

INCYTE CORP
Form 424B5
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Registration No. 333-152611

The information contained in this preliminary prospectus supplement is not complete and may be changed. This preliminary prospectus supplement and the accompanying prospectus are not an offer to sell nor do they seek an offer to buy these securities in any jurisdiction where the offer or sale is not permitted.

Subject to Completion. Dated July 29, 2008.

Prospectus Supplement To Prospectus dated July 29, 2008.

9,000,000 Shares

Incyte Corporation

Common Stock

Incyte Corporation is offering 9,000,000 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 1,000,000 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 July 29, 2008 was \$9.18 per share.

See "Risk Factors" beginning on page S-8 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	\$	\$
Underwriting discount	\$	\$
Proceeds, before expenses, to Incyte	\$	\$

To the extent that the underwriters sell more than 9,000,000 shares of common stock, the underwriters have the option to purchase up to an additional 1,350,000 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 _____, 2008.

Goldman, Sachs & Co.

Morgan Stanley

JPMorgan

Prospectus Supplement dated _____, 2008.

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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.

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.

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 pipeline with programs in oncology, inflammation, diabetes and human immunodeficiency virus (HIV).

Our wholly-owned pipeline includes the following compounds:

Drug Target	Drug Compound	Indication	Development Status
JAK	<i>INCB18424 (Oral)</i>	Myelofibrosis	Phase II
		Polycythemia vera/Essential thrombocythemia	Phase II
		Rheumatoid Arthritis	Phase IIa
		Refractory Prostate Cancer	Phase IIa
		Multiple Myeloma	Phase IIa
		Psoriasis	Phase IIa
	<i>INCB18424 (Topical)</i>		
	<i>INCB28050</i>	Rheumatoid Arthritis	Phase I
HSD1	<i>INCB13739</i>	Type 2 Diabetes	Phase IIb
	<i>INCB20817</i>	Type 2 Diabetes	Phase I
HM74a	<i>INCB19602</i>	Type 2 Diabetes	Phase IIa
Sheddase	<i>INCB7839</i>	Solid Tumors	Phase IIa
		Breast Cancer	Phase II
CCR2	<i>INCB8696</i>	Multiple Sclerosis	Phase I
CCR5	<i>INCB9471</i>	HIV	Phase II
	<i>INCB15050</i>	HIV	Phase I
Other			
	Lead clinical candidate	Oncology	Pre-clinical
	Lead clinical candidate	Oncology	Pre-clinical

We intend to develop and commercialize some of our compounds on our own in selected markets where we believe a company of our size can compete effectively, such as oncology and certain inflammatory conditions. For programs that target large primary care indications such as diabetes, or require lengthy and expensive clinical development plans, we intend to form strategic alliances with companies that have greater financial and commercial resources than we do, as we did with Pfizer Inc. in January 2006 for our CCR2 antagonist program.

Our productivity in drug discovery 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.

To succeed in our objective to create a pipeline of novel, orally available drugs that address serious unmet medical needs, we have established a broad range of discovery capabilities in-house, including target validation, high-throughput screening, medicinal chemistry, computational chemistry, and pharmacological and ADME (absorption, distribution, metabolism and excretion) assessment. We augment these capabilities through collaborations with academic and contract laboratory resources with relevant expertise.

Our current drug discovery and development programs include the following:

JAK Inhibitor Program

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, or MPDs, specifically myelofibrosis, polycythemia vera and essential thrombocythemia, inflammatory conditions such as rheumatoid arthritis and psoriasis, and certain other solid and liquid tumors. Additionally, the majority of MPD patients have a mutation in JAK2, V617F, as well as other JAK2 mutations, which result in increased JAK signaling. We believe the presence of these mutations further supports the hypothesis that hyperactivation of the JAK pathways is central to these disorders, and that inhibition of aberrant JAK signaling may have therapeutic value in treating these various diseases.

We have discovered multiple potent and orally bioavailable JAK inhibitors that are selective for JAK1 and JAK2 from multiple distinct chemical scaffolds. Our lead JAK inhibitor, INCB18424, is currently being developed as a treatment for several conditions, including myelofibrosis, polycythemia vera and essential thrombocythemia, rheumatoid arthritis and psoriasis. A lead follow-on JAK inhibitor compound, INCB28050, entered clinical trials in 2008.

INCB18424: Myelofibrosis. Results from our ongoing Phase II trial were the subject of oral presentations by the principal investigator at the American Society of Clinical Oncology meeting on June 2, 2008 and the European Hematology Association meeting on June 14, 2008. These presentations included data from 27 patients receiving 25 mg twice-daily and 12 patients receiving 10 mg twice-daily. Treatment with INCB18424 in these patients provided rapid reductions in splenomegaly and hepatomegaly, with mean organ size reductions of at least 50% in 71% of patients treated with 25 mg twice-daily and in 42% of patients treated with 10 mg twice-daily, as well as a greater than 50% reduction in constitutional symptoms, including fatigue, pruritus and night sweats in patients presenting these symptoms. INCB18424 was well tolerated at these doses. Adverse hematological effects of INCB18424 included grade 3 and 4 thrombocytopenia and anemia, seen in eight and two patients, respectively, with one patient experiencing both. These events were reversible and manageable through dose reduction and/or drug interruption in the majority of patients. Thrombocytopenia is a side effect that would be expected as a result of inhibition of JAK signaling.

We are continuing to expand this ongoing Phase II trial to further refine the dosing regimen and to assess a number of other potential endpoints for use in registration trials for INCB18424 in

myelofibrosis. This trial now includes over 100 patients, and we are seeking to enroll approximately 50 additional patients.

INCB18424: Polycythemia Vera and Essential Thrombocythemia. In the second quarter of 2008, we initiated an open-label multiple-dose Phase II trial to assess the safety and efficacy of INCB18424 in patients with advanced polycythemia vera and essential thrombocythemia. This multi-center trial is expected to include clinical sites in the United States and Europe, and is expected to enroll over 100 patients. Patients with polycythemia vera and essential thrombocythemia share many of the same symptoms as patients with myelofibrosis, including splenomegaly and the constitutional symptoms, fatigue, anemia, severe itching and an overall loss in the quality of their lives.

INCB18424: Rheumatoid Arthritis. In the first quarter of 2008, we completed the first treatment group of patients in a 28-day placebo-controlled dose-escalation Phase IIa trial, in which 12 patients received 15 mg twice-daily of INCB18424 and four received placebo. We have enrolled three additional treatment groups to evaluate two twice-daily doses and one once-daily dose. The results from the first treatment group were presented at the European League Against Rheumatism meeting on June 12, 2008. In these patients, INCB18424 was well tolerated and more effective than placebo in reducing the signs and symptoms of rheumatoid arthritis, as measured by the American College of Rheumatology, or ACR, improvement scores.

