INFINITY PHARMACEUTICALS, INC.
Form 10-K
March 14, 2008
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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, 2007

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: 0-31141

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 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 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 29, 2007 was $155,973,123 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 29, 2008: 19,737,359

Documents incorporated by reference:

Portions of our definitive proxy statement to be filed with the Securities and Exchange Commission no later than April 29, 2008 in connection with our 2008 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 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 such 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 processes, 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 proprietary rights for our products, our dependence on collaborative 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

Our mission is to discover, develop, and deliver to patients best-in-class medicines for the treatment of cancer and related conditions. A best-in-class drug refers to a drug, among all drugs within a class of drugs that operate through a particular target or molecular mechanism in the body to affect a particular disease, that is superior to all of the other drugs in the class by virtue of its superior efficacy, superior safety, ease of administration, or some combination of the foregoing. We have built a pipeline of innovative product candidates for multiple cancer indications, all of which represent proprietary applications of our expertise in small molecule drug technologies. We believe that our small molecule discovery and development capabilities, strategic alliances, team of highly experienced management and scientists, and corporate culture form the basis of our potential long-term competitive advantage in seeking to deliver best-in-class medicines to patients.

Our lead product candidate, retaspimycin hydrochloride for injection (formerly known as IPI-504), or retaspimycin, is an intravenously administered small molecule inhibitor of heat shock protein 90, or Hsp90. Hsp90 is a molecule that maintains the structure and activity of specific proteins, known as client proteins of Hsp90; specific mutations in, or the aberrant expression of, these client proteins result in many types of cancer. Hsp90 enables the survival of the cancer cell by allowing the client protein to continue functioning. We believe that the inhibition of Hsp90 has broad therapeutic potential for patients with solid tumors and blood-related cancers, including those that are resistant to other drugs. As of February 29, 2008, retaspimycin is being evaluated as a single agent in three disease-focused clinical trials, including a Phase 1 trial in patients with metastatic and/or unresectable gastrointestinal stromal tumors (GIST) and other soft tissue sarcomas (STS), the Phase 2 portion of a Phase 1/2 trial in patients with advanced non-small cell lung cancer (NSCLC), and a Phase 2 trial in patients with hormone-resistant prostate cancer (HRPC). We are also conducting a Phase 1b clinical trial of retaspimycin in combination with Taxotere® (docetaxel) in patients with advanced solid tumors. We currently expect to initiate additional clinical trials of retaspimycin during 2008, including a Phase 3 clinical trial in GIST in the third quarter of 2008 pending ongoing consultation with advisors and regulatory authorities and analysis of data from the ongoing Phase 1 trial, and one or more Phase 2 clinical trials in additional solid tumor indications. We also intend to begin a Phase 1 clinical trial of IPI-493, an orally available inhibitor of Hsp90, in the second quarter of 2008. We are pursuing our Hsp90 program in collaboration with MedImmune, Inc., a division of AstraZeneca plc. We use the term MedImmune/AZ to identify our Hsp90 collaborator.

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Our next most advanced program is directed against the Hedgehog signaling pathway, or Hedgehog pathway. Normally, the Hedgehog pathway regulates tissue and organ formation during embryonic development. When abnormally activated during adulthood, however, the Hedgehog pathway is believed to play a central role in allowing the proliferation and survival of certain cancer-causing cells, and is implicated in many of the most deadly cancers. The lead candidate in our Hedgehog pathway program, IPI-926, has shown potent and selective inhibition of the Hedgehog pathway as well as anti-tumor activity in preclinical models. We intend to file an investigational new drug, or IND, application for IPI-926 by the third quarter of 2008 and to commence a Phase 1 clinical trial shortly thereafter.

We also have other research programs that target cancer and related conditions, including a program being conducted in collaboration with the Novartis Institutes for BioMedical Research, or Novartis, to identify small molecule compounds that inhibit the Bcl-2 family of proteins.

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 Old Infinity, 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.

Upon completion of the merger, our common stock was issued to Old Infinity stockholders, and we assumed all of the stock options, stock warrants and restricted stock of Old Infinity outstanding as of September 12, 2006. Immediately following the closing of the merger, former Old Infinity stockholders, option holders and warrant holders owned approximately 69% of the combined company on a fully-diluted basis and former DPI stockholders, option holders and warrant holders owned approximately 31% of the combined company on a fully-diluted basis. In addition, after completion of the merger, the business conducted by the combined company became the one operated by Old Infinity prior to completion of the merger.

Since former Old Infinity security holders owned, immediately following the merger, approximately 69% of the combined company on a fully-diluted basis and as a result of certain other factors, including that former Old Infinity directors constituted a majority of the combined company s board of directors and all members of the combined company s executive management were from Old Infinity, Old Infinity was deemed to be the acquiring company for accounting purposes and the transaction was accounted for as a reverse acquisition of assets and a recapitalization in accordance with accounting principles generally accepted in the United States. Accordingly, for all purposes, including financial reporting, our financial statements for periods prior to the merger reflect the historical results of Old Infinity, and not DPI, and our financial statements for all subsequent periods reflect the results of the combined company. In addition, because the business conducted by the combined company became the one operated by Old Infinity prior to the completion of the merger, this annual report on Form 10-K describes the business of Old Infinity immediately prior to the completion of the merger and the business of the combined company after the merger. Unless specifically noted otherwise, as used herein, the terms Infinity, we, us and our refer to the combined company after the merger and the business of Old Infinity prior to the merger, and DPI refers to the business of DPI prior to completion of the merger.

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 subsidiaries in the United States and in other select countries. We 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.

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Business Strategy

We intend to accomplish our mission of discovering, developing and delivering to patients best-in-class medicines for the treatment of cancer and related conditions by executing on a strategy to:

Focus our efforts on cancer and related conditions. We have focused the majority of our efforts in the field of cancer, otherwise known as oncology, because we expect this focus will enable us to develop and build expertise and critical mass. Furthermore, we have chosen to focus our efforts strategically in oncology for scientific, clinical/regulatory and commercial reasons.

