INCYTE CORP
Form 10-K
March 06, 2008

Use these links to rapidly review the document
Table of Contents

UNITED STATES
SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

FORM 10-K

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

For the fiscal year ended December 31, 2007

or

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

For the transition period from to

Commission File Number: 0-27488

INCYTE CORPORATION

(Exact name of registrant as specified in its charter)

Delaware	**94-3136539**
(State of other jurisdiction of incorporation or organization)	(IRS Employer Identification No.)
Experimental Station, Route 141 & Henry Clay Road, Building E336, Wilmington, DE 19880	**(302) 498-6700**
(Address of principal executives offices)	(Registrant's telephone number, including area code)

Securities registered pursuant to Section 12(b) of the Act:

Title of each class	**Name of exchange on which registered**
Common Stock, par value $.001 per share	The NASDAQ Stock Market LLC
Series A Participating Preferred Stock Purchase Rights	The NASDAQ Stock Market LLC

Securities registered pursuant to Section 12(g) of the Act:

None

Indicate by check mark if the registrant is a well-known seasoned issuer, as defined in Rule 405 of the Securities Act. Yes ý No o

Indicate by check mark if the registrant is not required to file reports pursuant to Section 13 or Section 15 (d) of the Exchange Act. Yes o No ý

Indicate by check mark whether the registrant (1) has filed all reports required to be filed by Section 13 or 15(d) of the Securities Exchange Act of 1934 during the preceding 12 months (or for such shorter period that the registrant was required to file such reports), and (2) has been subject to such filing requirements for the past 90 days. Yes ý No o

Indicate by check mark if disclosure of delinquent filers pursuant to Item 405 of Regulation S-K (Section 229.405 of this chapter) is not contained herein, and will not be contained, to the best of registrant's knowledge, in definitive proxy or information statements incorporated by reference in Part III of this Form 10-K or any amendment to this Form 10-K. ý

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer or a smaller reporting company. See definitions of "large accelerated filer", "accelerated filer" and "smaller reporting company" in Rule 12b-2 of the Exchange Act.

Large accelerated filer o	Accelerated filer ý	Non-accelerated filer o (Do not check if a smaller reporting company)	Smaller reporting company o

Indicate by check mark whether the registrant is a shell company (as defined in Rule 12b-2 of the Exchange Act). Yes o No ý

The aggregate market value of Common Stock held by non-affiliates (based on the closing sale price on The Nasdaq Global Market on June 30, 2007) was approximately $443.3 million.

As of February 28, 2008 there were 84,618,917 shares of Common Stock, $.001 per share par value, outstanding.

DOCUMENTS INCORPORATED BY REFERENCE

Items 10 (as to directors and Section 16(a) Beneficial Ownership Reporting Compliance), 11, 12, 13 and 14 of Part III incorporate by reference information from the registrant's proxy statement to be filed with the Securities and Exchange Commission in connection with the solicitation of proxies for the registrant's 2008 Annual Meeting of Stockholders to be held on May 22, 2008.

Table of Contents

Item 1. ***Business***

This report contains forward-looking statements that involve risks and uncertainties. These statements relate to future periods, future events or our future operating or financial plans 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 U.S. Food and Drug Administration, or FDA, 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;

our history of operating losses; and

the risks set forth under "Risk Factors."

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.

In this report all references to "Incyte," "we," "us" or "our" mean Incyte Corporation and our subsidiaries, except where it is made clear that the term means only the parent company.

Incyte is our registered trademark. We also refer to trademarks of other corporations and organizations in this Annual Report on Form 10-K.

Overview

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).

Thus far in our drug discovery and development activities, which began in early 2002, we have filed twelve Investigational New Drug Applications (INDs) and have progressed eight internally developed proprietary compounds into clinical development. Currently, four of these compounds have advanced into Phase II clinical trials. Our wholly-owned pipeline includes the following compounds:

Drug Target	Drug Compound	Indication	Development Status
JAK	*INCB18424 (Oral)*	Myelofibrosis	Phase IIa
		Rheumatoid Arthritis	Phase IIa
		Refractory Prostate Cancer	Phase IIa
		Multiple Myeloma	Phase IIa
		Psoriasis	Phase I
	INCB18424 (Topical)	Psoriasis	Phase IIa
	INCB28050	Rheumatoid Arthritis	Preclinical
HSD1	*INCB13739*	Type 2 Diabetes	Phase IIa
	INCB20817	Type 2 Diabetes	Phase I
HM74a	*INCB19602*	Type 2 Diabetes	Phase I
CCR5	*INCB9471*	HIV	Phase II
		HIV	Phase I

Drug Target	Drug Compound	Indication	Development Status
	INCB15050		
Sheddase	*INCB7839*	Solid Tumors Breast Cancer	Phase IIa Phase II
CCR2	*INCB8696*	Multiple Sclerosis	Phase I
Other Lead clinical candidate Lead clinical candidate		Oncology Oncology	Pre-clinical Pre-clinical

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 (CROs), 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.

Incyte's Approach to Drug Discovery and Development

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.

We select drug targets with strong preclinical or clinical validation in areas where we have the potential to generate either first-in-class molecules or compounds that are highly differentiated from existing treatments.

