INCYTE CORP
Form 424B5
September 25, 2009

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Filed Pursuant to Rule 424(b)(5)
Registration Nos. 333-157751 and 333-162056

Prospectus Supplement To Prospectus dated April 16, 2009.

18,000,000 Shares

Incyte Corporation

Common Stock

Incyte Corporation is offering 18,000,000 shares to be sold in this offering.

Entities affiliated with one of our directors and principal stockholders, Julian C. Baker, have indicated an interest in purchasing up to 2,000,000 shares of common stock in this offering at the public offering price. Because indications of interest are not binding agreements or commitments to purchase, the Baker entities may purchase fewer or no shares in this offering.

The common stock is quoted on The NASDAQ Global Market under the symbol "INCY." The last reported sale price of the common stock on September 24, 2009 was $6.88 per share.

See "Risk Factors" beginning on page S-7 to read about factors you should consider before buying shares of the common stock.

Neither the Securities and Exchange Commission nor any other regulatory body has approved or disapproved of these securities or determined if this prospectus supplement or the accompanying prospectus is truthful or complete. Any representation to the contrary is a criminal offense.

	Per Share	Total

Initial price to public	$ 6.7500	$121,500,000
Underwriting discount	$ 0.3375	$ 6,075,000
Proceeds, before expenses, to Incyte	$ 6.4125	$115,425,000

To the extent that the underwriters sell more than 18,000,000 shares of common stock, the underwriters have the option to purchase up to an additional 2,700,000 shares from Incyte Corporation at the initial offering price less the underwriting discount.

The underwriters expect to deliver the shares against payment in New York, New York on September 30, 2009.

Sole Book-Running Manager

Goldman, Sachs & Co.

Co-Managers

Morgan Stanley **J.P.Morgan**

Prospectus Supplement dated September 24, 2009.

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Prospectus Supplement

Prospectus

No dealer, salesperson or other person is authorized to give any information or to represent anything not contained in this prospectus supplement or the accompanying prospectus. You must not rely on any unauthorized information or representations. This prospectus supplement and the accompanying prospectus are an offer to sell only the shares offered hereby, but only under circumstances and in jurisdictions where it is lawful to do so. The information contained in this prospectus supplement and the accompanying prospectus is current only as of their respective dates.

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ABOUT THIS PROSPECTUS SUPPLEMENT

This document consists of two parts. The first part is this prospectus supplement, which describes the specific terms of this offering and also adds to and updates information contained in the accompanying prospectus and the documents incorporated by reference into this prospectus supplement and the accompanying prospectus. The second part, the accompanying prospectus, gives more general information, some of which may not apply to this offering. If there is a conflict between the information contained in this prospectus supplement, on the one hand, and the information contained in the accompanying prospectus or any document incorporated by reference, on the other hand, the information in this prospectus supplement shall control.

You should rely only on the information contained or incorporated by reference in this prospectus supplement and the accompanying prospectus. We have not, and the underwriters have not, authorized anyone else to provide you with information that is in addition to or different from that contained or incorporated by reference in this prospectus supplement and the accompanying prospectus, along with the information contained in any permitted free writing prospectuses we have authorized for use in connection with this offering. We are offering to sell, and seeking offers to buy, shares of our common stock only in jurisdictions where offers and sales are permitted. The information contained in this prospectus supplement and the accompanying prospectus is accurate only as of the date of this prospectus supplement or the date of the accompanying prospectus, and the information in the documents incorporated by reference in this prospectus supplement and the accompanying prospectus is accurate only as of the date of those respective documents, regardless of the time of delivery of this prospectus supplement and the accompanying prospectus or of any sale of our common stock. Our business, financial condition, results of operations and prospects may have changed since those dates. It is important for you to read and consider all information contained or incorporated by reference in this prospectus supplement and the accompanying prospectus in making your investment decision. You should read both this prospectus supplement and the accompanying prospectus, as well as the documents incorporated by reference into this prospectus supplement and the accompanying prospectus and the additional information described under "Where You Can Find More Information" in this prospectus supplement and in the accompanying prospectus, before investing in our common stock.

In this prospectus supplement and the accompanying prospectus, unless otherwise indicated or the context otherwise requires, the terms "Incyte," "company," "we," "our," and "us" refer to Incyte Corporation and its consolidated subsidiaries.

This prospectus supplement and the accompanying prospectus, including the information incorporated by reference into this prospectus supplement and the accompanying prospectus, and any free writing prospectuses we have authorized for use in connection with this offering include trademarks, service marks and trade names owned by us or others. Incyte is a registered trademark of Incyte Corporation. The Incyte logo is a trademark of Incyte Corporation. All other trademarks, service marks and trade names included or incorporated by reference in this prospectus supplement and the accompanying prospectus are the property of their respective owners.

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PROSPECTUS SUPPLEMENT SUMMARY

This summary highlights selected information about us and this offering. Because it is a summary, it does not contain all of the information that you should consider before investing. Before you decide to invest in our common stock, you should read carefully and in their entirety this entire prospectus supplement and the accompanying prospectus, including information incorporated by reference, the section entitled "Risk Factors" in this prospectus supplement and our consolidated financial statements and related notes incorporated by reference in the accompanying prospectus.

Our Company

Incyte is a drug discovery and development company focused on developing proprietary small molecule drugs to treat serious unmet medical needs. We have a broad pipeline with programs focused primarily in the areas of oncology, inflammation, and diabetes. Our most advanced compound, INCB18424, is in Phase III development as a treatment for myelofibrosis.

Our wholly-owned pipeline includes the following compounds:

Drug Target	Drug Compound	Indication	Development Status
Active Programs			
JAK	*INCB18424 (Oral)*	Myelofibrosis Polycythemia Vera/ Essential Thrombocythemia	Phase III Phase II
	INCB18424 (Topical)	Psoriasis	Phase IIb
	INCB28050	Rheumatoid Arthritis	Phase II
HSD1	*INCB13739*	Type 2 Diabetes	Phase IIb
Sheddase	*INCB7839*	Breast Cancer	Phase II
Programs pending additional funding or seeking collaborative partner			
c-MET	*INCB28060*	Solid Cancers	IND Cleared
IDO	*INCB24360*	Oncology	IND Cleared
HM74a	*INCB19602*	Type 2 Diabetes	Phase IIa
CCR5	*INCB9471*	Human Immunodeficiency Virus (HIV)	Phase II
	INCB15050	HIV	Phase I

Since the beginning of 2009, we have focused our efforts on clinical programs that we believe have the greatest likelihood of creating near-term value and on compounds that we believe a company of our size can effectively develop and commercialize on its own, or that we can further develop and commercialize through strategic relationships. Currently, our highest priority program involves our JAK inhibitors. Our JAK inhibitor program includes an oral formulation of INCB18424 as a treatment for myeloproliferative disorders (myelofibrosis, polycythemia vera and essential thrombocythemia) and certain other oncology indications, a topical formulation of INCB18424 for psoriasis, and an oral formulation of INCB28050 for rheumatoid arthritis and other chronic inflammatory conditions.

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We intend to retain rights in the United States for INCB18424 for myeloproliferative disorders and other oncology indications, as we believe this is a market where a company of our size can effectively compete. For markets outside of the United States, we are currently evaluating strategic relationships. We may progress topical INCB18424 for psoriasis on our own, or we may seek to partner INCB18424 for this indication. For INCB28050 for rheumatoid arthritis and other chronic inflammatory conditions, we are evaluating a number of broad global alliances which may allow us to participate in the commercialization of INCB28050 and retain rights in certain indications. We are evaluating strategic relationships with respect to several of our programs and may enter into an agreement with respect to one or more of these programs in the near future. However, these arrangements and negotiations are complex and time consuming and there can be no assurance that we will reach agreement with a strategic partner with respect to any of these programs in the near future or at all.

We have several other oncology programs, including our sheddase inhibitor, INCB7839, that is under development as a treatment for breast cancer. We have two earlier stage oncology programs involving an oral c-MET inhibitor, INCB28060, and an indoleamine dioxygenase, or IDO, inhibitor, INCB24360. We do not intend to initiate clinical trials for either of these programs until we have either secured additional capital or found a strategic partner for these programs.

We have several other clinical programs that target either large primary care indications or require lengthy and expensive clinical development programs. These include: our 11ßHSD1 inhibitors, INCB13739 and INCB20817, for which we have shown positive results for the lead compound in a three-month Phase IIb trial in patients with type 2 diabetes; our HM74a agonist, INCB19602, also for type 2 diabetes; and our CCR5 receptor antagonists, INCB9471 and INCB15050, for HIV. Because these therapeutic areas require greater financial and commercial resources than we currently possess, we are seeking strategic relationships or collaborative partners for these programs.

Our productivity in drug discovery and development is primarily a result of our core competency in medicinal chemistry which is tightly integrated with and supported by an experienced team of biologists with expertise in multiple therapeutic areas. As a number of our compounds have progressed into clinical development, we have also built a clinical development and regulatory team. This team utilizes clinical research organizations, expert scientific advisory boards, and leading consultants and suppliers in relevant drug development areas in an effort to conduct our clinical trials as efficiently and effectively as possible while maintaining strategic control of the design and management of our programs.

Our highest priority programs include the following:

JAK Program for Myeloproliferative Disorders, Other Hematologic Malignancies and Cancers, and Inflammation

The JAK family is composed of four tyrosine kinases JAK1, JAK2, JAK3 and Tyk2 that are involved in signaling triggered by a number of cytokines and growth factors. JAKs are central to a number of biologic processes, including the formation and development of blood cells and the regulation of immune functions. Excessive signaling through the JAK pathways is believed to play a critical role in a number of disease states, including myeloproliferative disorders and other malignancies and cancers, and inflammatory conditions such as rheumatoid arthritis and psoriasis.

We have discovered multiple potent, selective and orally bioavailable JAK inhibitors that are selective for JAK1 and JAK2 from several distinct chemical scaffolds. Our lead JAK inhibitor, INCB18424, is currently being developed as an oral treatment for myelofibrosis, polycythemia vera and essential thrombocythemia, and as a topical treatment for psoriasis.

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Myelofibrosis. Our Phase II trial for myelofibrosis with INCB18424 includes data from over 150 myelofibrosis patients. In this trial, INCB18424 provided marked and durable reductions in splenomegaly, a condition that affects the majority of myelofibrosis patients. Patients in this trial treated with INCB18424 also showed clinically meaningful improvements in the symptoms of myelofibrosis including reductions in fatigue, night sweats, pruritus, abdominal discomfort, poor appetite and cachexia.

In July 2009, we obtained a Special Protocol Assessment from the U.S. Food and Drug Administration, or FDA, for the Phase III registration trial for INCB18424 for myelofibrosis. This Phase III trial is a double-blind, placebo-controlled trial, and is expected to include over 90 clinical sites in the United States, Canada and Australia and 240 patients with primary myelofibrosis, or PMF, post-polycythemia vera myelofibrosis, or PPV-MF, and post-essential thrombocythemia myelofibrosis, or PET-MF. We began screening and enrolling patients for this Phase III trial in September 2009.

The primary endpoint in this Phase III trial is the proportion of patients achieving at least 35% reduction in spleen volume, as measured by magnetic resonance imaging, or MRI, at 24 weeks. In the ongoing Phase II trial, in which we measured palpable spleen length, INCB18424 reduced palpable spleen length in the majority of patients, with over 50% of these treated patients receiving 15 mg and 25 mg twice-daily doses achieving at least a 50% reduction in palpable spleen length. In our Phase II trial we also measured spleen volume by MRI in a subset of patients, and established that half of these patients treated with INCB18424 achieved at least a 33% reduction in spleen volume compared to baseline after six months.