An ACR20 improvement score denotes a 20% improvement from the baseline assessment, based on the improvement in tender or swollen joint counts and improvement in three of five other criteria established by the American College of Rheumatology. ACR50, ACR70, and ACR90 improvement scores denote at least a 50% (ACR50) improvement, at least a 70% (ACR70) improvement, or at least a 90% (ACR90) improvement from the baseline assessment, based on the improvement in tender or swollen joint counts and improvement in three of the same five other criteria. ACR response rates seen after 28 days with INCB18424 were:

	INCB18424 (N=12)	Placebo (N=4)
% achieving ACR20	75	50
% achieving ACR50	50	0
% achieving ACR70	25	0
% achieving ACR90	17	0

There were no serious adverse events or patient withdrawals due to adverse events. Preliminary results from this Phase IIa trial have been accepted for oral presentation at the American Rheumatology Meeting, October 24-29, 2008.

INCB18424: Other Oncology Indications. We have initiated two Phase IIa trials, one in multiple myeloma patients and a second in hormone-refractory prostate cancer patients. We expect top-line data from these proof-of-concept trials later this year. Our abstract describing the preclinical effects of our JAK inhibitors in multiple myeloma was presented at the European Hematology Association meeting on June 15, 2008.

INCB18424: Psoriasis. In the first quarter of 2008, we completed a 28-day Phase IIa trial with a topical formulation of INCB18424 in mild-to-moderate psoriasis patients, in which the compound was well tolerated and provided comparable efficacy to the potent topical steroid, Diprolene. In addition, we completed three treatment groups in the 28-day sub-total inunction safety study of this topical formulation in which the compound continued to show efficacy and tolerability. Results from the 28-day Phase IIa trial were accepted for poster presentation at the European Academy of Dermatology and Venereology meeting in September 2008. We expect to initiate a

three-month Phase IIB trial with the topical formulation for this indication in the fourth quarter of 2008. We have decided to delay initiation of the 28-day Phase IIa trial in psoriasis with our orally administered JAK inhibitor until next year.

INCB28050: Follow-on compound for inflammation. In the second quarter of 2008, we completed the single-dose escalation Phase I trial of INCB28050 in healthy volunteers. INCB28050 was well tolerated and demonstrated appropriate pharmacokinetic and pharmacodynamic properties to begin a multiple dose escalation study.

11beta-HSD1 Inhibitor Program

We have developed a broad chemically-diverse series of novel proprietary oral inhibitors of 11 β HSD1, 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 11 β HSD1 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.

INCB13739: Type 2 Diabetes. Results from a 28-day Phase IIa trial of this compound in 32 patients with type 2 diabetes were presented by the principal investigator at the American Diabetes Association on June 9, 2008. Treatment with INCB13739, our orally bioavailable inhibitor of the 11 β HSD1 enzyme, significantly improved hepatic insulin sensitivity and decreased plasma LDL and total-cholesterol levels in these patients. Treatment with INCB13739 resulted in a placebo-adjusted mean 0.614 mg/kg/min decrease in glucose production (P = 0.018), indicating enhanced hepatic insulin sensitivity, and a mean 0.752 mg/kg/min trend toward increased insulin-stimulated glucose uptake (P = 0.177), an indicator of peripheral insulin sensitivity. Fasting blood tests were used to assess the secondary endpoints of the trial, plasma glucose concentrations and lipid profiles. INCB013739 treatment resulted in a trend toward reduced fasting plasma glucose (-19.5 mg/dL), with the treatment effect being of greater magnitude in patients with higher (greater than 160 mg/dL) baseline hyperglycemia (-45.0 mg/dL, P = 0.075), and a decrease in plasma total cholesterol (-26.9 mg/dL, P = 0.007) and LDL-cholesterol (-22.3 mg/dL, P = 0.001). INCB13739 was well tolerated over the course of the trial with no serious adverse events reported.

We initiated a three month Phase IIB trial in May 2008.

INCB20817: Type 2 Diabetes. We completed Phase I trials of this compound in the first quarter of 2008. Because we have observed positive results in our clinical trials with INCB13739, we do not currently plan to advance INCB20817 into Phase II development.

HM74a Agonist Program

HM74a is a G-protein-coupled receptor, or GPCR, that is expressed in adipocytes (fat cells). GPCRs are a large protein family of transmembrane receptors that sense molecules outside the cell, activate signal transduction pathways and, ultimately, cellular responses. GPCRs are involved in many diseases, and are the target of many existing drugs.

Agonism of HM74a by niacin causes a reduction in circulating free fatty acids, or FFAs. It is known that elevated levels of FFAs are associated with an increase in glucose production and a decrease in glucose uptake which leads to insulin resistance. While oral administration of niacin leads to a decrease in glucose production and an increase in glucose uptake, niacin treatments cannot be used to treat insulin resistance in type 2 diabetics because these compounds have very short half-lives that lead to intolerance and discomfort such as cutaneous flushing. Additionally, the short half-life of niacin treatments can cause FFA levels to rebound and actually lead to increased

glucose levels. In contrast to niacin containing treatments, our lead HM74a agonist, INCB19602, does not appear to cause flushing and has resulted in profound and sustained reductions in FFA levels without causing rebound. We therefore believe an HM74a agonist could prove to be an effective treatment for insulin resistance in type 2 diabetics without the adverse effect and limitations of niacin-containing treatments.

INCB19602: Type 2 Diabetes. In the first quarter of 2008, we completed Phase I trials in which the compound was well tolerated, lowered free fatty acids without rebound and did not produce the flushing seen with niacin and its derivatives. We have initiated a 28-day Phase IIa trial in type 2 diabetics that is expected to provide top-line proof-of-concept data early next year.

Sheddase Inhibitor Program

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, 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 currently available therapeutics 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 as a treatment of EGFR sensitive tumors.

INCB7839: Solid Tumors. This is in an ongoing dose-ranging study in a range of solid tumor types.

INCB7839: Breast Cancer. In the first quarter of 2008, we initiated a Phase II trial in combination with Herceptin with top-line results expected late this year.

CCR2 Receptor Antagonist Program for Inflammatory Diseases

CCR2 is a key chemokine receptor found on monocytes that controls their migration into sites of inflammation. Once inside the monocytes differentiate into tissue scavenger cells known as macrophages. In their normal role, macrophages scavenge foreign organisms or injured tissues; however, excessive or inappropriately triggered macrophage activity results in the production of pro-inflammatory mediators that can cause damage to tissues and can lead to a chronic

inflammatory response. There is substantial preclinical data from multiple academic centers suggesting that CCR2 antagonism could be of therapeutic benefit in multiple sclerosis, or MS. Activated macrophages accumulate in MS lesions, where they are associated with and presumed to be required for the destruction of the myelin sheath, the protective coating around the nerves which disrupts nerve signaling and leads to loss of muscle control, vision, balance and sensation. Blocking macrophage accumulation at these sites could thus lead to significant amelioration of this chronic and debilitating disease.