Scientific. In the last decade, advances in the basic molecular understanding of the pathways that drive the development of a cancer cell have grown. Many of the field s most important drug targets have only recently been discovered, and new approaches to drug development continue to evolve. We believe that our proprietary small molecule capabilities and the depth, breadth and experience of our scientific team provide us a competitive advantage in potentially overcoming the hurdles of cancer drug development.

Clinical/Regulatory. Because of the life-threatening nature of cancer and the side effects caused by many existing cancer drugs, there are several regulatory programs designed to provide an expedited path for developing and achieving marketing approval for cancer drugs which, if available for our drug candidates, may give us the opportunity to deliver new medicines to patients more rapidly.

Commercial. We believe that the large unmet medical need in oncology remains a significant market opportunity. Recently approved oncology drugs have experienced significant sales growth despite addressing relatively small patient populations. The American Cancer Society estimates that there were approximately 1.4 million newly diagnosed cases of cancer in the United States in 2007 and that approximately 560,000 people in the United States died of cancer in 2007.

Focus on therapies that serve an unmet medical need. To date, our strategy has been to focus on the discovery and development of drugs directed against specific molecular targets. These drugs, which are frequently referred to as targeted therapies, hold the promise of being more selective than traditional cytotoxic drugs, thus harming fewer normal cells, reducing side effects and improving the quality of life for patients. In selecting drug targets, we have focused on those that serve important unmet medical needs, are supported by strong science, leverage our small molecule discovery and development capabilities, and have clearly defined clinical development paths. We have also selected drug targets that, despite their high level of scientific validation, have not been adequately served by existing chemistries and generally do not have marketed drugs or late stage clinical product candidates directed against them. We believe this gives us the opportunity to develop a best-in-class medicine.

Focus our development efforts on rapidly obtaining product approval, while in parallel pursuing the broadest market opportunities. Our clinical development strategy is informed by our desire to reach the market with best-in-class drug candidates as rapidly as possible. Our clinical strategy with retaspimycin has been to initiate disease-focused Phase 1 trials, testing the drug candidate as a single agent in refractory settings where we believe there is a strong scientific rationale for the use of an Hsp90 inhibitor in the indication, substantial unmet medical need, and potential for accelerated approval. In addition to choosing targeted disease settings supported by strong science, we have also chosen indications in which we have the potential to observe signals of biological activity using surrogate markers, such as positron emission tomography, or PET, imaging. Combined, these strategies have the potential to markedly accelerate clinical development by producing valuable data on biological activity in a comparatively large sample of patients in the same indication, all in Phase 1. For more advanced stages of clinical development, we are making development decisions based on a rigorous scientific interpretation of clinical data, our growing understanding of the biology of our drug targets, and the interests of patients, all in an effort to expand our drug candidates into additional indications, earlier lines of therapy, and combination studies with other approved agents in order to enhance their market potential. Whenever possible, we will seek to obtain FastTrack designation, accelerated approval and priority review from the U.S. Food and Drug Administration, or FDA, for our drug candidates.

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Establish strategic alliances to accelerate and maximize the potential of our product portfolio. We believe that our long-term value will be driven by the medicines we create. We have adopted an efficient strategy for funding our research activities to provide us with the financial strength to support our scientific innovation. We have established alliances with leading pharmaceutical and biotechnology companies that have been instrumental in providing capital and complementary capabilities to support our internal research. We have product development alliances with MedImmune/AZ relating to our Hsp90 program and with Novartis relating to our Bcl-2 program. In both of these alliances, we have the right to take an active role in product development and to participate significantly in any downstream commercial activities and financial return generated by them. In addition, the cost-sharing provisions of these alliances help us control our cash burn rate, which enables us both to invest heavily in our programs and, potentially, to reach key development milestones before requiring additional financing.

Attract and develop outstanding scientists, clinicians, and business people. We believe that our people and the culture in which they operate are as important to our success as are our technologies, and that living our core values of diversity, citizenship, passionate innovation, transparent communication, mutual respect, social responsibility and integrity provides a key competitive advantage. Embracing a culture of citizen-ownership in which our employees work together as a community with the objective of bringing important new medicines to patients, we aspire to empower each individual to think innovatively and achieve his or her fullest potential. This culture has enabled us to use a relatively small team to perform virtually all of our discovery, development, and formulation sciences work internally, and to integrate our scientific and business teams to create value for shareholders and patients. In addition, our management team has an extensive track record in discovering, developing and commercializing innovative medicines and leading and/or managing successful biotechnology enterprises. This track record has also allowed us to attract and engage industry-leading external advisors and top clinical investigators to assist us in formulating our research and development strategies and conducting our clinical trials.

Product Development Pipeline

We focus our product development efforts on targeted therapies for cancer and related conditions. Our product development programs as of February 29, 2008 are illustrated in the following chart:

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During 2008, we expect to advance our product development pipeline by:

- launching a Phase 3 clinical trial of retaspimycin in refractory GIST, pending ongoing consultation with our advisors and regulatory authorities, and analysis of data from our ongoing Phase 1 clinical trial;
- initiating one or more Phase 2 clinical trials of retaspimycin in additional solid tumor indications;
- commencing a Phase 1 clinical trial of IPI-493;
- commencing a Phase 1 clinical trial of IPI-926; and
- making progress towards naming clinical candidates in our discovery-stage programs.

Hsp90 Program

Hsp90 is emerging as a significant 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. Many cancers result from specific mutations in, or aberrant expression of, these client proteins. Examples of cancer-promoting, or oncogenic, client proteins of Hsp90 include c-Kit in GIST, epidermal growth factor receptor, or EGFR, in NSCLC, and Her-2 in breast cancer. Hsp90 enables those cancers survival by maintaining the function of oncogenic client proteins.

In preclinical studies, inhibition of Hsp90 has been shown to lead to the degradation of these client proteins and to cell death, or apoptosis. Importantly, cancers featuring oncogenic client proteins that have become resistant to approved targeted therapies remain sensitive to Hsp90 inhibition in preclinical models. As a result, inhibition of Hsp90 is expected to have broad therapeutic potential for the treatment of patients with solid tumors and blood-related cancers, including cancers that are resistant to other drugs.