We began enrolling patients for a Phase III trial in Europe in June 2009. This trial is designed based on scientific advice from the European Medicines Agency, or EMEA, and is expected to include 150 patients with PMF, PPV-MF or PET-MF and involve approximately 70 clinical sites in 10 countries. The trial is an open-label study designed to evaluate the efficacy, safety and tolerability of INCB18424 as compared to the best-available therapy. The primary efficacy endpoint in the European Phase III trial is the proportion of patients achieving at least 35% reduction in spleen volume from baseline at 48 weeks.

We have received orphan drug status from the FDA for INCB18424 as a treatment for myelofibrosis and orphan medicinal product designation from the EMEA for INCB18424 for the treatment of chronic idiopathic myelofibrosis. In February 2009, the Committee for Orphan Medicinal Products of the EMEA informed us that it had adopted a positive opinion regarding our request for orphan medicinal product designation of INCB18424 for the treatment of PPV-MF and PET-MF.

Polycythemia Vera and Essential Thrombocythemia. We began a dose-ranging Phase II trial in advanced polycythemia vera and essential thrombocythemia to evaluate INCB18424 in these patients in 2008. This Phase II trial involves approximately 70 patients at six clinical sites in the United States and Europe. Results from this trial are expected later in 2009.

Rheumatoid Arthritis. In October 2008, we announced results from a 28-day Phase IIa dose-ranging trial using the oral formulation of INCB18424 in 50 rheumatoid arthritis patients whose conditions were not well-controlled with their existing therapy. In the 50-patient placebo-controlled trial three of the four doses of INCB18424 evaluated produced significant clinical benefits and all of the doses were well tolerated.

We also have a second JAK inhibitor, INCB28050, that has completed Phase I development. Based on both pre-clinical and clinical results to date, it appears INCB28050 may be as efficacious as INCB18424 and may offer some potential dosing advantages. Given the challenging economic environment and our objective to reduce spending in 2009, together with our desire to have a separate compound for inflammation, we have discontinued development of INCB18424 in

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rheumatoid arthritis and we intend to move INCB28050 forward as our lead oral anti-inflammatory compound. We recently initiated a six-month double-blind placebo-controlled dose-ranging Phase II trial that is scheduled to include 100 patients with active rheumatoid arthritis who have had inadequate response to currently available disease modifying therapies. Three-month results for efficacy and safety from this study are expected in the first half of 2010.

Psoriasis. In September 2008, we announced results from a completed 28-day Phase IIa dose-escalation trial with topical INCB18424, involving 28 patients with mild-to-moderate psoriasis and preliminary results from an ongoing 28-day sub-total inunction trial. In these trials topical INCB18424 in mild-to-moderate psoriasis patients was well tolerated at all doses tested thus far and significantly improved overall total lesion score (thickness, erythema, and scaling). In addition to the safety and efficacy results, transcriptional profiling data from the sub-total inunction trial indicated that topical INCB18424 inhibits two key pathways, Th1 and Th17, which play important roles in the pathogenesis of psoriasis. We recently completed a three-month multiple-dose Phase IIb trial involving approximately 200 psoriasis patients with mild-to-moderate disease, in which treatment with INCB18424 met the primary and secondary endpoints and was well tolerated at all doses. We intend to present full results from this Phase IIb trial at an appropriate future scientific meeting in 2010.

11ßHSD1 Program for Type 2 Diabetes and Related Disorders

We have developed a broad chemically diverse series of novel proprietary oral inhibitors of 11ßHSD1, an enzyme that converts the biologically-inactive steroid cortisone into the potent biologically-active hormone cortisol. Cortisol acts as a functional antagonist of insulin action in multiple tissue types, including the liver, adipose, skeletal muscle, and pancreas. Inhibition of 11ßHSD1 offers the potential to reduce insulin resistance and restore glycemic control in type 2 diabetes, and may also offer potential benefits in allied conditions such as dyslipidemia, atherosclerosis, and coronary heart disease.

In June 2009, we presented clinical results at the American Diabetes Association 69th Scientific Sessions from a three month placebo-controlled, dose-ranging Phase IIb trial involving approximately 300 patients with type 2 diabetes which demonstrated that treatment with once-daily doses of INCB13739 significantly improved glycemic control, as measured by hemoglobin A1c, insulin sensitivity and total-cholesterol levels.

Sheddase Inhibitor Program for Solid Tumors

As the fundamental biology of cancer has been explored at the molecular level, new therapeutics are emerging that distinguish themselves from the classic, relatively non-selective, cytotoxic agents. These new therapeutics are targeted specifically to pathways or proteins that are more critical for the growth of tumor cells than for the growth of normal cells, thereby having the potential to provide a greater therapeutic benefit, both when used alone and in combination with cytotoxic agents. Currently available therapeutics of this type have been shown to be effective in the treatment of certain important tumor types.

The signaling pathways that utilize the receptors and ligands of the epidermal growth factor receptor, or EGFR, family play a key role in the growth and survival of multiple tumor types, including breast, colorectal, and non-small cell lung cancers. The EGFR, or HER, signaling pathways consist of four known cellular receptors: HER1 (also known as EGFR), HER2, HER3, and HER4. Under normal conditions, these pathways are tightly regulated. However, in cancer, the pathways can become dysregulated and changes in the amount or the activity of HER family members, primarily HER1, HER2 and HER3, have been shown to impact the growth, proliferation,

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migration, and survival of cancer cells. Sheddase is an enzyme that is believed to activate all four EGFR pathways.

Currently approved therapies target one or more of the EGFR pathways. However, these existing therapies may not block all EGFR family-mediated signaling, even in the tumor types in which they are approved. In contrast, we believe our sheddase inhibitor targets all four EGFR signaling pathways and may provide meaningful advantages over therapies that target one or two.

We have identified novel, potent, and orally available small-molecule inhibitors of sheddase that, in preclinical models, show efficacy as single agents and show synergy with other targeted therapeutic agents and with cytotoxics. INCB7839, the lead compound from this program, is currently in a Phase II clinical trial designed to determine the effectiveness of INCB7839 when used in combination with Herceptin. Results from this trial are expected later in 2009.

c-MET for Solid Tumors

c-MET is a clinically validated receptor kinase cancer target and abnormal c-MET activation in cancer correlates with poor prognosis. Dysregulation of the c-MET pathway triggers tumor growth, formation of new blood vessels that supply the tumor with nutrients, and causes cancer to spread to other organs. Dysregulation of the c-MET pathway is seen in many types of cancers including kidney, liver, stomach, breast, and brain.

Several small molecule c-MET kinase inhibitors have demonstrated clinical efficacy in a number of cancers; however, these molecules have limited potency and are relatively non-selective, which could lead to off-target toxicities. We believe our lead c-MET inhibitor, INCB28060, has the requisite properties to overcome these limitations, including greater selectivity, improved potency and more effective inhibition of c-MET. We do not expect to initiate clinical trials for this program unless we are successful in securing additional funding or identify a strategic partner for this program.

IDO for Solid Tumors

The enzyme, indoleamine 2, 3-dioxygenase, IDO, is a key regulator of the mechanisms that are responsible for allowing tumors to escape from a patient's immune surveillance. IDO expression by tumor cells, or by antigen presenting cells such as macrophages and dendritic cells in tumors, creates an environment in which tumor specific cytotoxic T lymphocytes are rendered functionally inactive or are no longer able to attack a patient's cancer cells. By inhibiting IDO, it is proposed that this "brake" on the anti-tumor immune response is removed, allowing anti-tumor specific cytotoxic T cells, generated in a patient spontaneously in response to the tumor, or through a therapy designed to stimulate the immune response, to have greater anti-tumor efficacy.

We believe our compound, INCB24360, represents a novel, potent, and selective inhibitor of the enzyme IDO. It is efficacious in multiple mouse models of cancer and has been well-tolerated in preclinical safety studies. We do not expect to initiate clinical trials for this program unless we are successful in securing additional funding.

Corporate Information

We were incorporated in Delaware in 1991. Our principal executive offices are located at Experimental Station, Route 141 & Henry Clay Road, Building E336, Wilmington, DE 19880. Our telephone number at this location is (302) 498-6700. Our website is *www.incyte.com*. Information on our website is not a part of this prospectus supplement or the accompanying prospectus.

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The Offering

Common stock offered by us	18,000,000 shares
Common stock to be outstanding after the offering	115,785,047 shares
Use of proceeds	For general corporate purposes, including research and development activities. See "Use of Proceeds."
Risk factors	You should read the "Risk Factors" section of this prospectus supplement for a discussion of factors to consider before deciding to purchase shares of our common stock.
NASDAQ Global Market symbol	INCY

Information in the table above is based on 97,785,047 shares outstanding as of June 30, 2009. It does not include the following shares of our common stock as of June 30, 2009:

17,977,610 shares issuable upon the exercise of stock options outstanding with a weighted average exercise price of $7.72 per share;

3,595,333 shares reserved for issuance and available for future grant or sale under our stock plans;

1,250,537 shares reserved for issuance under our employee stock purchase plan;

13,531,224 shares issuable upon conversion of our 3 1/2% convertible senior notes due 2011;

22,284,625 shares issuable upon conversion of our 3 1/2% convertible subordinated notes due 2011;

1,461,496 shares issuable upon conversion of our convertible subordinated note due 2013 issued to Pfizer Inc.; and

1,025,641 shares issuable upon conversion of our convertible subordinated note due 2014 issued to Pfizer Inc.

Unless otherwise indicated, all information in this prospectus supplement assumes no exercise of the underwriters' option to purchase up to an additional 2,700,000 shares of common stock.

Concurrently with this offering, we are offering $350,000,000 principal amount of our 4.75% Convertible Senior Notes due 2015 (or a total of $400,000,000 principal amount if the initial purchasers in that offering exercise in full their option to purchase additional notes) in a separate private offering to qualified institutional buyers. The information above does not include shares of common stock, or shares of preferred stock in lieu of common stock, issuable upon conversion of our 4.75% Convertible Senior Notes due 2015 to be issued in the convertible notes offering. This offering is not contingent upon the completion of the convertible notes offering, and the convertible notes offering is not contingent upon the completion of this offering. The 4.75% Convertible Senior Notes due 2015 and the common stock, or shares of preferred stock in lieu of common stock, issuable upon conversion of the 4.75% Convertible Senior Notes due 2015 have not been and will not be registered under the Securities Act of 1933 and may not be offered or sold in the United States absent registration or an applicable exemption from registration. For more information about the preferred stock that may be issued in lieu of common stock upon conversion of the notes, see "Description of Capital Stock Series A Preferred Stock."

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RISK FACTORS

Investing in our common stock involves a high degree of risk. You should carefully consider the risk factors described below and the other information contained in or incorporated by reference into this prospectus supplement and the accompanying prospectus before deciding to invest in our common stock. The risks and uncertainties described below are not the only ones we face. Additional risks and uncertainties not presently known to us or that we currently deem immaterial may also impair our business operations. If any of the following risks actually occur, our business, financial condition and results of operations could be materially and adversely affected.

Risks Relating to our Business

We are at the early stage of our drug discovery and development efforts and we may be unsuccessful in our efforts.

We are in the early stage of building our drug discovery and development operations. Our ability to discover, develop and commercialize pharmaceutical products will depend on our ability to:

- hire and retain key scientific employees;
- identify high quality therapeutic targets;
- identify potential drug candidates;
- develop products internally or license drug candidates from others;
- identify and enroll suitable human subjects, either in the United States or abroad, for our clinical trials;
- complete laboratory testing and clinical trials on humans;
- obtain and maintain necessary intellectual property rights to our products;
- obtain and maintain necessary regulatory approvals for our products, both in the United States and abroad;
- enter into arrangements with third parties to provide services or to manufacture our products on our behalf;
- deploy sales and marketing resources effectively or enter into arrangements with third parties to provide these functions;
- lease facilities at reasonable rates to support our growth; and
- enter into arrangements with third parties to license and commercialize our products.