We established a collaborative research and license agreement with Pfizer Inc. in January 2006 in which Pfizer gained worldwide development and commercialization rights to our portfolio of CCR2 antagonist compounds. We retained rights to certain CCR2 antagonists for MS and lupus nephritis and other autoimmune nephritides.

INCB8696: Multiple Sclerosis. We have initiated a Phase I trial in healthy volunteers.

CCR5 Program for HIV

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. This decision reflects our objective to focus our resources on programs that we believe have the greatest near-term value.

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.

The Offering

Common stock offered by us	9,000,000 shares
Common stock to be outstanding after the offering	93,989,650 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.
The Nasdaq Global Market symbol	INCY

Information in the table above is based on 84,989,650 shares outstanding as of June 30, 2008. It does not include the following shares of our common stock as of June 30, 2008:

15,493,130 shares issuable upon the exercise of stock options outstanding with a weighted average exercise price of \$8.67 per share;

4,986,386 shares reserved for issuance and available for future grant or sale under our stock plans;

1,114,361 shares reserved for issuance under our employee stock purchase plan;

13,531,224 shares issuable upon conversion of our 3¹/₂% convertible senior notes due 2011;

22,284,625 shares issuable upon conversion of our 3¹/₂% 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 1,350,000 shares of common stock.

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.

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Our drug candidates in clinical trials are in early stage 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. 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

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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 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.

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 will be 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 expect that while we plan to conduct initial clinical trials on our drug candidates, we may need to seek collaborators for our drug candidates such as our chemokine receptor antagonists because of the expense, effort and expertise required to continue additional clinical trials and further develop those drug candidates. We may also seek 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. 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 or do not devote adequate resources to the program, 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.

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.

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 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.

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 Food and Drug Administration, or 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;

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

government or regulatory delays.

Regulatory authorities may delay or prevent the initiation of clinical trials for our drug candidates. For example, we may be unable to successfully complete discussions with the FDA regarding trial design, including agreement on appropriate dosing and specific endpoints, for the registration trials for our JAK inhibitor for myelofibrosis.

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. Our drug candidates in clinical trials are in early stage 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.

We may not obtain 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 currently intend to seek a special protocol assessment, or SPA, for the registration trials for our JAK inhibitor for myelofibrosis. The SPA process allows for 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. However, an SPA must be approved by the FDA before the trial can be initiated, and there is no guarantee that an SPA would be granted on a timely basis. Accordingly, if we submit a request for an SPA, the initiation of this trial may be delayed. If we believe that the submission of a request for an SPA will significantly delay the initiation of this trial, we may determine not to submit a request for an SPA. Without the FDA's concurrence on an SPA, we cannot be certain that the design, conduct and data analysis approach for this clinical trial will be sufficient to allow us to submit or receive approval of a JAK inhibitor for the treatment of myelofibrosis.

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 an 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.

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 the regulatory authority's approval.

We do not currently operate manufacturing facilities for clinical or commercial production of our drug candidates. We expect to continue to rely on third parties for the manufacture of our drug candidates and any drug products that we may develop. The FDA requires that drug products be manufactured according to its current Good Manufacturing Practices, or cGMP, regulations and a limited number of manufacturers comply with these requirements. If the other parties that we choose to manufacture our drug products are not compliant with cGMP, the FDA may not approve our application to manufacture our drug products. 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. Failure to comply with cGMP in the manufacture of our products could result in the FDA withdrawing or denying regulatory approval of our drug product or other enforcement actions.

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. Also, raw materials that may be required to manufacture any products we develop may only be available from a limited number of suppliers. 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. 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 might not be able to commercialize our drug candidates successfully, and we may spend significant time and money attempting to do so.

We have a limited number of drug candidates in early stage Phase I and Phase II clinical trials. 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. We recently 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 commercialize a product if the market does not accept the product because it is too expensive and 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.

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 intend to continue to explore opportunities to develop our clinical pipeline by in-licensing drug compounds that fit within our expertise and research and development capabilities. We may be unable to enter into any additional in-licensing agreements because suitable product candidates that are within our expertise may not be available to us on terms that are acceptable to us or because competitors with greater resources seek to in-license the same product candidates. Product candidates that we would like to develop may not be available to us because they are controlled by competitors who are unwilling to license the rights to the drug compound or candidate to us. In addition, we may enter into license agreements that are unsuccessful and our business and operations might be adversely affected by the termination of a drug candidate and termination and winding down of the related license agreement. For example, in April 2006, we announced the discontinuation of development of DFC and we gave notice of termination of our collaborative license agreement with Pharmasset, Inc., which licensed DFC to us. DFC was at the time our most advanced drug candidate. 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 candidates,

drug delivery technology or other technology or if these arrangements are unsuccessful, our research and development efforts could be adversely affected.

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 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.

We may encounter difficulties in integrating companies we acquire, which may harm our operations and financial results.

As part of our business strategy, we have in the past and may in the future acquire assets, technologies, compounds and businesses. Our past acquisitions, such as the acquisition of Maxia Pharmaceuticals, Inc. have involved, and our future acquisitions may involve, risks such as the following:

we may be exposed to unknown liabilities of acquired companies;

our acquisition and integration costs may be higher than we anticipated and may cause our quarterly and annual operating results to fluctuate;

we may experience difficulty and expense in assimilating the operations and personnel of the acquired businesses, disrupting our business and diverting our management's time and attention;

we may be unable to integrate or complete the development and application of acquired technology, compounds or drug candidates;

we may experience difficulties in establishing and maintaining uniform standards, controls, procedures and policies;

our relationships with key customers, suppliers or collaborative or license partners of acquired businesses may be impaired, due to changes in management and ownership of the acquired businesses;

we may be unable to retain key employees of the acquired businesses;

we may incur amortization or impairment expenses if an acquisition results in significant goodwill or other intangible assets;
or

our stockholders may be diluted if we pay for the acquisition with equity securities.

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 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 \$1.1 billion as of June 30, 2008. 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 2008 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. 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 or licensing of businesses, technologies or compounds, 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;

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. 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 would 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.

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 substantially all of our revenues for the six months ended June 30, 2008 from our collaborative research and license agreement with Pfizer and from licensing our intellectual property to others. We may be unable to enter into additional collaborative agreements. 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 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.

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, 2008, the aggregate principal amount of total consolidated debt was \$421.8 million and our stockholders' deficit was \$237.2 million. The documents pursuant to which our outstanding convertible senior and subordinated notes were issued do not limit the issuance of additional indebtedness. 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 debt service requirements with respect to our outstanding convertible senior notes and convertible subordinated notes. As of June 30, 2008, \$151.8 million aggregate principal amount of our 3¹/₂% convertible senior notes due 2011 was outstanding. Our annual interest payments, beginning in 2007, for the 3¹/₂% convertible 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, 2008, \$250.0 million aggregate principal amount of our 3¹/₂% convertible subordinated notes due 2011 was outstanding. Our annual interest payments for the 3¹/₂% convertible subordinated notes through 2010, 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, 2008, \$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.