Retaspimycin hydrochloride for injection. Retaspimycin is our lead Hsp90 inhibitor. It is a novel, small molecule, semi-synthetic analog of geldanamycin that is delivered as a water-based, intravenous infusion. To date, retaspimycin has been well-tolerated up to a dose of 400 mg/m^2, and has shown promising early evidence of biological activity in clinical trials in patients with metastatic and/or unresectable GIST and in patients with advanced NSCLC. Retaspimycin has also been shown in preclinical studies to inhibit Hsp90 potently and selectively, thereby killing cancer cells. In these preclinical studies, retaspimycin has demonstrated a broad potential to kill cancer cells as a single agent as well as in combination with existing anti-cancer drugs. In addition, preclinical studies suggest that retaspimycin preferentially targets and accumulates in tumor tissues. For these reasons, we believe that retaspimycin 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 are conducting multiple clinical trials with retaspimycin:

- *Gastrointestinal Stromal Tumors.* GIST is a life threatening type of sarcoma that is highly resistant to traditional cytotoxic chemotherapy or radiation treatment. The American Cancer Society estimates that between 4,500 and 6,000 Americans develop GIST each year. In the majority of GIST cases, there are specific mutations in cellular signaling enzymes, or kinases, such as c-Kit and platelet-derived growth factor receptor-alpha (PDGFRA), that are responsible for the growth and survival of the tumor. Kinase inhibitor drugs target these enzymes and have dramatically improved disease control and survival for patients with GIST. Resistance to kinase inhibitors is, however, an emerging problem, necessitating the development of new drugs with novel mechanisms of action. Both c-Kit and PDGFRA are also client proteins of Hsp90, and in preclinical experiments are degraded in cancer cells upon treatment with retaspimycin, leading to cancer cell death. These data suggest that Hsp90 inhibition with retaspimycin is a promising area for clinical investigation.

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We have completed enrollment and are analyzing data from the expansion phase of our open-label, dose-escalation Phase 1 clinical trial of retaspimycin in patients with metastatic and/or unresectable GIST or other soft tissue sarcomas. More than twenty patients with GIST or other soft tissue sarcomas were enrolled in the expansion phase of this trial, with retaspimycin being administered at the maximum tolerated dose of 400 mg/m^2 on a three-week cycle of twice-weekly treatment for two weeks followed by one week off treatment. We anticipate presenting data from the expansion phase of this trial at the American Society of Clinical Oncology s (ASCO) Annual Meeting in June 2008. Preliminary data from the dose-escalation portion of this trial were presented at the ASCO Annual Meeting in June 2007. The data presented showed that 16 of 21 evaluated patients, or 76%, had a best response of stable disease as measured by RECIST (Response Evaluation Criteria in Solid Tumors). In addition, an assessment of PET responses revealed that 15 of 18, or 83%, of evaluable patients achieved a partial response or stable disease using the European Organization for the Research and Treatment of Cancer s (EORTC) PET response criteria, which involves a quantitative measurement of the uptake of 18-fluorodeoxyglucose, an imaging agent.

We believe that stable disease is meaningful in patients with refractory GIST. Published data from a clinical trial of Gleevec® (imatinib) in this patient population reveal that overall survival in patients with stable disease is generally consistent with those having a radiographic response following administration with imatinib. Further, a statistically significant increase in time to disease progression in refractory GIST patients in response to administration with Sutent® (sunitinib) as compared to placebo formed the basis for approval of that drug for use in refractory GIST. On this basis, we are planning to launch a Phase 3 clinical trial of retaspimycin in refractory GIST in the third quarter of 2008, subject to our ongoing consultation with our advisors and regulatory authorities as well as our analysis of data emerging from the expansion phase of our ongoing Phase 1 clinical trial. In this regard, we submitted a special protocol assessment with the FDA in February 2008.

Non-Small Cell Lung Cancer. The American Cancer Society reports that lung cancer is the leading cause of cancer death for both men and women, estimating that approximately 215,000 new cases of lung cancer were diagnosed in the United States in 2007. NSCLC is the most common form of lung cancer, accounting for about 85% of all lung cancers, or approximately 170,000 new cases. Patients with NSCLC who have EGFR mutations (estimated to be approximately 15% of NSCLC patients in the United States and up to 30% of NSCLC patients outside of the United States) have been found to benefit from existing therapies that block EGFR signaling, including targeted kinase inhibitors. Unfortunately, additional resistance mutations in EGFR often lead to disease progression, even in patients who initially respond to kinase inhibitor therapy, necessitating the development of new therapeutics with novel mechanisms of action. Multiple cellular proteins or pathways have been linked to the progression and resistance to therapy of NSCLC, including mutated EGFR, Akt, and cMet. These proteins are all client proteins of Hsp90 and in preclinical experiments are degraded in cancer cells upon treatment with retaspimycin, leading to cancer cell death. This suggests that Hsp90 inhibition with retaspimycin in NSCLC is a promising area for clinical investigation. Furthermore, with a complementary, novel mechanism of action, inhibition of Hsp90 has the potential to aid in overcoming resistance to kinase inhibitor therapy.

We are currently conducting the Phase 2 portion of our open-label, multi-center Phase 1/2 clinical trial of retaspimycin in patients with NSCLC. In this portion of the study, a total of 20 patients are being enrolled in two equal groups: one group with known EGFR mutations and one group with unmutated, or wild-type, EGFR. Evidence of anti-tumor activity is being evaluated using RECIST criteria. If sufficient evidence of clinical benefit is observed in either cohort, 19 additional patients will be enrolled in that cohort. Retaspimycin is being administered intravenously at 400 mg/m^2 on a three-week cycle, consisting of twice-weekly treatment for two weeks followed by one week off treatment.

Preliminary data from the Phase 1 portion of this trial were presented at the American Association for Cancer Research-National Cancer Institute-European Organization for Research and Treatment of Cancer International Conference on Molecular Targets and Cancer Therapeutics in October 2007.