We have limited experience with the activities listed above and may not be successful in discovering, developing, or commercializing drug products.

Our efforts to discover and develop potential drug candidates may not lead to the discovery, development, commercialization or marketing of drug products.

All but one of our drug candidates in clinical trials are in Phase I and Phase II trials. Our other drug candidates are still undergoing preclinical testing. Discovery and development of potential drug candidates are expensive and time-consuming, and we do not know if our efforts will lead to discovery of any drug candidates that can be successfully developed and marketed. If our efforts do not lead to the discovery of a suitable drug candidate, we may be unable to grow our clinical pipeline or we may be unable to enter into agreements with collaborators who are willing to develop our drug candidates. Of the compounds that we identify as potential drug products or that

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we in-license from other companies, only a few, if any, are likely to lead to successful drug development programs. For example, in 2006, we discontinued the development of DFC, which was at the time our most advanced drug candidate and was in Phase IIb clinical trials. Prior to discontinuation of the DFC program, we expended a significant amount of effort and money on that program. We have also licensed to Pfizer our portfolio of CCR2 antagonist compounds. We have no control over the further clinical development of any compounds we licensed to Pfizer.

The success of our drug discovery and development efforts may depend on our ability to find suitable collaborators to fully exploit our capabilities. If we are unable to establish collaborations or if these future collaborations are unsuccessful, our research and development efforts may be unsuccessful, which could adversely affect our results of operations and financial condition.

An important element of our business strategy is to enter into collaborative or license arrangements with other parties, such as our collaboration with Pfizer, under which we license our drug candidates to those parties for development and commercialization. We are evaluating strategic relationships with respect to several of our programs and may enter into an agreement with respect to one or more of these programs in the near future. However, these arrangements and negotiations are complex and time consuming and there can be no assurance that we will reach agreement with a strategic partner with respect to any of these programs in the near future or at all.

Although we may conduct initial clinical trials on our drug candidates, we may need to seek collaborators for our drug candidates such as our 11ßHSD1 inhibitors because of the expense, effort and expertise required to continue additional clinical trials and further develop those drug candidates. We are seeking collaborators for our drug candidates that target large primary care indications such as diabetes because of the expense involved in further clinical development of these indications and in establishing a sales and marketing organization to address these indications. We are also currently evaluating strategic relationships for INCB18424 for myeloproliferative disorders and other oncology indications for markets outside the United States. Because collaboration arrangements are complex to negotiate, we may not be successful in our attempts to establish these arrangements. Also, we may not have drug compounds that are desirable to other parties, or we may be unwilling to license a drug compound because the party interested in it is a competitor. The terms of any such arrangements that we establish may not be favorable to us. Alternatively, potential collaborators may decide against entering into an agreement with us because of our financial, regulatory or intellectual property position or for scientific, commercial or other reasons. If we are not able to establish collaborative agreements, we may not be able to develop and commercialize a drug product, which would adversely affect our business and our revenues.

In order for any of these collaboration or license arrangements to be successful, we must first identify potential collaborators or licensees whose capabilities complement and integrate well with ours. We may rely on these arrangements for not only financial resources, but also for expertise or economies of scale that we expect to need in the future relating to clinical trials, manufacturing, sales and marketing, and for licenses to technology rights. However, it is likely that we will not be able to control the amount and timing of resources that our collaborators or licensees devote to our programs or potential products. If our collaborators or licensees prove difficult to work with, are less skilled than we originally expected, do not devote adequate resources to the program, or do not agree with our approach to development or manufacturing of the potential product, the relationship will not be successful. If a business combination involving a collaborator or licensees and a third party were to occur, the effect could be to diminish, terminate or cause delays in development of a potential product.

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Although we obtained a special protocol assessment for our JAK inhibitor for myelofibrosis, a special protocol assessment does not guarantee any particular outcome from regulatory review, including any regulatory approval.

We have obtained a special protocol assessment, or SPA, for the registration trial for our JAK inhibitor for the treatment of myelofibrosis in the United States. The SPA process allows for Food and Drug Administration, or FDA, evaluation of a clinical trial protocol intended to form the primary basis of an efficacy claim in support of a new drug application, or NDA, and provides a product sponsor with an agreement confirming that the design and size of the trial will be appropriate to form the primary basis of an efficacy claim for an NDA if the trial is performed according to the SPA. An SPA is not a guarantee of approval, and we cannot be certain that the design of, or data collected from, the trial will be adequate to demonstrate safety and efficacy, or otherwise be sufficient to support regulatory approval. There can be no assurance that the terms of an SPA will ultimately be binding on the FDA, and the FDA is not obligated to approve an NDA, if any, even if the clinical outcome is positive. The FDA retains significant latitude and discretion in interpreting the terms of an SPA and the data and results from a clinical trial, and can require trial design changes if issues arise essential to determining safety or efficacy. In addition, data may subsequently become available that causes the FDA to reconsider the previously agreed upon scope of review and the FDA may have subsequent safety or efficacy concerns that override an SPA, and we can give no assurance that as clinical trials proceed or as part of an NDA review process, if any, the FDA will determine that a previously approved SPA is still valid.

Additionally, an SPA may be changed only with written agreement of the FDA, and any further changes we may propose to the protocol will remain subject to the FDA's approval. The FDA may not agree to any such amendment and, even if they agree, they may request other amendments to the trial design that could require additional cost and time, as well as increase the degree of difficulty in reaching clinical endpoints. As a result, even with an SPA, we cannot be certain that the trial results will be found to be adequate to support an efficacy claim and product approval.

We depend heavily on the success of our most advanced product candidates. We might not be able to commercialize any of our drug candidates successfully, and we may spend significant time and money attempting to do so.

We have invested significant resources in the development of our most advanced product candidates. We have one drug candidate, INCB18424, in Phase III clinical trials. We have a number of drug candidates in Phase I and Phase II clinical trials. Our ability to generate product revenues will depend on the successful development and eventual commercialization of our most advanced product candidates. We have also licensed to Pfizer our portfolio of CCR2 antagonist compounds. We, or our collaborators or licensees, may decide to discontinue development of any or all of our drug candidates at any time for commercial, scientific or other reasons. We discontinued development of DFC in April 2006 for safety reasons. In March 2008, we announced that we would not advance our lead CCR5 antagonist into Phase IIb trials and that we are seeking to out-license this program. If a product is developed, but is not marketed, we may have spent significant amounts of time and money on it, which would adversely affect our operating results and financial condition. Even if a drug candidate that we develop receives regulatory approval, we may decide not to commercialize it if we determine that commercialization of that product would require more money and time than we are willing to invest. For example, drugs that receive approval are subject to post-regulatory surveillance and may have to be withdrawn from the market if previously unknown side effects occur. At this point, the regulatory agencies may require additional clinical trials or testing. Once a drug is marketed, if it causes side effects, the drug product may be recalled or may be subject to reformulation, additional studies, changes in labeling, warnings to the public and negative publicity. As a result, we may not continue to commercialize a product even though it has obtained regulatory approval. Further, we may decide not to continue to

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commercialize a product if the market does not accept the product because it is too expensive or because third parties such as insurance companies or Medicare have not approved it for substantial reimbursement. In addition, we may decide not to continue to commercialize a product if another product comes on the market that is as effective but has fewer side effects. There is also a risk that competitors may develop similar or superior products or have proprietary rights that preclude us from ultimately marketing our products.

Any drug products that we bring to the market, even if they receive marketing approval, may not gain market acceptance by physicians, patients, healthcare payors and others in the medical community.

Even if we are successful in gaining regulatory approval of our products, we may not generate significant product revenues and we may not become profitable if these drug products do not achieve an adequate level of acceptance. Physicians will not recommend our drug products until clinical data or other factors demonstrate the safety and efficacy of our drug products as compared to other alternative treatments. Even if the clinical safety and efficacy of our drug products is established, physicians may elect not to prescribe these drug products for a variety of reasons including the reimbursement policies of government and other third-party payors and the effectiveness of our competitors in marketing their products.

Market acceptance of our drug products, if approved for commercial sale, will depend on a number of factors, including:

- the willingness and ability of patients and the healthcare community to use our products;
- the ability to manufacture our drug products in sufficient quantities with acceptable quality and to offer our drug products for sale at competitive prices;
- the perception of patients and the healthcare community, including third-party payors, regarding the safety, efficacy and benefits of our drug products compared to those of competing products or therapies;
- the label and promotional claims allowed by the FDA;
- the pricing and reimbursement of our drug products relative to existing treatments; and
- marketing and distribution support for our drug products.

If conflicts arise between our collaborators, including Pfizer, licensees, or advisors and us, our collaborators, licensees, or advisors may act in their self-interest, which may adversely affect our business.

If conflicts arise between us and our collaborators or licensees, including Pfizer, or our scientific advisors, the other party may act in its self-interest and not in the interest of our stockholders. Conflicts may arise with our collaborators or licensees if they pursue alternative technologies or develop alternative products either on their own or in collaboration with others as a means for developing treatments for the diseases that we have targeted. Competing products, either developed by these future collaborators or licensees or to which these future collaborators or licensees have rights, may result in their withdrawal of support for our product candidates.

Additionally, conflicts may arise if there is a dispute about the achievement and payment of a milestone amount or the ownership of intellectual property that is developed during the course of the relationship. Similarly, the parties to a collaboration or license agreement may disagree as to which party owns newly developed products. Should an agreement be terminated as a result of a dispute and before we have realized the benefits of the collaboration or license, our reputation could be harmed and we may not obtain revenues that we anticipated receiving.

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We have limited expertise with and capacity to conduct preclinical testing and clinical trials, and our resulting dependence on other parties could result in delays in and additional costs for our drug development efforts.

We have only limited experience with clinical trials, formulation, manufacturing and commercialization of drug products. We also have limited internal resources and capacity to perform preclinical testing and clinical trials. As a result, we intend to continue to hire clinical research organizations, or CROs, to perform preclinical testing and clinical trials for drug candidates. If the CROs that we hire to perform our preclinical testing and clinical trials or our collaborators or licensees do not meet deadlines, do not follow proper procedures, or a conflict arises between us and our CROs, our preclinical testing and clinical trials may take longer than expected, may be delayed or may be terminated. If we were forced to find a replacement entity to perform any of our preclinical testing or clinical trials, we may not be able to find a suitable entity on favorable terms, or at all. Even if we were able to find another company to perform a preclinical test or clinical trial, the delay in the test or trial may result in significant additional expenditures. Events such as these may result in delays in our obtaining regulatory approval for our drug candidates or our ability to commercialize our products and could result in increased expenditures that would adversely affect our operating results.

In addition, for some of our drug candidates, we plan to contract with collaborators or licensees to advance those candidates through later-stage, more expensive clinical trials, rather than invest our own resources to perform these clinical trials. Depending on the terms of our agreements with these collaborators or licensees, we may not have any control over the conduct of these clinical trials, and in any event we would be subject to the risks associated with depending on collaborators or licensees to develop these drug candidates.

If we are unable to obtain regulatory approval to develop and market products in the United States and foreign jurisdictions, we will not be permitted to manufacture or commercialize products resulting from our research.

In order to manufacture and commercialize drug products in the United States, our drug candidates will have to obtain regulatory approval from the FDA. Satisfaction of regulatory requirements typically takes many years. To obtain regulatory approval, we must first show that our drug products are safe and effective for target indications through preclinical testing (animal testing) and clinical trials (human testing). Preclinical testing and clinical development are long, expensive and uncertain processes, and we do not know whether the FDA will allow us to undertake clinical trials of any potential drug products in addition to our compounds currently in clinical trials.

