2024 and 2028 as well as numerous pending patent applications and foreign counterpart patent filings which relate to our proprietary technologies. These patents and patent applications include claims directed to compositions of matter, pharmaceutical compositions, methods of treatment, and methods of making these compositions for multiple applications.

We have ten issued U.S. patents covering IPI-504 and related molecules, which expire on various dates between 2024 and 2025. IPI-493 and related formulations are protected by one issued or allowed U.S. patent, which expires no earlier than 2027. These patents and allowed patent applications include composition of matter, pharmaceutical composition, method of treatment, and synthetic method claims.

We have six issued or allowed U.S. patent applications covering IPI-926 and related molecules, which expire on various dates between 2025 and 2028. These patents include composition of matter, pharmaceutical composition, method of treatment, and synthetic method claims.

In addition, as of February 28, 2011, we had several hundred additional patents and patent applications filed worldwide, substantially all of which pertain to our product development programs. Any patents that may issue from our pending patent applications would expire between 2024 and 2030. These patents and patent applications disclose composition of matter, pharmaceutical composition, methods of use and synthetic methods.

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Our policy is to obtain and enforce the patents and proprietary technology rights that are key to our business. We intend to continue to file patent applications to protect technology and compounds that are commercially important to our business, and to do so 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 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 market commercial products, either on their own or through collaborative efforts.

We and our alliance partners 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 drug candidates, and there may be other companies working on competitive projects of which we are not aware. For example, we believe that the following companies, among others, are seeking to develop compounds targeting the Hedgehog pathway:

- Genentech, Inc., through its collaboration with Curis, Inc., which we believe is conducting several Phase 2 clinical trials of GDC-0449, including a pivotal Phase 2 clinical trial in patients with basal cell carcinoma;
- Bristol Myers Squibb Company, through its collaboration with Exelixis, Inc., which we believe is conducting multiple Phase 1 clinical trials of BMS-833923;
- Novartis AG, which we believe is conducting a Phase 2 and multiple Phase 1 clinical trials of LDE 225 and a Phase 1 trial of LEQ-506;
- Pfizer, Inc., which we believe is conducting two Phase 2 clinical trials of PF-04449913; and
- Millennium Pharmaceuticals, Inc. (a subsidiary of Takeda Pharmaceutical Company Limited), which we believe is conducting a Phase 1 clinical trial of TAK-441.

In addition, we believe that the following companies, among others, are seeking to develop compounds targeting Hsp90:

- Synta Pharmaceuticals Corp., which we believe is conducting Phase 2 clinical trials of STA-9090;
- Vernalis plc, which we believe is conducting multiple Phase 1 and 2 clinical trials of AUY-922 in collaboration with Novartis;
- Astex Therapeutics Limited, which we believe is conducting multiple Phase 1 clinical trials of AT-13387;

Exelixis, Inc., which we believe is conducting a Phase 1 clinical trial of XL888;

Myrexis, Inc., which we believe is conducting a Phase 1 clinical trial of MPC-3100;

Kyowa Hakko Kirin Co. Ltd., which we believe is conducting a Phase 1 clinical trial of KW-2478;

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Celgene Corporation, which we believe is conducting a Phase 1 clinical trial of ABI-010;

Novartis AG, which we believe is conducting a Phase 1 clinical trial of HSP990; and

Debiopharm Group, which we believe is conducting a Phase 1 clinical trial of Debio 0932.

We believe that the following companies, among others, are seeking to develop compounds targeting PI3K:

Calistoga Pharmaceuticals, which has entered into an agreement to be acquired by Gilead Sciences, Inc., and which we believe is conducting multiple Phase 1 and Phase 2 clinical trials of CAL-101 and a Phase 1 clinical trial of CAL-263;

Novartis AG, which we believe is conducting Phase 1 clinical trials of BEZ235, BGT226 and BKM120;

Pfizer, Inc., which we believe is conducting Phase 1 clinical trials of PF-04691502 and PF-05212384;

Semafore Pharmaceuticals, Inc., which we believe is conducting a Phase 1 clinical trial of SF1126;

Bayer AG, which we believe is conducting a Phase 1 clinical trial of an unnamed PI3K inhibitor;

GlaxoSmithKline plc., which we believe is conducting a Phase 1 clinical trial of GSK2126458;

Sanofi-aventis (through its collaboration with Exelixis, Inc.), which we believe is conducting multiple Phase 1 and Phase 2 clinical trials of XL147 and multiple Phase 1 clinical trials of XL765;

Genentech, Inc., which we believe is conducting multiple Phase 1 clinical trials of GDC-0941; and

Oncothyreon Inc., which we believe is conducting a Phase 1/2 clinical trial of PX-866.

Finally, we believe Ironwood Pharmaceuticals, Inc. is conducting a Phase 1/2 clinical trial of IW-6118.

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 collaborative partners may for our own drug candidates. These competitive products may have superior safety or efficacy, or be manufactured less expensively, than our drug 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 drug candidates or achieve a competitive position in the market. This would adversely affect our business.

Research and Development

As of February 28, 2011, our research and development group consisted of 133 individuals, of whom over 35 percent hold Ph.D. or M.D. degrees and over an additional 20 percent hold other advanced degrees. Our research and development group is focusing on drug discovery, preclinical research, clinical trials and manufacturing technologies. Our research and development expense for the years ended December 31, 2010, 2009 and 2008 was approximately $99.2 million, $77.9 million and $47.5 million, respectively. Reimbursement for our strategic collaborator-sponsored research and development expenses totaled approximately $67.0 million, $46.5 million and $20.1 million, for the years

ended December 31, 2010, 2009 and 2008, respectively. In calculating strategic collaborator-sponsored research and development expenses, we have included all reimbursement for our research and development efforts, whether the amounts are included in revenue or as a credit to research and development expense, and excluded license fees. Our remaining research and development expense is company-sponsored.

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

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clinical trial activities. Commercial quantities of any drugs we seek to develop will have to be manufactured in facilities and by processes that comply with FDA and other regulations, and we plan to rely on third parties to manufacture commercial quantities of any products we successfully develop.

A natural product is utilized in the production of IPI-926. This product is currently supplied from naturally available plant material. If IPI-926 is successfully developed we will need to acquire and process sufficient amounts of plant material to satisfy commercial demand for the product. We are currently seeking to identify locations where this plant naturally occurs and to establish a sustainable method for growing this plant or producing this natural product in a controlled environment.