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Preliminary evidence of biological activity was reported in a heavily pretreated population of patients. In seven of nine evaluable patients, disease stabilization by RECIST was achieved over at least one cycle of administration. One patient with a mutation in EGFR and prior history of progression on targeted kinase inhibitors experienced stable disease for more than six months. In addition, four of four evaluated patients who underwent positron emission tomography imaging revealed a decrease in tumor metabolic activity in response to retaspimycin administration as measured by uptake of 18-fluorodeoxyglucose; two of these patients achieved a partial response using the EORTC s PET response criteria.

Hormone Resistant Prostate Cancer. Prostate cancer is the most common noncutaneous malignancy diagnosed in men in the United States. According to the American Cancer Society, more than 218,000 American men are diagnosed with prostate cancer annually. Prostate tumors that are growing despite the reduction of circulating testosterone to very low levels are characterized as hormone-resistant. The only therapy at this time proven to improve survival for men with HRPC, also known as castration-resistant prostate cancer, is docetaxel-based chemotherapy. Multiple cellular proteins or pathways have been linked to the progression of hormone refractory disease in patients with prostate cancer, including the androgen receptor, the Her-2 receptor, and Akt. These proteins are all client proteins of Hsp90, and in preclinical experiments these proteins are degraded in prostate cancer cells upon treatment with retaspimycin, leading to cancer cell death. This suggests that Hsp90 inhibition with retaspimycin is a promising area for clinical investigation in HRPC.

We are conducting a Phase 2 clinical trial evaluating retaspimycin in patients with advanced HRPC. The goal of this open-label, multi-center study is to determine the anti-tumor activity of retaspimycin in patients with HRPC and to correlate prior treatment status with clinical response. Initially, two groups of patients will be enrolled: one group having no prior treatment with cytotoxic chemotherapy, and one group having had prior treatment with a docetaxel-based chemotherapy. Evidence of biological activity in both groups of patients is being evaluated by RECIST, bone scans, and measurement of prostate-specific antigen levels. The trial is expected to enroll 30 patients initially (15 per group) and will expand to enroll an additional 10 patients in each trial arm if a response is observed in at least one patient in that arm. In this study, retaspimycin is being administered by intravenous infusion at the recommended Phase 2 dose of 400 mg/m^2 on a three-week cycle of therapy, consisting of twice-weekly treatment for two weeks followed by one week off treatment.

Taxotere® (docetaxel) Combination. In preclinical models of prostate cancer and NSCLC, Taxotere® (docetaxel) demonstrates increased anti-tumor activity when administered in combination with retaspimycin. In addition, preclinical data suggest that retaspimycin may have anti-cancer properties in prostate, lung and breast cancers all tumors in which Taxotere has demonstrated clinical efficacy. These data provide a rationale for investigating retaspimycin in combination with Taxotere in multiple tumor types.

We are conducting a Phase 1b clinical trial of retaspimycin in combination with Taxotere in patients with advanced solid tumors. The goal of this open-label, dose-escalation study is to establish the safety, maximum tolerated dose and optimal schedule of administration for retaspimycin in combination with Taxotere. Initially, patients will receive 75 mg/m^2 of Taxotere followed by 300 mg/m^2 of retaspimycin on day one of each 21-day cycle. Once a maximum tolerated dose is reached, the trial will expand to enroll up to 20 additional patients. Additional schedules, including once-weekly dosing of retaspimycin and Taxotere, may also be explored as the trial progresses.

IPI-493. In parallel with the development of retaspimycin, we are pursuing development of IPI-493, a proprietary, orally available inhibitor of Hsp90. Like retaspimycin, IPI-493 is a semi-synthetic analog of geldanamycin. In preclinical models, IPI-493 has demonstrated high oral bioavailability in animals and selective and potent inhibition of Hsp90. We are currently preparing our IND application for IPI-493 and expect to initiate clinical development of this compound in the second quarter of 2008.

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Our Hsp90 program is being pursued in collaboration with MedImmune/AZ. For a description of this collaboration, see Strategic Alliances MedImmune/AZ below.

Hedgehog Pathway Inhibitor Program

The Hedgehog pathway is a target of growing interest in the oncology community. It represents a new way of understanding and potentially attacking the progression and reoccurrence of cancer. The Hedgehog pathway is normally active during embryonic development and regulates tissue and organ formation. When abnormally activated in adults, the Hedgehog pathway is believed to play a central role in allowing the proliferation and survival of cancer cells, including pancreatic cancer, prostate cancer, small cell lung cancer, breast cancer, hematologic cancers, skin cancers, and certain brain cancers. In addition, recent evidence points to a potentially important role for the Hedgehog pathway in tumor progenitor cells. Tumor progenitor cells are resistant to standard anti-cancer agents and radiation, and are therefore suspected to be responsible for disease relapse following treatment with conventional therapeutic agents.

We have developed a novel, proprietary Hedgehog pathway inhibitor, IPI-926. IPI-926 is a semi-synthetic derivative of the natural product, cyclopamine, that inhibits the Hedgehog pathway by binding to the Smoothened receptor. When systemically administered in multiple preclinical animal models, IPI-926 has shown potent and selective inhibition of the Hedgehog pathway, anti-tumor activity, and attractive pharmacologic properties including oral bioavailability and extended half-life. We are currently completing preclinical toxicology studies on IPI-926 and anticipate commencing clinical development of this compound in 2008.

In November 2007, we regained from MedImmune/AZ all development and worldwide commercialization rights for our Hedgehog pathway program, including for IPI-926. Additionally, we have the right to opt-in to the development and commercialization of certain Hedgehog pathway programs being developed by AstraZeneca. In exchange for these rights, we waived the non-competition clause contained in our collaboration agreement with MedImmune/AZ applicable to AstraZeneca s independent work in the Hedgehog pathway.