Completion of clinical trials may take several years and failure may occur at any stage of testing. The length of time required varies substantially according to the type, complexity, novelty and intended use of the product candidate. Interim results of a preclinical test or clinical trial do not necessarily predict final results, and acceptable results in early clinical trials may not be repeated in later clinical trials. For example, a drug candidate that is successful at the preclinical level may cause harmful or dangerous side effects when tested at the clinical level. Our rate of commencement and completion of clinical trials may be delayed by many factors, including:

- the high degree of risk associated with drug development;
- our inability to formulate or manufacture sufficient quantities of materials for use in clinical trials;
- variability in the number and types of patients available for each study;
- difficulty in maintaining contact with patients after treatment, resulting in incomplete data;
- unforeseen safety issues or side effects;

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poor or unanticipated effectiveness of drug candidates during the clinical trials; or

government or regulatory delays.

Data obtained from clinical trials are susceptible to varying interpretation, which may delay, limit or prevent regulatory approval. A number of companies in the pharmaceutical industry, including biotechnology companies, have suffered significant setbacks in advanced clinical trials, even after achieving promising results in earlier clinical trials. In addition, regulatory authorities may refuse or delay approval as a result of other factors, such as changes in regulatory policy during the period of product development and regulatory agency review. For example, the FDA has in the past required and could in the future require that we conduct additional trials of any of our product candidates, which would result in delays.

Due, in part, to the early stage of our drug candidate research and development process, we cannot predict whether regulatory approval will be obtained for any product we develop. All but one of our drug candidates in clinical trials are in Phase I and Phase II trials. Our other drug candidates are still undergoing preclinical testing. We have also licensed to Pfizer our portfolio of CCR2 antagonist compounds. We have no control over the further clinical development of any compounds we licensed to Pfizer. Compounds developed by us, alone or with other parties, may not prove to be safe and effective in clinical trials and may not meet all of the applicable regulatory requirements needed to receive marketing approval. If regulatory approval of a product is granted, this approval will be limited to those disease states and conditions for which the product is demonstrated through clinical trials to be safe and effective. Failure to obtain regulatory approval would delay or prevent us from commercializing products.

Outside the United States, our ability to market a product is contingent upon receiving a marketing authorization from the appropriate regulatory authorities. This foreign regulatory approval process typically includes all of the risks associated with the FDA approval process described above and may also include additional risks. The requirements governing the conduct of clinical trials, product licensing, pricing and reimbursement vary greatly from country to country and may require us to perform additional testing and expend additional resources. Approval by the FDA does not ensure approval by regulatory authorities in other countries, and approval by one foreign regulatory authority does not ensure approval by regulatory authorities in other countries or by the FDA.

We face significant competition for our drug discovery and development efforts, and if we do not compete effectively, our commercial opportunities will be reduced or eliminated.

The biotechnology and pharmaceutical industries are intensely competitive and subject to rapid and significant technological change. Our drug discovery and development efforts may target diseases and conditions that are already subject to existing therapies or that are being developed by our competitors, many of which have substantially greater resources, larger research and development staffs and facilities, more experience in completing preclinical testing and clinical trials, and formulation, marketing and manufacturing capabilities. As a result of these resources, our competitors may develop drug products that render our products obsolete or noncompetitive by developing more effective drugs or by developing their products more efficiently. Our ability to develop competitive products would be limited if our competitors succeeded in obtaining regulatory approvals for drug candidates more rapidly than we were able to or in obtaining patent protection or other intellectual property rights that limited our drug development efforts. Any drugs resulting from our research and development efforts, or from our joint efforts with collaborators or licensees, might not be able to compete successfully with our competitors' existing and future products, or obtain regulatory approval in the United States or elsewhere.

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Our reliance on other parties to manufacture our drug candidates could result in a short supply of the drugs, delays in clinical trials or drug development, increased costs, and withdrawal or denial of a regulatory authority's approval.

We do not currently operate manufacturing facilities for clinical or commercial production of our drug candidates. We currently rely on third parties for the manufacture of both the active pharmaceutical ingredient, or API, and finished drug product of our drug candidates for clinical trials. In addition, we expect to continue to rely on third parties for the manufacture of commercial supplies of API and finished drug product for any drugs that we successfully develop. For most of our drug candidates, including our lead drug candidate INCB18424, we rely on one third party to manufacture the API, another to make finished drug product and a third to package and label the finished product. The FDA requires that the API and finished product for each of our drug products be manufactured according to its current Good Manufacturing Practices, or cGMP, regulations and regulatory authorities in other countries have similar requirements. There are only a limited number of manufacturers that comply with these requirements. If the third parties that manufacture our drug candidates are not compliant with the applicable regulatory requirements, the FDA or a foreign regulatory authority may require us to halt ongoing clinical trials or not approve our application to market our drug products. Failure to comply with cGMP and the applicable regulatory requirements of other countries in the manufacture of our products could result in the FDA or foreign regulatory authority halting our clinical trials, withdrawing or denying regulatory approval of our drug product, enforcing product recalls or other enforcement actions, which could have a material adverse effect on our business.

We may not be able to obtain sufficient quantities of our drug candidates or any drug products we may develop if our designated manufacturers do not have the capacity or capability to manufacture our products according to our schedule and specifications. In addition, we may not be able to arrange for our drug candidates or any drug products that we may develop to be manufactured by one of these parties on reasonable terms, if at all. Also, raw materials that may be required to manufacture any products we develop may only be available from a limited number of suppliers. Generally, we have only a single source that is qualified to supply the API and finished product of our drug candidates. If any of these single source suppliers were to become unable or unwilling to supply us with API or finished product that complies with applicable regulatory requirements, we could incur significant delays in our clinical trials or interruption of commercial supply which could have a material adverse effect on our business. We are currently seeking to qualify a second source of supply for certain of our drug candidates, including a second source of supply for the API for INCB18424, however, there is no assurance that we will be able to identify and qualify a second source of supply for any of our drug candidates or drug products on a timely basis. If we have promised delivery of a new product and are unable to meet the delivery requirement due to manufacturing difficulties, our development programs would be delayed, and we may have to expend additional sums in order to ensure that manufacturing capacity is available when we need it even if we do not use all of the manufacturing capacity. This expense would adversely affect our operating results.

Manufacturers of pharmaceutical products often encounter difficulties in production, especially in scaling up initial production. These problems include difficulties with production costs and yields, quality control and assurance and shortages of qualified personnel, as well as compliance with strictly enforced federal, state and foreign regulations.

In order to obtain approval of our products, including INCB18424, by the FDA and foreign regulatory agencies, we need to complete testing on both the API and on the finished product in the packaging we propose for commercial sales. This includes testing of stability, identification of impurities and testing of other product specifications by validated test methods. In addition, we will be required to consistently produce the API in commercial quantities and of specified quality on a

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repeated basis and document our ability to do so. This requirement is referred to as process validation. With respect to INCB18424, although we have manufactured the product at commercial scale, we have started, but not yet completed, this process validation requirement. If the required testing or process validation is delayed or produces unfavorable results, we may not obtain approval to launch the product or product launch may be delayed.

We may not be able to adequately manage and oversee the manufacturers we choose, they may not perform as agreed or they may terminate their agreements with us. Foreign manufacturing approval processes typically include all of the risks associated with the FDA approval process for manufacturing and may also include additional risks.

We may incur additional expense in order to market our drug products.

We do not have experience marketing drug products. If the FDA grants regulatory approval to one or more of our drug candidates, we would have to employ additional personnel or engage another party to market our drug products, which would be an additional expense to us.

We depend on our collaboration with Pfizer for the development and commercialization of CCR2 antagonist compounds.

Under our collaborative research and license agreement with Pfizer, Pfizer gained worldwide development and commercialization rights to our portfolio of CCR2 antagonist compounds. Pfizer's rights extend to the full scope of potential indications, with the exception of multiple sclerosis and autoimmune nephritides.

Although Pfizer is required to use commercially reasonable efforts to develop and commercialize CCR2 antagonists for the indications for which they are responsible, we cannot control the amount and timing of resources Pfizer may devote to the development of CCR2 antagonists. Any failure of Pfizer to perform its obligations under our agreement could negatively impact the development of CCR2 antagonists, lead to our loss of potential revenues from product sales and milestones and delay our achievement, if any, of profitability.

Pfizer has certain rights to terminate the license agreement, including the right to terminate upon 90 days' notice for any reason. Pfizer also has the right to terminate its rights and obligations with respect to certain indications and licensed compounds. If Pfizer terminates the license agreement or its rights with respect to certain indications, we may not be able to find a new collaborator to replace Pfizer, and our business could be adversely affected.

If we fail to enter into additional licensing agreements or if these arrangements are unsuccessful, our business and operations might be adversely affected.

In addition to establishing collaborative or license arrangements under which other parties license our drug candidates for development and commercialization, we may also need to license drug delivery or other technology in order to continue to develop our drug candidate pipeline. If we are unable to enter into additional agreements to license drug delivery technology or other technology or if these arrangements are unsuccessful, our research and development efforts could be adversely affected.

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Our ability to generate revenues will be diminished if we are unable to obtain acceptable prices or an adequate level of reimbursement from payors of healthcare costs.

The continuing efforts of government and insurance companies, health maintenance organizations, or HMOs, and other payors of healthcare costs to contain or reduce costs of health care may affect our future revenues and profitability, and the future revenues and profitability of our potential customers, suppliers and collaborative or license partners and the availability of capital. For example, in certain foreign markets, pricing or profitability of prescription pharmaceuticals is subject to government control. In the United States, given recent federal and state government initiatives directed at lowering the total cost of health care, the U.S. Congress and state legislatures will likely continue to focus on health care reform, the cost of prescription pharmaceuticals and on the reform of the Medicare and Medicaid systems. While we cannot predict whether any such legislative or regulatory proposals will be adopted, the announcement or adoption of these proposals could reduce the price that we or any of our collaborators or licensees receive for any products in the future.

Our ability to commercialize our products successfully will depend in part on the extent to which appropriate reimbursement levels for the cost of our products and related treatment are obtained by governmental authorities, private health insurers and other organizations, such as HMOs. Third-party payors are increasingly challenging the prices charged for medical products and services. Also, the trend toward managed health care in the United States and the concurrent growth of organizations such as HMOs, which could control or significantly influence the purchase of health care services and products, as well as legislative proposals to reform health care or reduce government insurance programs, may all result in lower prices for or rejection of our products. The cost containment measures that health care payors and providers are instituting and the effect of any health care reform could materially and adversely affect our ability to generate revenues.

As our drug discovery and development operations are conducted at our headquarters in Wilmington, Delaware, the loss of access to this facility would negatively impact our business.

Our facility in Wilmington, Delaware is our headquarters and is also where we conduct all of our drug discovery operations and research and development activities. Our lease contains provisions that provide for its early termination upon the occurrence of certain events of default or upon a change of control. Further, our headquarters facility is located in a large research and development complex that may be temporarily or permanently shutdown if certain environmental or other hazardous conditions were to occur within the complex. In addition, actions of activists opposed to aspects of pharmaceutical research may disrupt our experiments or our ability to access or use our facilities. The loss of access to or use of our Wilmington, Delaware, facility, either on a temporary or permanent basis, or early termination of our lease would result in an interruption of our business and, consequently, would adversely affect the advancement of our drug discovery and development programs and our overall business.

We depend on key employees in a competitive market for skilled personnel, and the loss of the services of any of our key employees or our inability to attract and retain additional personnel would affect our ability to expand our drug discovery and development programs and achieve our objectives.

We are highly dependent on the principal members of our management, operations and scientific staff. We experience intense competition for qualified personnel. Our future success also depends in part on the continued service of our executive management team, key scientific and management personnel and our ability to recruit, train and retain essential scientific personnel for our drug discovery and development programs, including those who will be responsible for

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overseeing our preclinical testing and clinical trials as well as for the establishment of collaborations with other companies. If we lose the services of any of these people or if we are unable to recruit sufficient qualified personnel, our research and product development goals, including the identification and establishment of key collaborations, operations and marketing efforts could be delayed or curtailed. We do not maintain "key person" insurance on any of our employees.