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 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 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 new collaborative relationships by us or our competitors;

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;

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.

We intend generally to use the net proceeds from this offering for general corporate purposes, including research and development activities. 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 an assumed public offering price of \$9.18 per share, if you purchase shares of common stock in this offering, you will suffer immediate and substantial dilution of \$10.88 per share in the net tangible book value of the common stock. If the underwriters exercise their option to purchase additional shares in full, you will experience suffer immediate and substantial dilution of \$10.74 per share. See "Dilution" on page S-28 for a more detailed discussion of the dilution you will incur in this 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.

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.

In addition, our board of directors has adopted a stockholder rights plan, the provisions of which could make it more difficult for a potential acquirer of Incyte to consummate an acquisition transaction. Also, Section 203 of the Delaware General Corporation Law may prohibit large stockholders, in particular those owning 15% or more of our outstanding voting stock, from merging or consolidating with us. In connection with this offering, our board of directors has delegated to the disinterested members of the finance committee of our board of directors the authority to approve an amendment to the stockholder rights plan increasing the percentage of beneficial ownership that would trigger the operation of the plan from 15% to 20%. Under the stockholder rights plan, our board of directors has express authority to amend the rights plan without stockholder approval.

FORWARD-LOOKING STATEMENTS

This prospectus supplement, the accompanying prospectus, the documents we have filed with the SEC that are incorporated herein by reference and any free writing prospectuses we have authorized for use in connection with this offering 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 alliance 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 gene and genomics-related 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; our ability to in-license a potential drug compound or drug candidate; the cost of accessing, licensing or acquiring potential drug compounds or drug candidates developed by other companies; the costs of terminating any licensing or access arrangement for third party 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; 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 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 when needed; 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 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.

USE OF PROCEEDS

We estimate that the net proceeds from the sale of the 9,000,000 shares of our common stock that we are offering will be approximately \$77.3 million, after deducting the estimated underwriting discount and estimated offering expenses we expect to pay and assuming a public offering price of \$9.18 per share (based on the last reported sale price on July 29, 2008). If the underwriters exercise their over-allotment option in full, we estimate that the net proceeds will be approximately \$89.0 million. A \$1.00 increase or decrease in the assumed public offering price of \$9.18 per share would increase or decrease the net proceeds to us from this offering by \$8.5 million, assuming that the number of shares offered by us, as set forth on the cover page of this preliminary prospectus supplement, remains the same and after deducting the estimated underwriting discount and estimated offering expenses we expect to pay. We may also increase or decrease the number of shares we are offering. An increase of 100,000 shares in the number of shares offered by us, to a total of 9,100,000 shares, would increase the estimated net proceeds to us from this offering by approximately \$0.9 million. Similarly, a decrease of 100,000 shares in the number of shares offered by us, to a total of 8,900,000 shares, would decrease the estimated net proceeds to us from this offering by approximately \$0.9 million. We do not expect that a change in the offering price or the number of shares by these amounts would have a material effect on our uses of the proceeds from this offering, although it may impact the amount of time prior to which we will need to seek additional capital.

We intend to use the net proceeds of this offering for general corporate purposes, including research and development activities.

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.

DILUTION

Our net tangible book value (deficit) as of June 30, 2008 was approximately \$(237.4) million, or \$(2.79) 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 9,000,000 shares of our common stock offered in this offering, at an assumed public offering price of \$9.18 per share (based on the last reported sale price on July 29, 2008) 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, 2008 would have been \$(160.1) million, or \$(1.70) per share of our common stock. This represents an immediate increase in the net tangible book value of \$1.09 per share to our existing stockholders and an immediate and substantial dilution in net tangible book value of \$10.88 per share to new investors. The following table illustrates this per share dilution:

Assumed public offering price per share	\$ 9.18
Net tangible book value (deficit) per share	\$(2.79)
Increase per share attributable to new investors	1.09
Net tangible book value (deficit) per share after this offering	(1.70)
Dilution per share to new investors	\$ 10.88

A \$1.00 increase or decrease in the assumed public offering price of \$9.18 per share would increase or decrease our net tangible book value per share after this offering by \$0.09 per share and the dilution per share to new investors in this offering by \$0.91 per share, assuming that the number of shares offered by us, as set forth on the cover page of this preliminary prospectus supplement, remains the same and after deducting the estimated underwriting discount and estimated offering expenses we expect to pay. We may also increase or decrease the number of shares we are offering. An increase of 100,000 shares in the number of shares offered by us, to a total of 9,100,000 shares, would increase our net tangible book value per share after this offering by \$0.01 per share, and decrease the dilution per share to new investors in this offering by \$0.01 per share. Similarly, a decrease of 100,000 shares in the number of shares offered by us, to a total of 8,900,000 shares, would decrease our net tangible book value per share after this offering by \$0.01 per share, and increase the dilution per share to new investors in this offering by \$0.01 per share.

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 \$(1.56), which represents an increase in the net tangible book value of \$1.23 per share to our existing stockholders and an immediate dilution in net tangible book value of \$10.74 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, 2008, and does not take into effect further dilution to new investors that could occur as a result of:

15,493,130 shares of common stock issuable upon the exercise of stock options outstanding with a weighted average exercise price of \$8.67 per share;

4,986,386 shares of common stock available for future issuance under our stock plans;

1,114,361 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

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

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
2006		
First Quarter	\$ 6.25	\$5.01
Second Quarter	4.62	3.51
Third Quarter	5.20	3.85
Fourth Quarter	6.10	4.12
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 (through July 29, 2008)	9.34	7.01

On July 29, 2008, the last reported sale price for the common stock on The Nasdaq Global Market was \$9.18. As of June 30, 2008, there were approximately 315 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.

CAPITALIZATION

The following table shows our unaudited cash, cash equivalents and marketable securities and capitalization as of June 30, 2008:

on an actual basis; and

on an as adjusted basis to give effect to the sale of 9,000,000 shares of common stock in this offering at an assumed public offering price of \$9.18 per share (based on the last reported sale price on July 29, 2008), after deducting the estimated underwriting discount and estimated offering expenses we expect to pay.