Bcl-2 Program

Bcl-2 and the related protein Bcl-xL act as brakes on programmed cell death, or apoptosis, and are key regulators of this process. Many cancer cells have higher than normal levels of Bcl-2 and/or Bcl-xL. This allows them to evade apoptosis and potentially become resistant to chemotherapy. We are developing compounds that target Bcl-2 alone, and Bcl-2/Bcl-xL together, to inhibit their protective effect on cancer cells. Inhibitors of Bcl family proteins are expected to work as single agents in B-cell malignancies that are dependent on Bcl-2 for their survival, such as follicular lymphoma, chronic lymphocytic leukemia, and diffuse large B-cell lymphoma. Bcl inhibitors are also expected to work in combination with chemotherapies to sensitize a broad range of solid tumors to treatment with chemotherapy.

We have developed highly potent compounds that either selectively target Bcl-2 or target both Bcl-2 and Bcl-xL. In cells, these compounds disrupt the protein-protein interactions between Bcl-2 and its pro-apoptotic binding partners and selectively induce apoptosis in cancer cells that depend on Bcl-2 for survival. In preclinical studies in a variety of tumor types, antagonism of Bcl-2 using our compounds also results in synergy with multiple chemotherapeutic agents. These drug candidates are currently being optimized based on potency or specificity against Bcl-2, as well as for pharmaceutical properties such as solubility, metabolism and absorption, in collaboration with Novartis. For a description of our collaboration with Novartis, see Strategic Alliances Novartis below.

Diversity Oriented Synthesis Technology

Our diversity oriented synthesis chemistry technology consists of methods to create collections of novel, diverse, natural product-like compounds potentially able to interact with biological targets that have not been accessible to traditional synthetic chemistries. We have produced large libraries of structurally diverse and complex molecules for pharmaceutical screening. We believe these libraries embody all of the advantages of natural products, such as diversity and structural complexity, without the historic difficulties of synthesis and

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replication. We have entered into technology access alliances with Amgen Inc., Novartis International Pharmaceutical Ltd. and Johnson & Johnson Pharmaceutical Research & Development, a division of Janssen Pharmaceutical N.V., relating to our diversity oriented synthesis technology. As of December 31, 2007, we have successfully completed all of our obligations to our partners under these agreements. We do, however, have the right to receive milestone payments under two of these agreements if our alliance partner develops and successfully commercializes products based upon certain compounds licensed to them under the applicable agreement.

Strategic Alliances

Developing alliances has been a key strategic element in our evolution. Our alliances complement our expertise in small molecule drug discovery and development with important scientific, clinical, and business capabilities. We have developed significant alliances with leading pharmaceutical and biotechnology companies that enable us to drive forward our proprietary programs while retaining significant value in their downstream potential. These alliances have brought in over $150 million in capital, allowing us to continue to advance our pipeline of novel small molecules and pursue potential additional product opportunities. Since our inception, all of our revenue has been derived from our strategic alliances. For the fiscal year ended December 31, 2007, our collaborations with Novartis accounted for 59% of our revenue and our collaboration with MedImmune/AZ accounted for 41% of our revenue.

MedImmune/AZ. In August 2006, we entered into a product development and commercialization agreement with MedImmune/AZ to jointly develop and commercialize cancer drugs targeting Hsp90 and the Hedgehog pathway. In November 2007, we regained from MedImmune/AZ all development and worldwide commercialization rights under our Hedgehog pathway program.

Under the terms of this agreement, we share equally with MedImmune/AZ all development costs, as well as potential profits and losses, from any future marketed products. MedImmune/AZ made non-refundable, up-front payments totaling $70 million to us in order to obtain co-exclusive rights to the Hsp90 and Hedgehog pathway development programs. Because we have continuing involvement in the development program, we are recognizing the up-front license fee as revenue on a straight-line basis over seven years, which is based on our estimate of the period under which product candidates would be developed by us under the collaboration. During the year ended December 31, 2007, we recognized $10 million in revenue from such fee. In addition, we could receive up to $215 million in milestone payments if certain late-stage development and sales objectives are achieved for products resulting from the Hsp90 program. Further, because the agreement is a cost-sharing arrangement rather than one in which research and development expenses are reimbursed, we record amounts reimbursable by MedImmune/AZ with respect to research and development as a reduction to research and development expense, and not as revenue. For the year ended December 31, 2007, we offset approximately $13.7 million in amounts reimbursable by MedImmune/AZ against research and development expense.

We will retain primary responsibility for discovery and preclinical development of drug candidates targeting Hsp90. The parties will jointly lead clinical development through first product approval, if any. The parties will jointly develop a worldwide marketing and sales strategy for commercialized products, if any. MedImmune/AZ will have the initial right to market and sell such products worldwide, while we have the option to co-promote any future products in the United States, contributing up to 35% of the total promotional effort and with our promotional costs being included among those shared under the collaboration.

The parties will jointly own any invention and know-how that may be developed by either or both parties during the term of the agreement that is directed to the development, manufacture, use or sale of an active pharmaceutical ingredient of a product directed to Hsp90, or is developed in the course of performing activities under the research and development plan. The parties will also jointly own any patent rights that claim such an invention.

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The agreement with MedImmune/AZ will expire in August 2066. Either party may opt out of a project, as MedImmune/AZ did with respect to the Hedgehog pathway project in November 2007, by giving six months written notice to the other party. If one party gives such notice, the other party has 20 days to also opt-out of the project, in which case the parties will seek to out-license or sell the project assets or seek to otherwise maximize the value of the project. We did not elect to opt out of the Hedgehog pathway project. Upon expiration of the six month notice period, the opting-out party is no longer obligated to perform work under the research and development plan and marketing plan for the project, nor pay development costs for the project. Thus, MedImmune/AZ s research and funding obligations with respect to the Hedgehog pathway project terminate in May 2008. An opting-out party is no longer entitled to share profits arising from the project; instead, such party is entitled to receive royalties at a rate based on when such party opted out. MedImmune/AZ agreed to waive these royalties in connection with its decision to opt-out of the Hedgehog pathway project. The collaboration agreement terminates with respect to a project if both parties opt out. If a party materially breaches the agreement with respect to a project and does not cure the breach within a specified period of time, the breaching party is deemed to have opted-out of such project. If a party which opted-out of a project materially breaches the agreement and does not cure the breach within a specified period of time, the breaching party shall no longer be entitled to royalties or milestones with respect to such project. In addition, either party is permitted to terminate the collaboration agreement with respect to a product if it believes there are safety concerns with respect to such product and the parties do not agree on the course of action to be taken, in which case the terminating party gives up all rights in such product.