If we fail to manage our growth effectively, our ability to develop and commercialize products could suffer.

We expect that if our clinical drug candidates continue to progress in development, we continue to build our development organization and our drug discovery efforts continue to generate drug candidates, we will require significant additional investment in personnel, management and resources. Our ability to commercialize our drug candidates and to achieve our research and development objectives depends on our ability to respond effectively to these demands and expand our internal organization, systems and controls to accommodate additional anticipated growth. If we are unable to manage our growth effectively, our business could be harmed and our ability to execute our business strategy could suffer.

If product liability lawsuits are brought against us, we could face substantial liabilities and may be required to limit commercialization of our products and our results of operations could be harmed.

The clinical trials and marketing of medical products that are intended for human use entails an inherent risk of product liability. If any product that we or any of our collaborators or licensees develops causes or is alleged to cause injury or is found to be unsuitable during clinical trials, manufacturing or sale, we may be held liable. If we cannot successfully defend ourselves against product liability claims, we may incur substantial liabilities, including substantial damages to be paid to the plaintiffs and legal costs, or we may be required to limit commercialization of our products. Our product liability insurance policy that provides coverage for liabilities arising from our clinical trials may not fully cover our potential liabilities. In addition, we may determine that we should increase our coverage upon the undertaking of new clinical trials, and this insurance may be prohibitively expensive to us or our collaborators or licensees and may not fully cover our potential liabilities. Our inability to obtain sufficient product liability insurance at an acceptable cost to protect against potential product liability claims could prevent or inhibit the commercialization of pharmaceutical products we develop, alone or with our collaborators. Additionally, any product liability lawsuit could cause injury to our reputation, recall of products, participants to withdraw from clinical trials, and potential collaborators or licensees to seek other partners, any of which could impact our results of operations.

Because our activities involve the use of hazardous materials, we may be subject to claims relating to improper handling, storage or disposal of these materials that could be time consuming and costly.

We are subject to various environmental, health and safety laws and regulations governing, among other things, the use, handling, storage and disposal of regulated substances and the health and safety of our employees. Our research and development processes involve the controlled use of hazardous and radioactive materials and biological waste resulting in the production of hazardous waste products. We cannot completely eliminate the risk of accidental contamination or discharge and any resultant injury from these materials. If any injury or contamination results from our use or the use by our collaborators or licensees of these materials, we may be sued and our liability may exceed our insurance coverage and our total assets. Further, we may be required to indemnify our collaborators or licensees against all damages and other

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liabilities arising out of our development activities or products produced in connection with these collaborations or licenses. Compliance with the applicable environmental and workplace laws and regulations is expensive. Future changes to environmental, health, workplace and safety laws could cause us to incur additional expense or may restrict our operations or impair our research, development and production efforts.

Risks Relating to our Financial Results

We expect to incur losses in the future and we may not achieve or maintain profitability in the future.

We had net losses from inception in 1991 through 1996 and in 1999 through 2008. Because of those losses, we had an accumulated deficit of $1.3 billion as of June 30, 2009. We will continue to spend significant amounts on our efforts to discover and develop drugs. As a result, we expect to continue to incur losses in 2009 and in future periods as well.

We anticipate that our drug discovery and development efforts and related expenditures will increase as we focus on the studies, including preclinical tests and clinical trials prior to seeking regulatory approval, that are required before we can sell a drug product.

The development of drug products will require us to spend significant funds on research, development, testing, obtaining regulatory approvals, manufacturing and marketing. To date, we do not have any drug products that have generated revenues and we cannot assure you that we will generate revenues from the drug candidates that we license or develop for several years, if ever. We cannot be certain whether or when we will achieve profitability because of the significant uncertainties relating to our ability to generate commercially successful drug products. Even if we were successful in obtaining regulatory approvals for manufacturing and commercializing a drug candidate, we expect that we will continue to incur losses if our drug products do not generate significant revenues. If we achieve profitability, we may not be able to sustain or increase profitability.

We will need additional capital in the future. The capital markets may not permit us to raise additional capital at the time that we require it, which could result in limitations on our research and development or commercialization efforts or the loss of certain of our rights in our technologies or drug candidates.

Our future funding requirements will depend on many factors and we anticipate that we will need to raise additional capital to fund our business plan and research and development efforts going forward and to repay our existing indebtedness. Additional factors that may affect our future funding requirements include:

- any changes in the breadth of our research and development programs;
- the results of research and development, preclinical testing and clinical trials conducted by us or our future collaborative partners or licensees, if any;
- the acquisition of technologies, if any;
- our ability to maintain and establish new corporate relationships and research collaborations;
- competing technological and market developments;
- the amount of revenues generated from our business activities, if any;
- the time and costs involved in filing, prosecuting, defending and enforcing patent and intellectual property claims;

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the receipt of contingent licensing or milestone fees or royalties on product sales from our current or future collaborative and license arrangements, if established; and

the timing of regulatory approvals, if any.

If we require additional capital at a time when investment in companies such as ours, or in the marketplace generally, is limited due to the then prevailing market or other conditions, we may have to scale back our operations, eliminate one or more of our research or development programs, or attempt to obtain funds by entering into an agreement with a collaborative partner that would result in terms that are not favorable to us or relinquishing our rights in certain of our proprietary technologies or drug candidates. For example, we recently decided not to advance compounds from our c-MET and IDO programs into Phase I clinical trials until additional funding is obtained. If we are unable to raise funds at the time that we desire or at any time thereafter on acceptable terms, we may not be able to continue to develop our potential drug products. The sale of equity or additional convertible debt securities in the future may be dilutive to our stockholders, and debt financing arrangements may require us to pledge certain assets or enter into covenants that could restrict our operations or our ability to incur further indebtedness.

We have a large amount of debt and our debt service obligations may prevent us from taking actions that we would otherwise consider to be in our best interests.

As of June 30, 2009, the aggregate principal amount of our total consolidated debt was $421.8 million and our stockholders' deficit was $291.4 million. The documents pursuant to which our outstanding convertible senior and subordinated notes were issued do not limit the issuance of additional indebtedness. If our concurrent offering of convertible notes closes, we will incur $350.0 million of additional indebtedness, or up to $400.0 million if the initial purchasers exercise in full their option to purchase additional notes, significantly increasing our leverage. Our substantial leverage could have significant negative consequences for our future operations, including:

increasing our vulnerability to general adverse economic and industry conditions;

limiting our ability to obtain additional financing for working capital, capital and research and development expenditures, and general corporate purposes;

requiring the dedication of a substantial portion of our expected cash flow or our existing cash to service our indebtedness, thereby reducing the amount of our cash available for other purposes, including working capital, capital expenditures and research and development expenditures;

limiting our flexibility in planning for, or reacting to, changes in our business and the industry in which we compete; or

placing us at a possible competitive disadvantage compared to less leveraged competitors and competitors that have better access to capital resources;

In the past five years, we have had negative cash flow from operations. We likely will not generate sufficient cash flow from our operations in the future to enable us to meet our anticipated fixed charges, including our obligations with respect to our outstanding convertible senior notes and convertible subordinated notes. As of June 30, 2009, $151.8 million aggregate principal amount of our convertible senior notes due 2011 was outstanding and is due in February 2011. Our annual interest payments, beginning in 2007, for the 2011 senior notes through 2010, assuming none of these notes are converted, redeemed, repurchased or exchanged, are $5.3 million, and an additional $2.6 million in interest is payable in 2011. As of June 30, 2009, $250.0 million aggregate principal amount of our convertible subordinated notes due 2011 was outstanding and is due in February 2011. Our annual interest payments for the 2011 subordinated notes through 2010,

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assuming none of these notes are converted, redeemed, repurchased or exchanged, are $8.8 million, and an additional $4.4 million in interest is payable in 2011. As of June 30, 2009, $20.0 million aggregate principal amount of the non-interest bearing convertible subordinated notes held by Pfizer was outstanding, of which $10.0 million is due in 2013 and $10.0 million is due in 2014. If we are unable to generate cash from our operations or raise additional cash through financings sufficient to meet these obligations, we will need to use existing cash or liquidate marketable securities in order to fund these obligations, which may delay or curtail our research, development and commercialization programs. We may from time to time seek to repurchase or refinance our outstanding convertible notes that mature in February 2011. Repurchases might occur through cash purchases and/or exchanges for other securities in open market transactions, privately negotiated transactions or otherwise. Such repurchases or exchanges, if any, will depend on prevailing market conditions, our cash position, our liquidity requirements, contractual restrictions and other factors. The amounts involved in any such transactions, individually or in the aggregate, may be material. Any issuance of equity securities in exchange for our outstanding convertible notes may be dilutive to our stockholders.

The indenture governing the notes being offered in our concurrent offering of convertible notes includes limitations on our ability to incur additional indebtedness, issue certain preferred stock, and incur liens on our assets, including on intellectual property concerning our JAK inhibitor program. These limitations could interfere with our ability to raise additional capital in the future or engage in activities that may be in our long-term best interest.

Our marketable securities are subject to certain risks that could adversely affect our overall financial position.

We invest our cash in accordance with an established internal policy and customarily in instruments which historically have been highly liquid and carried relatively low risk. However, with recent credit market conditions, similar types of investments have experienced losses in value or liquidity issues which differ from their historical pattern. Should a portion of our marketable securities lose value or have their liquidity impaired, it could adversely affect our overall financial position by imperiling our ability to fund our operations and forcing us to seek additional financing sooner than we would otherwise. Such financing, if available, may not be available on commercially attractive terms.

Our current revenues are derived from collaborations and from licensing our intellectual property. If we are unable to achieve milestones, develop products or renew or enter into new collaborations, our revenues may decrease, and future milestone and royalty payments from our gene and genomics-related intellectual property may not contribute significantly to revenues for several years, and may never result in revenues.

We derived all of our revenues for the three and six months ended June 30, 2009 from licensing our intellectual property to others. We are currently evaluating collaboration arrangements for several of our programs, and may be unable to enter into additional collaborative agreements on acceptable terms or at all. Revenues from research and development collaborations depend upon continuation of the collaborations, the achievement of milestones and royalties we earn from any future products developed from our research. If we are unable to successfully achieve milestones or our collaborators fail to develop successful products, we will not earn the revenues contemplated under our collaborative agreements. Part of our prior strategy was to license to our database customers and to other pharmaceutical and biotechnology companies our know-how and patent rights associated with the information we have generated in the creation of our proprietary databases, for use in the discovery and development of potential pharmaceutical, diagnostic or other products. Any potential product that is the subject of such a license will require several years

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of further development, clinical trials and regulatory approval before commercialization, all of which is beyond our control, and possibly beyond the control of our licensee. These licensees may not develop the potential product if they do not devote the necessary resources or decide that they do not want to expend the resources to do the clinical trials necessary to obtain the necessary regulatory approvals. Therefore, milestone or royalty payments from these licenses may not contribute to our revenues for several years, if at all. We have decided to discontinue some of our gene and genomics-related patent prosecution and maintenance, and may in the future decide to discontinue additional gene and genomics-related patent prosecution and maintenance, which could limit our ability to receive license-based revenues from our gene and genomics-related patent portfolio.

Risks Relating to Intellectual Property and Legal Matters

If we are subject to arbitration, litigation and infringement claims, they could be costly and disrupt our drug discovery and development efforts.

The technology that we use to make and develop our drug products, the technology that we incorporate in our products, and the products we are developing may be subject to claims that they infringe the patents or proprietary rights of others. The success of our drug discovery and development efforts will also depend on our ability to develop new compounds, drugs and technologies without infringing or misappropriating the proprietary rights of others. We are aware of patents and patent applications filed in certain countries claiming intellectual property relating to some of our drug discovery targets and product candidates. While the validity of issued patents, patentability of pending patent applications and applicability of any of them to our programs are uncertain, if any of these patents are asserted against us or if we choose to license any of these patents, our ability to commercialize our products could be harmed or the potential return to us from any product that may be successfully commercialized could be diminished.