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, 2008	
	Actual	As Adjusted
	(unaudited)	
	(in thousands)	
Cash, cash equivalents and short-term and long-term marketable securities	\$ 188,032	\$ 265,345
Long-term debt	\$ 391,279	\$ 391,279
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; 84,989,650 shares issued and outstanding actual, 93,989,650 shares issued and outstanding as adjusted	85	94
Additional paid-in capital	850,692	927,996
Accumulated other comprehensive loss	(1,857)	(1,857)
Accumulated deficit	(1,086,115)	(1,086,115)
Total stockholders' deficit	(237,195)	(159,882)
Total capitalization	\$ 154,084	\$ 231,397

The number of shares of common stock shown as issued and outstanding in the table above excludes, as of June 30, 2008:

15,493,130 shares issuable upon the exercise of stock options outstanding with a weighted average exercise price of \$8.67 per share;

4,986,386 shares reserved for issuance and available for future grant or sale under our stock plans;

1,114,361 shares reserved for issuance under our employee stock purchase plan;

13,531,224 shares issuable upon conversion of our 3¹/₂% convertible senior notes due 2011;

22,284,625 shares issuable upon conversion of our 3¹/₂% convertible subordinated notes due 2011;

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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.

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UNDERWRITING

The company and the underwriters named below have entered into an underwriting agreement with respect to the shares being offered. Subject to certain conditions, each underwriter has severally agreed to purchase the number of shares indicated in the following table. Goldman, Sachs & Co. is the representative of the underwriters.

Underwriters	Number of Shares
Goldman, Sachs & Co.	
Morgan Stanley & Co. Incorporated	
J.P. Morgan Securities Inc.	
Total	9,000,000

The underwriters are committed to take and pay for all of the shares being offered, if any are taken, other than the shares covered by the option described below unless and until this option is exercised.

If the underwriters sell more shares than the total number set forth in the table above, the underwriters have an option to buy up to an additional 1,350,000 shares from the company. They may exercise that option for a period of 30 days after the date of the underwriting agreement. If any shares are purchased pursuant to this option, the underwriters will severally purchase shares in approximately the same proportion as set forth in the table above.

The following table shows the per share and total underwriting discounts and commissions to be paid to the underwriters by the company. Such amounts are shown assuming both no exercise and full exercise of the underwriters' option to purchase 1,350,000 additional shares.

Paid by the Company

	No Exercise	Full Exercise
Per Share	\$	\$
Total	\$	\$

Shares sold by the underwriters to the public will initially be offered at the initial public offering price set forth on the cover of this prospectus supplement. Any shares sold by the underwriters to securities dealers may be sold at a discount of up to \$ per share from the initial public offering price. If all the shares are not sold at the initial public offering price, the representative may change the offering price and the other selling terms. The offering of the shares by the underwriters is subject to receipt and acceptance and subject to the underwriters' right to reject any order in whole or in part.

The company and its directors and executive officers have agreed with the underwriters, subject to certain exceptions, not to dispose of or hedge any of their common stock or securities convertible into or exchangeable for shares of common stock during the period from the date of this prospectus supplement continuing through the date 90 days after the date of this prospectus supplement, except with the prior written consent of the representative. This agreement does not apply to any existing employee benefit plans.

In connection with the offering, the underwriters may purchase and sell shares of common stock in the open market. These transactions may include short sales, stabilizing transactions and purchases to cover positions created by short sales. Short sales involve the sale by the underwriters of a greater number of shares than they are required to purchase in the offering. "Covered" short sales are sales made in an amount not greater than the underwriters' option to

purchase additional shares from the company in the offering. The underwriters may close out any covered short position by either exercising their option to purchase additional shares or purchasing shares in the open market. In determining the source of shares to close out the covered short position, the underwriters will consider, among other things, the price of shares available for purchase in the open market as compared to the price at which they may purchase additional shares pursuant to the option granted to them. "Naked" short sales are any sales in excess of such option. The underwriters must close out any naked short position by purchasing shares in the open market. A naked short position is more likely to be created if the underwriters are concerned that there may be downward pressure on the price of the common stock in the open market after pricing that could adversely affect investors who purchase in the offering. Stabilizing transactions consist of various bids for or purchases of common stock made by the underwriters in the open market prior to the completion of the offering.

The underwriters may also impose a penalty bid. This occurs when a particular underwriter repays to the underwriters a portion of the underwriting discount received by it because the representatives have repurchased shares sold by or for the account of such underwriter in stabilizing or short-covering transactions.

Purchases to cover a short position and stabilizing transactions, as well as other purchases by the underwriters for their own accounts, may have the effect of preventing or retarding a decline in the market price of the company's stock, and together with the imposition of the penalty bid, may stabilize, maintain or otherwise affect the market price of the common stock. As a result, the price of the common stock may be higher than the price that otherwise might exist in the open market. If these activities are commenced, they may be discontinued at any time. These transactions may be effected on The Nasdaq Global Market, in the over-the-counter market or otherwise.

European Economic Area

In relation to each Member State of the European Economic Area which has implemented the Prospectus Directive (each, a Relevant Member State), each underwriter has represented and agreed that with effect from and including the date on which the Prospectus Directive is implemented in that Relevant Member State (the Relevant Implementation Date) it has not made and will not make an offer of shares to the public in that Relevant Member State prior to the publication of a prospectus in relation to the shares which has been approved by the competent authority in that Relevant Member State or, where appropriate, approved in another Relevant Member State and notified to the competent authority in that Relevant Member State, all in accordance with the Prospectus Directive, except that it may, with effect from and including the Relevant Implementation Date, make an offer of shares to the public in that Relevant Member State at any time:

- (a) to legal entities which are authorized or regulated to operate in the financial markets or, if not so authorized or regulated, whose corporate purpose is solely to invest in securities;
- (b) to any legal entity which has two or more of (1) an average of at least 250 employees during the last financial year; (2) a total balance sheet of more than €43,000,000 and (3) an annual net turnover of more than €50,000,000, as shown in its last annual or consolidated accounts;
- (c) to fewer than 100 natural or legal persons (other than qualified investors as defined in the Prospectus Directive) subject to obtaining the prior consent of the representatives for any such offer; or
- (d) in any other circumstances which do not require the publication by the Company of a prospectus pursuant to Article 3 of the Prospectus Directive.

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For the purpose of this provision, the expression an "offer of shares to the public" in relation to any shares in any Relevant Member State means the communication in any form and by any means of sufficient information on the terms of the offer and the shares to be offered so as to enable an investor to decide to purchase or subscribe the shares, as the same may be varied in that Relevant Member State by any measure implementing the Prospectus Directive in that Relevant Member State and the expression Prospectus Directive means Directive 2003/71/EC and includes any relevant implementing measure in each Relevant Member State.

Each underwriter has represented and agreed that:

(a) it has only communicated or caused to be communicated and will only communicate or cause to be communicated an invitation or inducement to engage in investment activity (within the meaning of Section 21 of the Financial Services and Markets Act 2000, or FSMA) received by it in connection with the issue or sale of the shares in circumstances in which Section 21(1) of the FSMA does not apply to the company; and

(b) it has complied and will comply with all applicable provisions of the FSMA with respect to anything done by it in relation to the shares in, from or otherwise involving the United Kingdom.