Novartis. In February 2006, we entered into a collaboration agreement with Novartis to discover, develop and commercialize drugs targeting Bcl protein family members for the treatment of a broad range of cancers. Under the terms of this agreement, we granted to Novartis an exclusive, worldwide license to research, develop and commercialize pharmaceutical products that are based upon our proprietary Bcl inhibitors. Novartis paid us a $15 million up-front license fee, an affiliate of Novartis made a $5 million equity investment in us, and Novartis committed to provide us research funding of approximately $10 million over the initial two-year research term, which expired in February 2008. Pursuant to this agreement, we conducted joint research with Novartis to identify molecules for clinical development. For the year ended December 31, 2007, we recognized $3.75 million in revenue related to the amortization of the up-front license fee and $4.8 million in revenue related to the reimbursable research and development services we performed for Novartis under the agreement.

Novartis had the right to extend the research term for up to two additional one-year terms, under which Novartis could have obligated us to provide up to five full-time equivalents, at Novartis expense, to enable the full transition of the Bcl inhibitor program to Novartis. Novartis chose not to exercise its option for these one-year extensions; thus, Novartis now has responsibility for further pre-clinical, clinical development and commercialization of any products based upon compounds discovered under the joint research program. We may request to participate in clinical development of any such products and, if such request is agreed upon by Novartis, Novartis will fund agreed-upon development costs that are incurred by us. We also have a non-exclusive right to detail Bcl-2 family inhibitor products in the United States, with our detailing costs to be reimbursed by Novartis.

Novartis has agreed to make milestone payments totaling over $370 million if certain specified research, development and commercialization milestones are achieved for multiple products for multiple indications, such that total payments to us could exceed $400 million. Novartis has also agreed to pay us royalties upon successful commercialization of any products developed under the alliance. Novartis has the right to terminate the agreement at any time upon 60 days prior written notice. In addition, Novartis has the right to terminate the agreement in the event of a material breach by us that remains uncured for a period of 120 days after notice. We can terminate specified programs under this agreement as to breaches by Novartis relating solely to such programs that remain uncured for a period of 120 days after notice or can terminate the agreement in its entirety in the event of a material breach by Novartis that remains uncured for a period of 120 days after notice.

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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 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.

Retaspimycin and related molecules are protected by U.S. Patent No. 7,282,493, which expires in March 2025. This patent includes composition of matter, pharmaceutical composition, method of treatment, and synthetic method claims. IPI-926 is protected by U.S. Patent No. 7,230,004, which expires in October 2025. In addition, as of February 29, 2008 we had approximately 145 other patents and patent applications worldwide, substantially all of which pertain to our key product development programs. Any patents that may issue from our pending patent applications would expire between 2024 and 2028.

Our practice is 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 considerable experience 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 Hsp90:

Kosan Biosciences Incorporated, which we believe is conducting a Phase 3 and multiple Phase 2 clinical trials of tanespimycin and a Phase 2 and multiple Phase 1 clinical trials of alvespimycin;

Biogen Idec Inc., which we believe is conducting a Phase 2 clinical trial of BIIB021;

Vernalis plc, which we believe is conducting a Phase 1 clinical trial of an Hsp90 inhibitor in collaboration with Novartis;

Serenex, Inc., which we believe is conducting two Phase 1 clinical studies of SNX-5422;

Synta Pharmaceuticals Corp., which we believe is conducting two Phase 1 clinical studies of STA-9090; and

Astex Therapeutics Limited, which we believe is conducting a Phase 1 clinical trial of AT-13387 in collaboration with Novartis.

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In addition, we believe that Curis, Inc., in collaboration with Genentech Inc., is intending to advance its Hedgehog pathway antagonist into Phase 2 clinical development in advanced solid tumors in 2008. Exelixis, Inc. and Bristol-Myers Squibb Co. are jointly conducting preclinical development of XL139, a Hedgehog pathway inhibitor.

Finally, we believe that Gemin-X Biosciences is conducting clinical trials of one or more Bcl-2 inhibitors in multiple cancer indications, that Abbott Laboratories, Inc. (in collaboration with Genentech) is conducting a Phase 1/2 clinical trial of its Bcl-2 inhibitor, ABT-263, and that Ascenta Therapeutics, Inc. is in Phase 2 clinical development of AT-101, also a Bcl-2 inhibitor.

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 29, 2008, our research and development group consisted of 99 individuals, of whom over 40 percent hold Ph.D. or M.D. degrees and over 64 percent hold 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, 2007, 2006 and 2005 was approximately $33.8 million, $35.8 million and $31.5 million, respectively. Our strategic collaborator-sponsored research and development expenses totaled approximately $18.5 million, $8.1 million and $0 for the years ended December 31, 2007, 2006 and 2005, respectively. In calculating strategic collaborator-sponsored research and development expenses, we have included net reimbursement for our research and development efforts, excluding license fees. Our remaining research and development expense is company-sponsored.

Manufacturing and Supply

We rely primarily on third parties to manufacture critical raw materials, drug substance and final drug product for our research, preclinical development and clinical trial activities. Commercial quantities of any drugs we seek to develop will have to be manufactured in facilities and by processes that comply with FDA and other regulations, and we plan to rely on third parties to manufacture commercial quantities of any products we successfully develop. We do not currently have relationships for redundant supply or a second source for any of our drug candidates.

Sales and Marketing

We currently have no marketing, sales or distribution capabilities. We do, however, have the right to co-promote in the United States any products arising from our collaborations with MedImmune/AZ and Novartis. In order to participate in the commercialization of these drugs if and when they are approved for sale in the United States, we will need to, and we intend to, develop these capabilities.