From time to time we have received, and we may in the future receive, notices from third parties offering licenses to technology or alleging patent, trademark, or copyright infringement, claims regarding trade secrets or other contract claims. Receipt of these notices could result in significant costs as a result of the diversion of the attention of management from our drug discovery and development efforts. Parties sending these notices may have brought and in the future may bring litigation against us or seek arbitration relating to contract claims.

We may be involved in future lawsuits or other legal proceedings alleging patent infringement or other intellectual property rights or contract violations. In addition, litigation or other legal proceedings may be necessary to:

assert claims of infringement;

enforce our patents or trademarks;

protect our trade secrets or know-how; or

determine the enforceability, scope and validity of the proprietary rights of others.

We may be unsuccessful in defending or pursuing these lawsuits, claims or other legal proceedings. Regardless of the outcome, litigation or other legal proceedings can be very costly and can divert management's efforts. For example, we settled patent litigation with Invitrogen Corporation in 2006. We incurred significant expenses related to this litigation and, as part of the settlement, paid Invitrogen $3.4 million. An adverse determination may subject us to significant liabilities or require us or our collaborators or licensees to seek licenses to other parties' patents or proprietary rights. We or our collaborators or licensees may also be restricted or prevented from manufacturing or selling a drug or other product that we or they develop. Further, we or our future

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collaborators or licensees may not be able to obtain any necessary licenses on acceptable terms, if at all. If we are unable to develop non-infringing technology or license technology on a timely basis or on reasonable terms, our business could be harmed.

We may be unable to adequately protect or enforce our proprietary information, which may result in its unauthorized use, a loss of revenue under a collaboration agreement or loss of sales to generic versions of our products or otherwise reduce our ability to compete in developing and commercializing products.

Our business and competitive position depends in significant part upon our ability to protect our proprietary technology, including any drug products that we create. Despite our efforts to protect this information, unauthorized parties may attempt to obtain and use information that we regard as proprietary. For example, one of our collaborators may disclose proprietary information pertaining to our drug discovery efforts. In addition, while we have filed numerous patent applications with respect to our product candidates in the United States and in foreign countries, our patent applications may fail to result in issued patents. In addition, because patent applications can take several years to issue as patents, there may be pending patent applications of others that may later issue as patents that cover some aspect of our drug candidates. Our existing patents and any future patents we may obtain may not be broad enough to protect our products or all of the potential uses of our products, or otherwise prevent others from developing competing products or technologies. In addition, our patents may be challenged and invalidated or may fail to provide us with any competitive advantages if, for example, others were first to invent or first to file a patent application for the technologies and products covered by our patents.

Additionally, when we do not control the prosecution, maintenance and enforcement of certain important intellectual property, such as a drug compound in-licensed to us or subject to a collaboration with a third party, the protection of the intellectual property rights may not be in our hands. If we do not control the intellectual property rights in-licensed to us with respect to a compound and the entity that controls the intellectual property rights does not adequately protect those rights, our rights may be impaired, which may impact our ability to develop, market and commercialize the in-licensed compound.

Our means of protecting our proprietary rights may not be adequate, and our competitors may:

- independently develop substantially equivalent proprietary information, products and techniques;
- otherwise gain access to our proprietary information; or
- design around patents issued to us or our other intellectual property.

We pursue a policy of having our employees, consultants and advisors execute proprietary information and invention agreements when they begin working for us. However, these agreements may not provide meaningful protection for our trade secrets or other proprietary information in the event of unauthorized use or disclosure. If we fail to maintain trade secret and patent protection, our potential, future revenues may be decreased.

If the effective term of our patents is decreased due to changes in the United States patent laws or if we need to refile some of our patent applications, the value of our patent portfolio and the revenues we derive from it may be decreased.

The value of our patents depends in part on their duration. A shorter period of patent protection could lessen the value of our rights under any patents that we obtain and may decrease the revenues we derive from our patents. The United States patent laws were amended in 1995 to

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change the term of patent protection from 17 years from patent issuance to 20 years from the earliest effective filing date of the application. Because the time from filing to issuance of biotechnology applications may be more than three years depending on the subject matter, a 20-year patent term from the filing date may result in substantially shorter patent protection. Also, we may need to refile some of our applications filed before 1995 that claim large numbers of genes or other additional subject matter and, in these situations, the patent term will be measured from the date of the earliest priority application. This would shorten our period of patent exclusivity and may decrease the revenues that we might derive from the patents.

International patent protection is particularly uncertain and costly, and if we are involved in opposition proceedings in foreign countries, we may have to expend substantial sums and management resources.

Biotechnology and pharmaceutical patent law outside the United States is even more uncertain and costly than in the United States and is currently undergoing review and revision in many countries. Further, the laws of some foreign countries may not protect our intellectual property rights to the same extent as United States laws. For example, certain countries do not grant patent claims that are directed to the treatment of humans. We may participate in opposition proceedings to determine the validity of our foreign patents or our competitors' foreign patents, which could result in substantial costs and diversion of our efforts.

Risks Related to the Common Stock and this Offering

Because the price of our common stock has been volatile historically, it may be difficult for you to resell the common stock at a price that is acceptable to you or at all.

The market price of our common stock, like that of the common stock of many other pharmaceutical and biotechnology companies, has been and is likely to be highly volatile. In addition, the stock market has experienced extreme price and volume fluctuations. This volatility has significantly affected the market prices of securities of many pharmaceutical and biotechnology companies for reasons frequently unrelated to or disproportionate to the operating performance of the specific companies. These broad market fluctuations may adversely affect the market price of our common stock. Prices for our common stock will be determined in the market place and may be influenced by many factors, including:

- announcements of data from, or material developments in, our clinical trials or those of our collaborators or competitors, including delays in the commencement, progress or completion of a clinical trial or adverse results in a clinical trial;
- actions taken by FDA or other regulatory agencies with respect to our, our collaborators' or our competitors' clinical trials;
- announcements of new products by us or our competitors;
- announcements of collaborative relationships by us or our competitors and our ability to enter into and maintain existing collaborative relationships;
- litigation and other developments relating to our products and our patents or other proprietary rights or those of our competitors or other litigation against us and our directors and officers;
- variations in our financial results;
- conditions in the life sciences, biotechnology or pharmaceutical industries;
- governmental regulation and legislation;

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sales of a substantial amount of our securities; and

investors' perceptions of us, changes in recommendations by securities analysts, and investors' and securities analysts' perceptions of general economic, industry and market conditions.

In the past, companies that have experienced volatility in the market prices of their stock have been the object of securities class action litigation. If we were the object of securities class action litigation, it could result in substantial costs and a diversion of management's attention and resources.

Our management has significant flexibility in using the net proceeds of this offering and the concurrent convertible notes offering.

We have not designated the amount of net proceeds from this offering or the convertible notes offering that we will use for any purpose. We intend to use the net proceeds of this offering for general corporate purposes, including research and development activities. We intend to use the net proceeds of the concurrent convertible notes offering to repurchase or otherwise retire outstanding debt and, to the extent not used to repurchase or otherwise retire outstanding debt, for general corporate purposes. However, depending on future developments and circumstances, we may use some of the proceeds for other purposes. Therefore, our management will have significant flexibility in applying the net proceeds of this offering. The actual amounts and timing of expenditures will vary significantly depending on a number of factors, including the amount of cash used in our operations and our drug discovery and development efforts. Management's failure to use these funds effectively would have an adverse effect on the value of our common stock and could make it more difficult and costly to raise funds in the future.

You will experience immediate dilution in the book value per share of the common stock you purchase.

Because the price per share of our common stock being offered is substantially higher than the net tangible book value (deficit) per share of our common stock, you will suffer substantial dilution in the net tangible book value of the common stock you purchase in this offering. Based on a public offering price of $6.75 per share, if you purchase shares of common stock in this offering, you will suffer immediate and substantial dilution of $8.28 per share in the net tangible book value of the common stock. If the underwriters exercises their option to purchase additional shares in full, you will suffer immediate and substantial dilution of $8.10 per share. See "Dilution" on page S-29 for a more detailed discussion of the dilution you will incur in this offering.

Because we do not now and may never have enough shares of common stock authorized to accommodate the full conversion of the notes being sold in our concurrent convertible notes offering, we may be required to issue shares of a new series of preferred stock upon conversion of the notes instead of common stock and pay additional interest on the notes.

The maximum number of shares of common stock into which notes being sold in our concurrent convertible notes offering may be convertible exceeds the number of shares of common stock currently available for us to issue upon conversion of the notes. In order to increase the number of shares of common stock we are authorized to issue, we must obtain the approval of stockholders holding a majority of our outstanding shares of common stock, and we have agreed to use reasonable efforts to obtain stockholder approval and to increase the shares of common stock reserved to a level sufficient for conversion of all notes. We cannot guarantee that such stockholder approval will be obtained. In the event we have not established a sufficient reserve by January 1, 2010, the interest rate on the notes will increase to 10%. If we have not established a

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sufficient reserve by June 30, 2010, the interest rate on the notes will increase to 15%. The interest rate on the notes will increase an additional 5% each June 30 thereafter until maturity or until we have established a sufficient reserve.

For so long as we do not have enough shares of common stock authorized and available for issuance upon conversion of these notes, we will issue a combination of shares of our common stock and shares of newly created series A preferred stock upon such conversion. Under the terms of the indenture governing these notes, until we have reserved a sufficient number of shares of our common stock for conversion of all of the notes, we will not be able to raise additional capital through a subsequent sale of common stock or securities convertible into common stock. Until a reserve of common stock sufficient for conversion of all notes is established, our ability to raise additional capital will be severely limited.

Although we will issue shares of series A preferred stock based on a ratio of 1.1 shares of series A preferred stock for every 1,000 shares of common stock otherwise issuable upon conversion of the notes, in the event of any dividends or distributions, any liquidation or dissolution, or in the event of a consolidation, merger, sale or other similar transaction, each whole share of series A preferred stock will have the same economic rights as 1,000 shares of common stock. In addition, if certain tender or exchange offers occur before we establish a sufficient common stock reserve for the notes, as a result of which a third party or group own beneficially more than 50% of our voting stock, then the interest rate on the notes will increase to 15% (or remain at any higher rate then in effect as a result of our inability to establish a sufficient common stock reserve for the notes as described above), with an additional 5% increase in the interest rate on each anniversary of that occurrence, until we have established a sufficient reserve.

Conversion of the notes offered and sold pursuant to the concurrent convertible notes offering will dilute the ownership interests of existing stockholders.

The issuance of shares of our common stock, or a combination of shares of our common stock and shares of newly created series A preferred stock, in connection with conversions of the convertible senior notes being sold in our concurrent convertible notes offering will dilute the ownership interests of our existing stockholders. Any sales in the public market of our common stock issuable upon such conversion could adversely affect prevailing market prices of our common stock. In addition, the existence of the notes may encourage short-selling by holders of the notes engaged in hedging or arbitrage, and by other market participants.

This offering is not conditioned on the concurrent convertible notes offering.

Although the convertible notes offering is scheduled to close concurrently with this offering of common stock, this offering of common stock is not conditioned on the closing of the notes offering. Accordingly, the sale of common stock in this offering may be completed without the convertible notes offering. If the convertible notes offering is not consummated, we will not have the additional liquidity that we expect from the convertible notes offering.

We do not expect to pay dividends in the foreseeable future. As a result, you must rely on stock appreciation for any return on your investment.