The shares may not be offered or sold by means of any document other than (i) in circumstances which do not constitute an offer to the public within the meaning of the Companies Ordinance (Cap. 32, Laws of Hong Kong), (ii) to "professional investors" within the meaning of the Securities and Futures Ordinance (Cap. 571, Laws of Hong Kong) and any rules made thereunder, or (iii) in other circumstances which do not result in the documents being a "prospectus" within the meaning of the Companies Ordinance (Cap. 32, Laws of Hong Kong), and no advertisement, invitation or document relating to the shares may be issued or may be in the possession of any person for the purpose of issue (in each case whether in Hong Kong or elsewhere), which is directed at, or the contents of which are likely to be accessed or read by, the public in Hong Kong (except if permitted to do so under the Laws of Hong Kong) other than with respect to shares which are intended to be disposed of only to persons outside Hong Kong or only to "professional investors" within the meaning of the Securities and Futures Ordinance (Cap. 571, Laws of Hong Kong) and any rules made thereunder.

This prospectus supplement has not been registered as a prospectus with the Monetary Authority of Singapore. Accordingly, this prospectus supplement and any other document or material in connection with the offer or sale, or invitation for subscription or purchase, of the shares may not be circulated or distributed, nor may the shares be offered or sold, or be made the subject of an invitation for subscription or purchase, whether directly or indirectly, to persons in Singapore other than (i) to an institutional investor under Section 274 of the Securities and Futures Act, Chapter 289 of Singapore (the "SFA"), (ii) to a relevant person, or any person pursuant to Section 275(1A), and in accordance with the conditions, specified in Section 275 of the SFA or (iii) otherwise pursuant to, and in accordance with the conditions of, any other applicable provision of the SFA.

Where the shares are subscribed or purchased under Section 275 by a relevant person which is: (a) a corporation (which is not an accredited investor) the sole business of which is to hold investments and the entire share capital of which is owned by one or more individuals, each of whom is an accredited investor; or (b) a trust (where the trustee is not an accredited investor) whose sole purpose is to hold investments and each beneficiary is an accredited investor, shares, debentures and units of shares and debentures of that corporation or the beneficiaries' rights and interest in that trust shall not be transferable for 6 months after that corporation or that trust has acquired the shares under Section 275 except: (1) to an institutional investor under Section 274 of the SFA or to a relevant person, or any person pursuant to Section 275(1A), and in accordance

with the conditions, specified in Section 275 of the SFA; (2) where no consideration is given for the transfer; or (3) by operation of law.

The securities have not been and will not be registered under the Securities and Exchange Law of Japan (the Securities and Exchange Law) and each underwriter has agreed that it will not offer or sell any securities, directly or indirectly, in Japan or to, or for the benefit of, any resident of Japan (which term as used herein means any person resident in Japan, including any corporation or other entity organized under the laws of Japan), or to others for re-offering or resale, directly or indirectly, in Japan or to a resident of Japan, except pursuant to an exemption from the registration requirements of, and otherwise in compliance with, the Securities and Exchange Law and any other applicable laws, regulations and ministerial guidelines of Japan.

The company estimates that its share of the total expenses of the offering, excluding underwriting discounts and commissions, will be approximately \$350,000.

The company has agreed to indemnify the several underwriters and their controlling persons against certain liabilities, including liabilities under the Securities Act of 1933.

Certain of the underwriters and their respective affiliates have, from time to time, performed, and may in the future perform, various financial advisory and investment banking services for the company, for which they received or will receive customary fees and expenses.

LEGAL MATTERS

The validity of the shares of common stock offered by this prospectus supplement will be passed upon for us by Pillsbury Winthrop Shaw Pittman LLP. Certain legal matters in connection with this offering will be passed on for the underwriter by Ropes & Gray LLP, Boston, Massachusetts.

WHERE YOU CAN FIND MORE INFORMATION

We have filed a registration statement on Form S-3 with the SEC under the Securities Act of 1933. This prospectus supplement and the accompanying prospectus are part of the registration statement but the registration statement includes and incorporates by reference additional information and exhibits. We file annual, quarterly and current reports, proxy statements and other information with the SEC. You may read and copy the registration statement and any document we file with the SEC at the public reference room maintained by the SEC at 100 F Street, N.E., Washington, D.C. 20549. You may obtain information on the operation of the public reference room by calling the SEC at 1-800-SEC-0330. The SEC also maintains a web site that contains reports, proxy and information statements and other information regarding companies, such as ours, that file documents electronically with the SEC. The address of that site on the world wide web is <http://www.sec.gov>. The information on the SEC's web site is not part of this prospectus supplement or the accompanying prospectus, and any references to this web site or any other web site are inactive textual references only.

PROSPECTUS

INCYTE CORPORATION

Common Stock

We may, from time to time, offer and sell shares of our common stock in one or more offerings. We will specify in the accompanying prospectus supplement more specific information about any such offering.

We may offer shares of common stock directly to investors or through underwriters, dealers or agents. We will set forth the names of any underwriters, dealers or agents and their compensation in the accompanying prospectus supplement.

This prospectus may not be used to sell any of these securities unless accompanied by a prospectus supplement.

Our common stock is traded on The Nasdaq Global Market under the symbol "INCY." On July 28, 2008, the closing price of our common stock on The Nasdaq Global Market was \$8.97 per share.

Investing in our securities involves risks. See the section entitled "Risk Factors" in the accompanying prospectus supplement and in the documents we incorporate by reference in this prospectus.

Neither the Securities and Exchange Commission nor any state securities commission has approved or disapproved of these securities or passed upon the adequacy or accuracy of this prospectus. Any representation to the contrary is a criminal offense.

The date of this prospectus is July 29, 2008.

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You should rely only on the information incorporated by reference or provided in this prospectus, any prospectus supplement and the registration statement. We have not authorized anyone else to provide you with different information. If anyone provides you with different or inconsistent information, you should not rely on it. We are not making an offer to sell these securities in any state where the offer or sale is not permitted. You should assume that the information in this prospectus and any prospectus supplement, or incorporated by reference, is accurate only as of the dates of those documents. Our business, financial condition, results of operations and prospects may have changed since those dates.

ABOUT THIS PROSPECTUS

This prospectus is part of a registration statement that we filed with the Securities and Exchange Commission, or SEC, using a "shelf" registration, or continuous offering, process. Under this shelf registration process, we may, from time to time, issue and sell shares of our common stock in one or more offerings.

This prospectus describes our common stock and the general manner in which we will offer our common stock. Each time we offer shares of our common stock, we will provide a prospectus supplement that will contain specific information about the terms of that offering. Any prospectus supplement may also add, update or change information contained in this prospectus. Any statement that we make in this prospectus will be modified or superseded by any inconsistent statement made by us in a prospectus supplement. The registration statement we filed with the SEC includes exhibits that provide more detail of the matters discussed in this prospectus. You should read this prospectus and the related exhibits filed with the SEC and any prospectus supplement, together with additional information described under the heading "Where You Can Find More Information," before making your investment decision.