Government Regulation

Government authorities in the United States and in other countries extensively regulate, among other things, the research, development, testing, manufacturing, labeling, promotion, advertising, distribution, marketing, and export and import of pharmaceutical products such as those we are developing. There is no assurance that any of our drug candidates will prove to be safe or effective, will receive regulatory approvals or will be successfully commercialized.

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New Drug Approval in the United States

In the United States, drugs and drug testing are regulated by the FDA and other federal agencies, as well as by state and local government authorities. Before any of our products may be marketed in the United States, we must comply with the Federal Food, Drug and Cosmetic Act, which generally involves the following:

- preclinical laboratory and animal tests performed under the FDA s Good Laboratory Practices regulations;
- submission and acceptance of an IND application, which must become effective before clinical trials may begin in the United States;
- adequate and well-controlled human clinical trials to establish the safety and efficacy of the drug candidate for its intended use;
- development of manufacturing processes which conform to FDA-mandated current Good Manufacturing Practices, or cGMPs; and
- FDA review and approval of a New Drug Application, or NDA, prior to any commercial sale or shipment of a product.

The testing and approval process requires substantial time, effort and financial resources, and we cannot be certain that any approval will be granted on a timely basis, if at all.

Preclinical testing. Preclinical tests include laboratory evaluation of a drug candidate, its chemistry, formulation, safety and stability, as well as animal studies to assess the potential safety and efficacy of the drug candidate. The results of the preclinical tests, together with manufacturing information, analytical data and other available information about the drug candidate, are submitted to the FDA as part of an IND. An IND is 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 new drug application. Preclinical tests and studies can take several years to complete, and despite completion of those tests and studies, the FDA may not permit clinical testing to begin.

The IND process. The FDA requires a 30-day waiting period after the filing of each IND application 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 or at any time thereafter, 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 or continue. The IND application process may become extremely costly and substantially delay development of our products. Moreover, positive results of preclinical tests will not necessarily indicate positive results in clinical trials.

Prior to initiation of clinical studies, an independent Institutional Review Board, or IRB, at each medical site proposing to conduct the clinical trial must review and approve each study protocol and study subjects must provide informed consent.

Clinical trials. Human clinical trials are typically conducted in three sequential phases that may overlap or be combined:

- Phase 1: The drug candidate is initially introduced into healthy human subjects or patients and tested for safety, dosage tolerance, bioavailability, absorption, distribution, excretion and metabolism. For cancer drugs such as those we are developing, this phase of study is generally conducted in patients.
- Phase 2: The drug candidate is introduced into a limited patient population to: (1) assess the efficacy of the candidate in specific, targeted indications; (2) assess dosage tolerance and optimal dosage; and (3) identify possible adverse effects and safety risks.

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Phase 3: These are commonly referred to as pivotal studies. If a drug candidate is found to have an acceptable safety profile and to be potentially effective in Phase 1 and 2 trials, Phase 3 clinical trials will be initiated to further demonstrate clinical efficacy, optimal dosage and safety within an expanded and diverse patient population at geographically dispersed clinical study sites.

We cannot be certain that we will successfully complete Phase 1, Phase 2 or Phase 3 testing of our drug candidates within any specific time period, if at all. Clinical testing must meet requirements for IRB oversight, informed consent and good clinical practices. The FDA and the IRB at each institution at which a clinical trial is being performed may suspend a clinical trial at any time for various reasons, including a belief that the subjects are being exposed to an unacceptable health risk.

The NDA process. If clinical trials are successful, the next step in the drug regulatory approval process is the preparation and submission to the FDA of an NDA. The NDA is the vehicle through which drug sponsors formally propose that the FDA approve a new pharmaceutical for marketing and sale in the United States. 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. A substantial user fee must also be paid with the NDA, unless an exemption applies. Every new drug must be the subject of an approved NDA before commercialization in the United States.

Upon submission of the NDA, the FDA will make a threshold determination of whether the application is sufficiently complete to permit review, and, if not, will issue a refuse-to-file letter. If the application is accepted for filing, the FDA will attempt to review and take action on the application in accordance with performance goal commitments the FDA has made in connection with the user fee law. Current timing commitments under the user fee laws vary depending on whether an NDA is for a priority drug or not, and in any event are not a guarantee that an application will be approved or even acted upon by any specific deadline. The review process is often significantly extended by FDA requests for additional information or clarification. The FDA may refer the NDA to an advisory committee for review, evaluation and recommendation as to whether the application should be approved, but the FDA is not bound by the recommendation of an advisory committee. The FDA may deny or delay approval of applications that do not meet applicable regulatory criteria or if the FDA determines that the clinical data do not adequately establish the safety and efficacy of the drug. In addition, the FDA may approve a drug candidate subject to the completion of post-marketing studies, referred to as Phase 4 trials, to monitor the effect of the approved product. The FDA may also grant approval with restrictive product labeling, or may impose other restrictions on marketing or distribution such as the adoption of a special risk management plan. The FDA has broad post-market regulatory and enforcement powers, including the ability to issue warning letters, levy fines and civil penalties, suspend or delay issuance of approvals, seize or recall products, and withdraw approvals.

Manufacturing and post-marketing requirements. If approved, a drug may only be marketed in the dosage forms and for the indications approved in the NDA. Special requirements also apply to any drug samples that are distributed in accordance with the Prescription Drug Marketing Act. The manufacturers of approved products and their manufacturing facilities are subject to continual review and periodic inspections by the FDA and other authorities where applicable, and must comply with ongoing requirements, including the FDA s cGMP requirements. Once the FDA approves a product, a manufacturer must provide certain updated safety and efficacy information, submit copies of promotional materials to the FDA, and make certain other required reports. Product and labeling changes, as well as certain changes in a manufacturing process or facility or other post-approval changes, may necessitate additional FDA review and approval. Failure to comply with the statutory and regulatory requirements subjects the manufacturer to possible legal or regulatory action, such as untitled letters, warning letters, suspension of manufacturing, seizure of product, voluntary recall of a product, injunctive action or possible criminal or civil penalties. Product approvals may be withdrawn if compliance with regulatory requirements is not maintained or if problems concerning safety or efficacy of the product occur following approval. Because we intend to contract with third parties for manufacturing of our products, our ability to control third party compliance with FDA requirements will be limited to contractual remedies and

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rights of inspection. Failure of third party manufacturers to comply with cGMP or other FDA requirements applicable to our products may result in, among other things, total or partial suspension of production, failure of the government to grant approval for marketing, and withdrawal, suspension, or revocation of marketing approvals.