We do not anticipate paying cash dividends on our common stock in the foreseeable future. Any payment of cash dividends will also depend on our financial condition, results of operations, capital requirements and other factors and will be at the discretion of our board of directors. Accordingly, you will have to rely on capital appreciation, if any, to earn a return on your investment in our common stock. Furthermore, we may in the future become subject to contractual restrictions on, or prohibitions against, the payment of dividends.

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We have various mechanisms in place to discourage takeover attempts, which may reduce or eliminate our stockholders' ability to sell their shares for a premium in a change of control transaction.

Various provisions of our certificate of incorporation and bylaws and of Delaware corporate law may discourage, delay or prevent a change in control or takeover attempt of our company by a third party that is opposed by our management and board of directors. Public stockholders who might desire to participate in such a transaction may not have the opportunity to do so. These anti-takeover provisions could substantially impede the ability of public stockholders to benefit from a change of control or change in our management and board of directors. These provisions include:

- no cumulative voting for directors, which would otherwise allow less than a majority of stockholders to elect director candidates;
- control by our board of directors of the size of our board of directors;
- limitations on the ability of stockholders to call special meetings of stockholders;
- advance notice requirements for nominations of candidates for election to our board of directors or for proposing matters that can be acted upon by our stockholders at stockholder meetings; and
- the ability of our board of directors to issue, without stockholder approval, preferred stock with rights that are senior to those of our common stock.

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FORWARD-LOOKING STATEMENTS

This prospectus supplement, the accompanying prospectus and the documents we have filed with the Securities and Exchange Commission, or SEC, that are incorporated herein by reference contain forward-looking statements that involve risks and uncertainties. These statements relate to future periods, future events or our future operating or financial plan or performance. These statements can often be identified by the use of forward-looking terminology such as "expects", "believes", "intends", "anticipates", "estimates", "plans", "may", or "will", or the negative of these terms, and other similar expressions. These forward-looking statements include statements as to: the discovery, development, formulation, manufacturing and commercialization of our compounds and our product candidates; focus on our drug discovery and development efforts; conducting clinical trials internally, with collaborators, or with clinical research organizations; our collaboration and strategic relationship strategy; anticipated benefits and disadvantages of entering into collaboration agreements; our licensing, investment and commercialization strategies; the regulatory approval process, including determinations to seek FDA and other international health authorities approval for, and plans to commercialize, our products in the United States and abroad; the safety, effectiveness and potential benefits and indications of our product candidates and other compounds under development; potential uses for our product candidates and our other compounds; the timing and size of our clinical trials; the compounds expected to enter clinical trials; timing of clinical trial results; our ability to manage expansion of our drug discovery and development operations; future required expertise relating to clinical trials, manufacturing, sales and marketing; obtaining and terminating licenses to products, compounds or technology, or other intellectual property rights; the receipt from or payments pursuant to collaboration or license agreements resulting from milestones or royalties; the decrease in revenues from our information product-related activities; plans to develop and commercialize products on our own; plans to use third party manufacturers; expected expenses and expenditure levels; expected uses of cash; expected revenues and sources of revenues; expected losses; fluctuation of losses; our profitability; the adequacy of our capital resources to continue operations; the need to raise additional capital; the costs associated with resolving matters in litigation; our expectations regarding competition; our investments, including anticipated expenditures, losses and expenses; our patent prosecution and maintenance efforts; and our indebtedness, and debt service obligations.

These forward-looking statements reflect our current views with respect to future events, are based on assumptions and are subject to risks and uncertainties. These risks and uncertainties could cause actual results to differ materially from those projected and include, but are not limited to, our ability to discover, develop, formulate, manufacture and commercialize a drug candidate or product; the risk of unanticipated delays in research and development efforts; the risk that previous preclinical testing or clinical trial results are not necessarily indicative of future clinical trial results; risks relating to the conduct of our clinical trials; changing regulatory requirements; the risk of adverse safety findings; the risk that results of our clinical trials do not support submission of a marketing approval application for our product candidates; the risk of significant delays or costs in obtaining regulatory approvals; risks relating to our reliance on third party manufacturers, collaborators, and clinical research organizations; risks relating to the development of new products and their use by us and our current and potential collaborators; risks relating to our inability to control the development of out-licensed drug compounds or drug candidates; costs associated with prosecuting, maintaining, defending and enforcing patent claims and other intellectual property rights; our ability to maintain or obtain adequate product liability and other insurance coverage; the risk that our product candidates may not obtain regulatory approval; the impact of technological advances and competition; the ability to compete against third parties with greater resources than ours; risks relating to changes in pricing and reimbursements in the markets in which we may compete; competition to develop and commercialize similar drug products; our ability to obtain patent protection and freedom to operate for our discoveries and to continue to be effective in

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expanding our patent coverage; the impact of changing laws on our patent portfolio; developments in and expenses relating to litigation; the impact of past or future acquisitions on our business; the results of businesses in which we have made investments; our ability to obtain additional capital, including the proposed concurrent offering of convertible notes; fluctuations in net cash used by investing activities; and our history of operating losses. You should also consider carefully the statements set forth in the section entitled "Risk Factors" and other sections of this prospectus supplement, the accompanying prospectus and in the other documents we have filed with the SEC and that are incorporated in this prospectus supplement and the accompanying prospectus by reference, which address additional factors that could cause results or events to differ from those set forth in the forward-looking statements. Given these risks and uncertainties, you should not place undue reliance on these forward-looking statements. Except as required by federal securities laws, we undertake no obligation to update any forward-looking statements for any reason, even if new information becomes available or other events occur in the future.

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USE OF PROCEEDS

We estimate that the net proceeds from the sale of the 18,000,000 shares of our common stock that we are offering will be approximately $114.7 million, after deducting the estimated underwriting discount and estimated offering expenses we expect to pay. If the underwriters exercise their option to purchase additional shares in full, we estimate that the net proceeds will be approximately $132.0 million.

Concurrently with this offering, we are offering $350,000,000 principal amount of our 4.75% Convertible Senior Notes due 2015 (or a total of $400,000,000 principal amount if the initial purchasers in that offering exercise in full their option to purchase additional notes) in a separate private offering to qualified institutional buyers. We estimate that the net proceeds from our concurrent private offering of convertible notes will be approximately $338.8 million, or $387.3 million if the initial purchasers' option is exercised in full. The 4.75% Convertible Senior Notes due 2015 and the common stock, or shares of preferred stock in lieu of common stock, issuable upon conversion of the 4.75% Convertible Senior Notes due 2015 have not been and will not be registered under the Securities Act of 1933 and may not be offered or sold in the United States absent registration or applicable exemption from registration requirements.

We intend to use the net proceeds from this offering for general corporate purposes, including research and development activities. We intend to use the net proceeds of the concurrent convertible notes offering to repurchase or otherwise retire outstanding debt, including our 3 1/2% convertible senior notes due 2011 and 3 1/2% convertible subordinated notes due 2011, through open market transactions, negotiated transactions or otherwise, and, to the extent not used to repurchase or otherwise retire outstanding debt, for general corporate purposes. We have agreed to repurchase $38.3 million aggregate principal amount of our 3 1/2% convertible senior notes due 2011 and $59.1 million aggregate principal amount of our 3 1/2% convertible subordinated notes due 2011 from entities affiliated with Julian C. Baker, one of our directors and principal stockholders, and expect to repurchase, upon the closing of this offering, an additional $48.0 million aggregate principal amount of our 3 1/2% convertible senior notes due 2011 and an additional $40.9 million aggregate principal amount of our 3 1/2% convertible subordinated notes due 2011 pursuant to privately negotiated transactions with other holders, and intend to use a portion of the net proceeds from the offering of the notes for these repurchases. We also intend to use a portion of the net proceeds from the convertible notes offering to fund the escrow account to be used for the first six semi-annual interest payments on those notes.

Our board of directors has broad discretion in determining how the proceeds of this offering will be applied. The timing and amount of our actual expenditures cannot be precisely determined at this time and will be based upon many factors, including the following:

- our research and development activities;
- competitive developments;
- technological advances;
- our future growth, if any;
- our future capital expenditures;
- the availability of alternative methods of financing; and
- the amount of cash required by our operations.

A portion of the proceeds may be used to acquire or invest in complementary businesses, products or technologies, although we have no current agreements or commitments for any such acquisition or investment.

Until we use the net proceeds of this offering, we intend to invest the funds in money market funds and other short-term, investment grade, interest bearing obligations.

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DILUTION

Our net tangible book value (deficit) as of June 30, 2009 was approximately $(291.4) million, or $(2.98) per share of our common stock. Net tangible book value (deficit) per share is calculated by subtracting our total liabilities from our total tangible assets, which is total assets less intangible assets, and dividing this amount by the number of shares of our common stock outstanding. After giving effect to the sale by us of the 18,000,000 shares of our common stock offered in this offering, at a public offering price of $6.75 per share and after deducting the estimated underwriting discount and estimated offering expenses we expect to pay, our net tangible book value (deficit) as of June 30, 2009 would have been $(176.8) million, or $(1.53) per share of our common stock. This represents an immediate increase in the net tangible book value of $1.45 per share to our existing stockholders and an immediate and substantial dilution in net tangible book value of $8.28 per share to new investors. The following table illustrates this per share dilution:

Public offering price per share		$ 6.75
Net tangible book value (deficit) per share	$(2.98)	
Increase per share attributable to new investors	1.45	
Net tangible book value (deficit) per share after this offering		(1.53)
Dilution per share to new investors		$ 8.28

If the underwriters exercise their option to purchase additional shares in full, our net tangible book value per share after this offering will increase to $(1.35), which represents an increase in the net tangible book value of $1.63 per share to our existing stockholders and an immediate dilution in net tangible book value of $8.10 per share to new investors purchasing shares of common stock in this offering.

The foregoing table and discussion is based on the number of shares of common stock outstanding as of June 30, 2009, and does not take into effect further dilution to new investors that could occur as a result of:

- 17,977,610 shares of common stock issuable upon the exercise of stock options outstanding with a weighted average exercise price of $7.72 per share;
- 3,595,333 shares of common stock available for future issuance under our stock plans;
- 1,250,537 shares reserved for issuance under our employee stock purchase plan;
- 1,461,496 shares issuable upon conversion of our convertible subordinated note due 2013 issued to Pfizer Inc.; and
- shares issuable upon conversion of any of the convertible notes sold in our concurrent convertible notes offering.

The foregoing table and discussion does not take into effect the issuance of the convertible notes in our concurrent convertible notes offering nor any repurchase or retirement of outstanding debt.

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PRICE RANGE OF COMMON STOCK

Our common stock is traded on The NASDAQ Global Market under the symbol "INCY." The following table sets forth for the periods indicated the high and low sales prices for the common stock on The NASDAQ Global Market.

	High	Low
2007		
First Quarter	$ 7.70	$ 5.84
Second Quarter	8.30	5.79
Third Quarter	7.76	4.75
Fourth Quarter	10.93	7.02
2008		
First Quarter	$12.83	$ 8.33
Second Quarter	11.69	7.45
Third Quarter	10.42	7.01
Fourth Quarter	7.67	1.85
2009		
First Quarter	$ 4.21	$ 2.03
Second Quarter	4.10	1.96
Third Quarter (through September 24, 2009)	8.18	3.22

On September 24, 2009, the last reported sale price for the common stock on The NASDAQ Global Market was $6.88. As of June 30, 2009, there were approximately 302 holders of record of our common stock.

DIVIDEND POLICY

We have never declared or paid dividends on our capital stock. We do not expect to pay any dividends in the foreseeable future. We currently intend to retain our earnings, if any, for the development of our business.