Unless the context otherwise requires, references in this prospectus and the accompanying prospectus supplement to "Incyte," "we," "us" and "our" refer to Incyte Corporation and its subsidiaries.

RISK FACTORS

Investing in our common stock involves risk. The prospectus supplement relating to a particular offering will contain a discussion of risks applicable to an investment in our common stock. Prior to making a decision about investing in our common stock, you should carefully consider the specific factors discussed under the heading "Risk Factors" in the applicable prospectus supplement together with all of the other information contained in the prospectus supplement or appearing or incorporated by reference in this prospectus.

INCYTE CORPORATION

Incyte is a drug discovery and development company focused on developing proprietary small molecule drugs to treat serious unmet medical needs. We have a pipeline with programs in oncology, inflammation, diabetes and human immunodeficiency virus.

Incyte was incorporated in Delaware in 1991. Our principal executive offices are located at Experimental Station, Route 141 & Henry Clay Road, Building E336, Wilmington, Delaware 19880, and our telephone number is (302) 498-6700.

FORWARD-LOOKING STATEMENTS

When used in this prospectus, the words "expects," "believes," "anticipates," "estimates," "may," "could," "intends," and similar expressions are intended to identify forward-looking statements. These statements are subject to known and unknown risks and uncertainties that could cause actual results to differ materially from those projected or otherwise implied by the forward-looking statements. These forward-looking statements speak only as of the date of this prospectus. Given these risks and uncertainties, you should not place undue reliance on these forward-looking statements. We will discuss many of these risks and uncertainties in greater detail in any prospectus supplement under the heading "Risk Factors." Additional cautionary statements or discussions of risks and uncertainties that could affect our results or the achievement of the expectations described in forward-looking statements may also be contained in the documents we incorporate by reference into this prospectus.

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These forward-looking statements speak only as of the date of this prospectus. We expressly disclaim any obligation or undertaking to release publicly any updates or revisions to any forward-looking statements contained herein to reflect any change in our expectations with regard thereto or any change in events, conditions or circumstances on which any such statement is based. You should, however, review additional disclosures we make in our Annual Report on Form 10-K, Quarterly Reports on Form 10-Q, and Current Reports on Form 8-K filed with the SEC.

USE OF PROCEEDS

Unless we state otherwise in the accompanying prospectus supplement, we intend to use the net proceeds from the sale of the shares of our common stock offered by this prospectus for research and development and other general corporate purposes. General corporate purposes may include additions to working capital, financing of capital expenditures, repayment or redemption of existing indebtedness, and future acquisitions and strategic investment opportunities. Pending the application of net proceeds, we expect to invest the net proceeds in investment grade, interest-bearing securities.

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. 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, 2008, there were 84,989,650 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, 2008, no shares of preferred stock were issued and outstanding. Of the authorized shares, 250,000 shares have been designated series A participating preferred stock, which have been authorized for issuance as described below. 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.

Stockholder Rights Plan

In September 1998, we adopted a stockholder rights plan. Under the rights plan, we will issue one right with respect to each share of common stock that is issued prior to the distribution date described below. Except as set forth below, each right, when exercisable, entitles the holder to purchase from us one one-thousandth of a share of our series A participating preferred stock at a price of \$100.00, subject to adjustment. The rights are not exercisable until a distribution date. Until a right is exercised, the holder of the right, as such, will have no rights as a stockholder of ours and will not have the right to vote or to receive dividends.

In general, the rights separate from the common stock and a "distribution date" will occur upon the earlier of:

the public announcement of the acquisition by a person or group of 15% or more of our common stock or

ten days after the commencement of, or public announcement of an intention to make, a tender offer or exchange offer that would result in the acquisition of 15% or more of our common stock.

If a person or group acquires 15% or more of our common stock, all rightholders except the buyer will be entitled to acquire our common stock at a discount and, under certain circumstances, to acquire shares of the acquiring company at a discount. Also, in the event our board of directors may authorize the exchange of all or part of the then outstanding and exercisable rights for shares of our common stock at a rate of one share of our common stock per right if the buyer has not acquired 50% or more of our common stock.

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Our board of directors may authorize the redemption of the rights, at a price of \$0.01 per right, at any time before a person or group acquires 15% or more of our common stock. The rights will expire on September 25, 2008.

On July 29, 2008, our board of directors approved a form of amendment to the rights plan that would increase the threshold of beneficial ownership that would trigger a distribution date under the rights plan from 15% to 20%. Our board delegated authority to effect the amendment to the finance committee of our board, with the intention that the amendment would become effective in connection with an offering of our common stock.

Certain Provisions of Delaware Law and of the Charter and Bylaws

The provisions of Delaware law, our certificate of incorporation and our bylaws described below may have the effect of delaying, deferring or discouraging another party from acquiring control of us.

Delaware Law. We are subject to the provisions of Section 203 of the Delaware General Corporation Law regulating corporate takeovers. In general, those provisions prohibit a Delaware corporation from engaging in any business combination with any interested stockholder for a period of three years following the date that the stockholder became an interested stockholder, unless:

the transaction is approved by the board before the date the interested stockholder attained that status;

upon consummation of the transaction that resulted in the stockholder becoming an interested stockholder, the interested stockholder owned at least 85% of the voting stock of the corporation outstanding at the time the transaction commenced; or

on or after the date the business combination is approved by the board and authorized at a meeting of stockholders by at least two-thirds of the outstanding voting stock that is not owned by the interested stockholder.

Section 203 defines "business combination" to include the following:

any merger or consolidation involving the corporation and the interested stockholder;

any sale, transfer, pledge or other disposition of 10% or more of the assets of the corporation involving the interested stockholder;

subject to certain exceptions, any transaction that results in the issuance or transfer by the corporation of any stock of the corporation to the interested stockholder;

any transaction involving the corporation that has the effect of increasing the proportionate share of the stock of any class or series of the corporation beneficially owned by the interested stockholder; or

the receipt by the interested stockholder of the benefit of any loans, advances, guarantees, pledges or other financial benefits provided by or through the corporation.

In general, Section 203 defines an interested stockholder as any entity or person beneficially owning 15% or more of the outstanding voting stock of the corporation and any entity or person affiliated with or controlling or controlled by any of these entities or persons.

A Delaware corporation may opt out of these provisions either with an express provision in its original certificate of incorporation or in an amendment to its certificate of incorporation or bylaws approved by its stockholders. However, we have not opted out, and do not currently intend to opt out of, these provisions. The statute could prohibit or delay mergers or other takeover or change in control attempts and, accordingly, may discourage attempts to acquire us.