The FDA s policies may change and additional government regulations may be enacted which could prevent or delay regulatory approval of our potential products. Moreover, increased attention to the containment of health care costs in the United States and in foreign markets could result in new government regulations that could have a material adverse effect on our business. We cannot predict the likelihood, nature or extent of adverse governmental regulation that might arise from future legislative or administrative action, either in the United States or abroad.

New Drug Approval Outside of the United States

Approval of a drug in the United States does not guarantee approval in any other country and vice versa. Thus, we will have to complete approval processes that are similar to those in the United States in virtually every foreign market in order to conduct clinical or preclinical research and to commercialize our drug candidates in those countries. The approval procedures and the time required for approvals vary from country to country, may involve additional testing, and may take longer than in the United States. Foreign approvals may not be granted on a timely basis, or at all. In addition, regulatory approval of drug prices is required in most countries other than the United States. We face the risk that the resulting prices would be insufficient to generate an acceptable return to us or our collaborators.

In common with the United States, the various phases of preclinical and clinical research are subject to significant regulatory controls within the European Union. Variations in the national regimes exist. Most jurisdictions, however, require regulatory and institutional review board approval of interventional clinical trials. Most European regulators also require the submission of adverse event reports during a study and a copy of the final study report. Under European Union regulatory systems, products that have an Orphan Drug designation or which target cancer, such as the drug candidates we are currently developing, marketing authorizations must be submitted under a centralized procedure that provides for the grant of a single marketing authorization that is valid for all European Union member states.

Orphan Drug Designation

Under the Orphan Drug Act and corresponding European Union regulations, the FDA and European Union regulatory authorities may grant Orphan Drug designation to drugs intended to treat a rare disease or condition. In the United States, a rare disease or condition is one that affects fewer than 200,000 individuals, or more than 200,000 individuals but for which there is no reasonable expectation that the cost of developing and making available in the United States a drug for this type of disease or condition will be recovered from sales in the United States of that drug. In the European Union, a rare disease or condition is one that affects fewer than 5 in 10,000 individuals. In the United States, Orphan Drug designation must be requested before submitting an NDA. After the FDA grants Orphan Drug designation, the identity of the therapeutic agent and its potential orphan use are disclosed publicly by the FDA. Orphan Drug designation does not convey any advantage in or shorten the duration of the regulatory review and approval process, nor does it assure approval.

In the United States, if a product that has Orphan Drug designation receives the first FDA approval for the disease for which it has such designation, the product is entitled to orphan product exclusivity, which means that the FDA may not approve any other applications to market the same drug for the same indication, except in very limited circumstances, for seven years. In the European Union, the period of product exclusivity is ten years. Orphan Drug exclusivity, however, also could block the approval of one of our products in the United States for seven years for an Orphan Drug indication if a competitor obtains approval of the same drug, as defined by the FDA, for such Orphan Drug indication or if our product candidate is determined to be contained within the

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competitor s product for the same indication or disease. We have obtained Orphan Drug designation for retaspimycin for GIST in both the United States and the European Union and intend to seek Orphan Drug status for our other product candidates as appropriate. Orphan Drug designation may not, however, provide us with a material commercial advantage.

Other Regulatory Matters

In the United States, manufacturing, sales, promotion and other activities following the approval of a new drug are subject to regulation by regulatory authorities in addition to the FDA, including the Federal Trade Commission, the Department of Justice, the Centers for Medicare & Medicaid Services, other divisions of the Department of Health and Human Services, and state and local governments. Among other laws and requirements, our sales, marketing and scientific/educational programs would need to comply with the anti-kickback provisions of the Social Security Act, the False Claims Act and similar state laws. Our pricing and rebate programs would need to comply with pricing and reimbursement rules, including the Medicaid rebate requirements of the Omnibus Budget Reconciliation Act of 1990. If products are made available to authorized users of the Federal Supply Schedule of the General Services Administration, additional laws and requirements apply. All of our activities are potentially subject to federal and state consumer protection and unfair competition laws. Finally, certain jurisdictions have other trade regulations from time to time to which our business is subject such as technology or environmental export controls and political trade embargoes. Depending on the circumstances, failure to meet these applicable regulatory requirements can result in criminal prosecution, fines or other penalties, injunctions, private qui tam actions brought by individual whistleblowers in the name of the government, or refusal to allow us to enter into supply contracts, including government contracts.

In addition to regulations enforced by the FDA, we also are subject to regulation under the Occupational Safety and Health Act, the Toxic Substances Control Act, the Resource Conservation and Recovery Act, and other present and potential future foreign, federal, state, and local laws and regulations. Our research and development involves the controlled use of hazardous materials, including corrosive, explosive and flammable chemicals, various radioactive compounds, and compounds known to cause birth defects. Although we believe that our safety procedures for storing, handling, using, and disposing of such materials comply with the standards prescribed by applicable regulations, the risk of contamination or injury from these materials cannot be completely eliminated. In the event of an accident, we could be held liable for any damages that result, and any such liability could materially affect our ongoing business.

Employees

We refer to our employees as citizen-owners. As of February 29, 2008, we had 125 full-time citizen-owners, 99 of whom were engaged in research and development and 26 of whom were engaged in management, administration and finance. Over 60 percent of our citizen-owners 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 doing so in the future. None of our citizen-owners 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 citizen-owners are good.

Executive Officers

The following table lists the positions, names and ages of our executive officers as of February 29, 2008:

Name	Age	Position
Steven H. Holtzman	54	President, Chair and Chief Executive Officer
Julian Adams, Ph.D.	53	