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CAPITALIZATION

The following table shows our unaudited cash, cash equivalents and marketable securities and capitalization as of June 30, 2009:

- on an actual basis; and
- on an as adjusted basis to give effect to the sale of 18,000,000 shares of common stock in this offering at a public offering price of $6.75 per share after deducting the underwriting discount and estimated offering expenses we expect to pay;
- on an as further adjusted basis to give effect to the foregoing and the receipt of the estimated net proceeds (includes approximately $49.0 million of net proceeds to be invested and held in escrow for the payment of the first six semi-annual interest payments on the notes) from our concurrent offering of $350,000,000 principal amount of our 4.75% Convertible Senior Notes due 2015.

You should read this information in conjunction with our consolidated financial statements and other financial information that are included in or incorporated by reference in this prospectus supplement and the accompanying prospectus.

	As of June 30, 2009 (unaudited)		
	Actual	As Adjusted	As Further Adjusted
	(in thousands)		
Cash, cash equivalents and short-term and long-term marketable securities	$ 147,485	$ 262,160	$ 600,910
Long-term debt	$ 401,225	$ 401,225	$ 751,225
Stockholders' deficit:			
Preferred stock, $.001 par value; 5,000,000 shares authorized; none issued and outstanding actual and as adjusted			
Common stock, $.001 par value; 200,000,000 shares authorized; 97,785,047 shares issued and outstanding actual, 115,785,047 shares issued and outstanding as adjusted	98	116	116
Additional paid-in capital	967,964	1,082,621	1,082,621
Accumulated other comprehensive loss	(107)	(107)	(107)
Accumulated deficit	(1,259,385)	(1,259,385)	(1,259,385)
Total stockholders' deficit	(291,430)	(176,755)	(176,755)
Total capitalization	$ 109,795	$ 224,470	$ 574,470

We have designated 100,000 shares of preferred stock as series A preferred stock, none of which is outstanding as of the date hereof.

The number of shares of common stock shown as issued and outstanding in the table above excludes, as of June 30, 2009:

- 17,977,610 shares issuable upon the exercise of stock options outstanding with a weighted average exercise price of $7.72 per share;

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3,595,333 shares reserved for issuance and available for future grant or sale under our stock plans;

1,250,537 shares reserved for issuance under our employee stock purchase plan;

13,531,224 shares issuable upon conversion of our 3 1/2% convertible senior notes due 2011;

22,284,625 shares issuable upon conversion of our 3 1/2% convertible subordinated notes due 2011;

1,461,496 shares issuable upon conversion of our convertible subordinated note due 2013 issued to Pfizer Inc.;

1,025,641 shares issuable upon conversion of our convertible subordinated note due 2014 issued to Pfizer Inc; and

shares issuable upon conversion of our 4.75% Convertible Senior Notes due 2015 to be issued in the convertible notes offering.

The table above does not take into effect the repurchase of our 3 1/2% convertible senior notes due 2011 and our 3 1/2% convertible subordinated notes due 2011.

Although the convertible notes offering is scheduled to close concurrently with this offering of common stock, this offering of common stock is not conditioned on the closing of the notes offering and the notes offering is not contingent upon the closing of this offering. Accordingly, the sale of common stock in this offering may be completed without the convertible notes offering.

DESCRIPTION OF CAPITAL STOCK

This section describes the general terms and provisions of the shares of our common stock, $.001 par value per share, and preferred stock, $.001 par value per share. This description is only a summary. Our certificate of incorporation and our bylaws have been filed as exhibits to our periodic reports filed with the SEC, which are incorporated by reference in this prospectus supplement. You should read our certificate of incorporation and our bylaws for additional information before you buy any of our common stock. See "Where You Can Find More Information."

Common Stock

General. We are authorized to issue up to 200,000,000 shares of common stock. As of June 30, 2009, there were 97,785,047 shares of common stock issued and outstanding.

Voting Rights. The holders of our common stock are entitled to one vote for each share held of record on all matters submitted to a vote of the stockholders, including the election of directors, and do not have cumulative voting rights. Accordingly, the holders of a majority of the shares of common stock entitled to vote in any election of directors can elect all of the directors standing for election, if they so choose.

Dividends. Subject to preferences that may be applicable to any then outstanding preferred stock, holders of common stock are entitled to receive ratably dividends, if any, as may be declared by our board of directors out of funds legally available therefor.

Other Rights. Upon our liquidation, dissolution or winding up, the holders of common stock will be entitled to share ratably in the net assets legally available for distribution to stockholders after the payment of all of our debts and other liabilities, subject to the prior rights of any preferred stock then outstanding. Holders of common stock have no preemptive or conversion rights or other subscription rights and there are no redemption or sinking fund provisions applicable to the common stock. All outstanding shares of common stock are, and the common stock offered, when issued, will be, fully paid and nonassessable.

Preferred Stock

We are authorized to issue up to 5,000,000 shares of preferred stock. As of June 30, 2009, no shares of preferred stock were outstanding and we have no current plans to issue any shares of such stock other than the potential issuance of series A preferred stock in the event that we have insufficient shares of common stock upon the conversion of the notes being offered in our concurrent convertible notes offering. Our board of directors has the authority, without further action by our stockholders, to issue from time to time the preferred stock in one or more series, and to fix the number of shares, designations, preferences, powers, and other rights and qualifications, limitations or restrictions as our board of directors may authorize, including:

- the distinctive designation of each series and the number of shares that will constitute the series;
- the voting rights, if any, of shares of the series and the terms and conditions of the voting rights;
- the dividend rate on the shares of the series, the dates on which dividends are payable, any restriction, limitation or condition upon the payment of dividends, whether dividends will be cumulative, and the dates from and after which dividends shall accumulate;
- the prices at which, and the terms and conditions on which, the shares of the series may be redeemed, if the shares are redeemable;

the terms and conditions of a sinking or purchase fund for the purchase or redemption of shares of the series, if such a fund is provided;

any preferential amount payable upon shares of the series in the event of the liquidation, dissolution or winding up of, or upon the distribution of any of our assets; and

the prices or rates of conversion or exchange at which, and the terms and conditions on which, the shares of the series may be converted or exchanged into other securities, if the shares are convertible or exchangeable.

The issuance of preferred stock could decrease the amount of earnings and assets available for distribution to holders of common stock or adversely affect the rights and powers, including voting rights, of the holders of common stock. The issuance of preferred stock could have the effect of delaying, deferring or preventing a change in control of our company, which could depress the market price of our common stock.

Series A Preferred Stock

To date, no shares of series A preferred stock have been issued and we have no current plans to issue any shares of series A preferred stock other than the potential issuance of series A preferred stock in the event that we have insufficient shares of common stock upon the conversion of our 4.75% Convertible Senior Notes due 2015 to be issued in the concurrent convertible notes offering.

We do not currently have enough authorized shares of common stock to issue the full number shares of our common stock issuable upon conversion of our 4.75% Convertible Senior Notes due 2015. We have agreed to use reasonable efforts to obtain the approval of our stockholders of an increase in our authorized common stock and to increase the authorized shares underlying our 4.75% Convertible Senior Notes due 2015 to equal or exceed the full number of shares that may be issuable upon conversion of the notes.

If we receive the favorable vote of our stockholders on our proposal to increase our authorized common stock at our proposed special stockholders meeting, or if we are able to increase the number of shares of our common stock that we have set aside for issuance under our 4.75% Convertible Senior Notes due 2015 to equal or exceed the full number of shares underlying the notes, whether through repurchases of our common stock, repurchases of our other indebtedness convertible into shares of our common stock or otherwise, we will not need to issue series A preferred stock in lieu of shares of our common stock. In addition, if and when we do obtain stockholder approval, we will no longer have the option to issue shares of series A preferred stock in lieu of shares of our common stock upon conversion of our 4.75% Convertible Senior Notes due 2015.

Voting Rights. Except as required by law and as to matters that would adversely affect the rights of the series A preferred stock relative to the common stock, the series A preferred stock will have no voting rights.

Dividends or Distributions. Subject to the preferences that may be applicable to any senior preferred stock outstanding at the time, each share of series A preferred stock will be entitled to dividends or distributions equal to the common conversion number times any dividends or distributions paid or made on each share of common stock. The "common conversion number" is initially 1,000, and will be subject to proportionate adjustment for stock dividends, stock splits and share combinations of our common stock. We may not pay dividends or make distributions on the common stock without making a comparable dividend or distribution on the series A preferred stock.

Cumulative Dividends on Qualifying Tender Offer. If a qualifying tender offer (as defined below) occurs, then holders of shares of series A preferred stock will be entitled to receive, when, as and if declared by our board of directors, or an authorized committee of our board, out of funds legally available for payment, cumulative dividends, payable in cash, at the rate per annum (the "dividend rate") equal to the then applicable interest rate per annum payable on our 4.75% Convertible Senior Notes due 2015, including additional interest that will accrue upon the occurrence of a qualifying tender offer, subject to increase at the same time and same rate as increases in the additional interest on our 4.75% Convertible Senior Notes due 2015. The dividend per share of series A preferred stock will equal the dividend rate multiplied by an amount equal to the product of the common conversion number and the then applicable conversion price of our 4.75% Convertible Senior Notes due 2015. Dividends on the series A preferred stock will be payable quarterly in arrears on January 1, April 1, July 1, and October 1 of each year, each of which we refer to as a "dividend payment date," or the following business day if such date is not a business day, commencing on the dividend payment date immediately following the occurrence of a qualifying tender offer, at such annual rate, and will accumulate from the most recent date as to which dividends shall have been paid or, if no dividends have been paid, from the date of occurrence of the qualifying tender offer, whether or not in any dividend period or periods there have been funds legally available for the payment of such dividends.

Dividends will be payable to holders of record as they appear on our stock register on the immediately preceding December 15, March 15, June 15 and September 15, each of which we refer to as a "dividend record date," or the following business day if such date is not a business day. Accumulations of dividends on shares of series A preferred stock do not bear interest. Dividends payable on the series A preferred stock for any period other than a full dividend period (based upon the number of days elapsed during the period) will be computed on the basis of a 360-day year consisting of twelve 30-day months.

No dividend will be declared or paid upon, or any sum set apart for the payment of dividends upon, any outstanding shares of the series A preferred stock with respect to any dividend period unless all dividends for all preceding dividend periods have been declared and paid or declared and a sufficient sum of money has been set apart for the payment of such dividend, upon all outstanding shares of series A preferred stock.

We are only obligated to pay a dividend on our series A preferred stock if our board of directors or an authorized committee of our board declares the dividend payable and we have assets that legally can be used to pay the dividend.

A "qualifying tender offer" will be deemed to have occurred if at any time after our 4.75% Convertible Senior Notes due 2015 are originally issued and prior to the date on which the shares of our common stock reserved for issuance upon conversion of our 4.75% Convertible Senior Notes due 2015 equal or exceed the full number of shares that may be issuable upon conversion of the notes, a "person" or "group" within the meaning of Section 13(d) of the Securities Exchange Act of 1934, or the Exchange Act, other than us, our subsidiaries or our or their employee benefit plans, files a Schedule TO or any schedule, form or report under the Exchange Act disclosing that such person or group acquired in a tender or exchange offer direct or indirect "beneficial ownership," as defined in Rule 13d-3 under the Exchange Act, of our common equity representing more than 50% of the voting power of all classes of our common equity entitled to vote generally in the election of our directors.

Conversion. The series A preferred stock is not convertible at the election of the holders, but will be converted automatically, without any further action of any holder, at such time that the company has authorized and reserved a sufficient number of shares of common stock to permit the full conversion of all outstanding shares of series A preferred stock into common stock. Each 1.1

shares of series A preferred stock will convert into the number of shares of common stock equal to the common conversion number.

No Redemption. The series A preferred stock is not redeemable.

Liquidation, Dissolution or Winding Up. In the event of our liquidation, dissolution or winding up, the holders of shares of series A preferred stock will be entitled to receive, before any payment or distribution is made to holders of our common stock, accumulated and unpaid dividends on such shares to the date fixed for