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Charter and Bylaws. Our certificate of incorporation and bylaws provide that:

stockholders may not call special meetings of the stockholders or fill vacancies on the board;

our board of directors is authorized to issue preferred stock without stockholder approval; and

we will indemnify officers and directors against losses that they may incur in investigations and legal proceedings resulting from their services to us, which may include services in connection with takeover defense measures.

Transfer Agent

The transfer agent and registrar for our common stock is BNY Mellon Shareowner Services.

PLAN OF DISTRIBUTION

We may sell the securities offered by this prospectus to one or more underwriters or dealers for public offering and sale by them or to investors directly or through agents. The accompanying prospectus supplement will set forth the terms of the offering and the method of distribution and will identify any firms acting as underwriters, dealers or agents in connection with the offering, including:

the name or names of any underwriters, dealers or agents;

the purchase price of the securities and the proceeds to us from the sale;

any underwriting discounts and other items constituting compensation to underwriters, dealers or agents;

any public offering price;

any discounts or concessions allowed or reallocated or paid to dealers; and

any securities exchange or market on which the securities offered in the prospectus supplement may be listed.

Only those underwriters identified in such prospectus supplement are deemed to be underwriters in connection with the securities offered in the prospectus supplement.

The distribution of the securities may be effected from time to time in one or more transactions at a fixed price or prices, which may be changed, or at prices determined as the applicable prospectus supplement specifies. The securities may be sold through a rights offering, forward contracts or similar arrangements. In connection with the sale of the securities, underwriters, dealers or agents may be deemed to have received compensation from us in the form of underwriting discounts or commissions and also may receive commissions from securities purchasers for whom they may act as agent. Underwriters may sell the securities to or through dealers, and the dealers may receive compensation in the form of discounts, concessions or commissions from the underwriters or commissions from the purchasers for whom they may act as agent. Some of the underwriters, dealers or agents who participate in the securities distribution may engage in other transactions with, and perform other services for, us or our subsidiaries in the ordinary course of business.

We will provide in the applicable prospectus supplement information regarding any underwriting discounts or other compensation that we pay to underwriters or agents in connection with the securities offering, and any discounts, concessions or commissions which underwriters allow to dealers. Underwriters, dealers and agents participating in the securities distribution may be deemed to be underwriters, and any discounts and commissions they receive and any profit they realize on the resale of the securities may be deemed to be underwriting discounts

and commissions under the Securities Act of 1933. Underwriters and their controlling persons, dealers and agents may be entitled, under

agreements entered into with us, to indemnification against and contribution toward specific civil liabilities, including liabilities under the Securities Act.

In connection with an offering, the underwriters may purchase and sell securities in the open market. These transactions may include short sales, stabilizing transactions and purchases to cover positions created by short sales. Short sales involve the sale by the underwriters of a greater number of securities than they are required to purchase in an offering. Stabilizing transactions consist of bids or purchases made for the purpose of preventing or retarding a decline in the market price of the securities while an offering is in progress. The underwriters also may impose a penalty bid. This occurs when a particular underwriter repays to the underwriters a portion of the underwriting discount received by it because the underwriters have repurchased securities sold by or for the account of that underwriter in stabilizing or short-covering transactions. These activities by the underwriters may stabilize, maintain or otherwise affect the market price of the securities. As a result, the price of the securities may be higher than the price that otherwise might exist in the open market. If these activities are commenced, they may be discontinued by the underwriters at any time.

LEGAL MATTERS

The validity of the shares of common stock offered by this prospectus will be passed upon for us by Pillsbury Winthrop Shaw Pittman LLP.

EXPERTS

Ernst & Young LLP, independent registered public accounting firm, has audited our consolidated financial statements and schedule appearing in our Annual Report on Form 10-K for the year ended December 31, 2007, and the effectiveness of our internal control over financial reporting as of December 31, 2007, as set forth in their reports, which are incorporated by reference in this prospectus and elsewhere in this registration statement. Our consolidated financial statements and schedule are incorporated by reference in reliance on Ernst & Young LLP's reports, given on their authority as experts in accounting and auditing.

WHERE YOU CAN FIND MORE INFORMATION

We have filed a registration statement on Form S-3 with the SEC under the Securities Act of 1933. This prospectus is part of the registration statement but the registration statement includes and incorporates by reference additional information and exhibits. We file annual, quarterly and current reports, proxy statements and other information with the SEC. You may read and copy the registration statement and any document we file with the SEC at the public reference room maintained by the SEC at 100 F Street, N.E., Washington, D.C. 20549. You may obtain information on the operation of the public reference room by calling the SEC at 1-800-SEC-0330. The SEC also maintains a web site that contains reports, proxy and information statements and other information regarding companies, such as ours, that file documents electronically with the SEC. The address of that site on the world wide web is <http://www.sec.gov>. The information on the SEC's web site is not part of this prospectus, and any references to this web site or any other web site are inactive textual references only.

The SEC permits us to "incorporate by reference" the information contained in documents we file with the SEC, which means that we can disclose important information to you by referring you to those documents rather than by including them in this prospectus. Information that is incorporated by reference is considered to be part of this prospectus and you should read it with the same care that you read this prospectus. Later information that we file with the SEC will automatically update and supersede the information that is either contained, or incorporated by reference, in this prospectus, and

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will be considered to be a part of this prospectus from the date those documents are filed. We have filed with the SEC, and incorporate by reference in this prospectus:

our Annual Report on Form 10-K for the year ended December 31, 2007;

our Quarterly Report on Form 10-Q for the quarter ended March 31, 2008;

our Current Reports on Form 8-K filed February 14, 2008 and May 22, 2008;

the description of our common stock contained in our Registration Statement on Form 8-A filed January 5, 1996, including any amendment or report filed for the purpose of updating such description; and

the description of our series A participating preferred stock purchase rights contained in our Registration Statement on Form 8-A filed September 30, 1998.

We also incorporate by reference all additional documents that we file with the SEC under the terms of Sections 13(a), 13(c), 14 or 15(d) of the Exchange Act that are made after the initial filing date of the registration statement of which this prospectus is a part and the effectiveness of the registration statement, as well as between the date of this prospectus and the termination of any offering of securities offered by this prospectus. We are not, however, incorporating, in each case, any documents or information that we are deemed to furnish and not file in accordance with SEC rules.

You may request a copy of any or all of the documents incorporated by reference but not delivered with this prospectus, at no cost, by writing or telephoning us at the following address and number: Investor Relations, Incyte Corporation, Experimental Station, Route 141 & Henry Clay Road, Building E336, Wilmington, DE 19880, telephone (302) 498-6700. We will not, however, send exhibits to those documents, unless the exhibits are specifically incorporated by reference in those documents.

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9,000,000 Shares

Incyte Corporation

Common Stock

PROSPECTUS SUPPLEMENT

Goldman, Sachs & Co.

Morgan Stanley

JPMorgan

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