Our chemistry and biology efforts are highly integrated and are characterized by the rapid generation of relevant data on a broad and diverse range of compounds for each therapeutic target we pursue. This process allows our scientists to better understand, in real time, the potency and selectivity of the compounds, how they are likely to be absorbed and eliminated in the body, and to assess the potential safety of the compounds. We believe that this approach, along with stringent criteria for the selection of clinical candidates, will help us to select appropriate candidates for clinical development and rapidly assess key characteristics required for success.

Given our chemistry-driven discovery process, our pipeline has grown to encompass multiple therapeutic areas: oncology, inflammation, diabetes and HIV. While our productivity has created a diverse pipeline, we conduct a limited number of discovery programs in parallel at any one time. This focus allows us to allocate resources to our selected programs at a level that we believe is competitive with much larger pharmaceutical companies. We believe this level of resource allocation, applied to the discovery process outlined above, has been critical to our success in our current programs, and that it remains a meaningful competitive advantage.

Additionally, in all of our programs we strive to generate a diverse and broad range of proprietary compounds which we believe enhances the overall probability of success for our programs and creates the potential for multiple products.

Once our compounds reach clinical development, our objective, whenever possible, is to rapidly progress the lead candidate into a proof-of-concept clinical trial prior to initiating larger definitive Phase IIb clinical trials to quickly assess the therapeutic potential of the clinical candidate itself and its underlying mechanism. This information is then used to evaluate the commercial potential of the compound and the most appropriate indication or indications to pursue.

Incyte's Development Teams

Our development teams are responsible for ensuring that our clinical candidates are expeditiously progressed from preclinical development and IND-enabling studies into Phase I and Phase II development. To efficiently and effectively keep pace with the growth in our clinical pipeline, we have added new members to the development teams by internal transfers and by recruiting new employees

with expertise in drug development including clinical trial design, statistics, regulatory affairs, and project management. We have also built core internal process chemistry and formulation teams using this same strategy. Our internal multi-disciplinary project teams also work with experienced external CROs with expertise in managing clinical trials, process chemistry, product formulation, and the manufacture of clinical trial supplies to support our drug development efforts.

Clinical Pipeline

Our pipeline includes compounds in various stages of development in the areas of oncology, inflammation, diabetes and HIV. The following summarizes the status of and rationale for our most advanced compounds.

JAK 2 Program for Inflammation, Hematologic Malignancies, and Solid Tumors

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

We have discovered multiple potent, selective 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 of these conditions, including MF, RA and psoriasis. A lead follow-on JAK inhibitor compound, INCB28050, is expected to enter clinical trials in 2008.

Thus far, our clinical trial results with INCB18424 include positive interim results from several Phase IIa clinical trials in MF, RA and psoriasis patients and the compound has been well tolerated.

Myelofibrosis

In December 2007, we reported positive interim results involving 11 MF patients from a dose-escalation Phase Ib/IIa trial with orally administered INCB18424. We also announced that we reached a maximum tolerated dose in this first Phase Ib/IIa trial and have expanded the study to include an additional 21 patients at this dose. If the compound continues to be well tolerated and demonstrates comparable efficacy in additional patients, we intend to begin discussions with the Food and Drug Administration (FDA) to define the potential registration pathway for INCB18424 as a treatment for MF. Provided the FDA agrees with our development plan, our objective is to initiate these trials in the second half of 2008.

Rheumatoid Arthritis

In January 2008, we announced positive interim results from a 28-day Phase IIa dose-ranging trial using the oral formulation of INCB18424 in six RA patients whose conditions were not well-controlled with their existing therapy. This trial is expected to involve a total of 48 patients with final results expected in the first half of 2008. Provided these results are positive, we plan to begin a six-month Phase IIb trial in RA patients in the second half of 2008.

Psoriasis (Topical)

In September 2007, we announced positive interim results from a 28-day Phase IIa dose-escalation trial with topical INCB18424, involving 24 patients with mild-to-moderate psoriasis. In this trial the compound was well tolerated with no adverse events reported at any dose administered and with rapid and sustained improvement observed in all subjects. These results suggest that topical intervention in the JAK pathway could be an effective way to treat psoriasis. If the compound continues to be well tolerated in the ongoing safety studies, we expect to begin a three-month Phase IIb trial in psoriasis using this topical formulation in the second half of 2008.

Refractory Prostate Cancer and Multiple Myeloma

We recently initiated Phase IIa clinical trials in refractory prostate cancer patients, as well as patients with multiple myeloma. Results from these trials are expected in the second half of 2008.

We intend to complete our IND-enabling studies and initiate Phase I clinical trials with our follow-on JAK inhibitor compound INCB28050 in mid-2008.

11ßHSD1 Program for Type 2 Diabetes and Related Disorders

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

In September 2007, we reported positive interim results from the ongoing 28-day Phase IIa placebo-controlled clinical trial in type 2 diabetes. In the patients included in this interim analysis, we observed positive effects on multiple clinically relevant endpoints such as fasting plasma glucose and on dyslipidemia, including reduction of LDL, total cholesterol and triglycerides. A three-month Phase IIb trial in type 2 diabetes is scheduled to begin in the first half of 2008.

For INCB20817, our follow on 11ßHSD1 compound, the Investigational New Drug Application (IND) has been accepted and Phase I trials are expected to begin in the first half of 2008.

HM74a for Type 2 Diabetes

HM74a is a G-protein-coupled receptor (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 (FFA). 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 level. In contrast to niacin containing treatments, our lead HM74a agonist, INCB19602, which is in Phase I clinical trials in healthy volunteers, 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. If the results from the Phase I trials continue to support development of INCB19602, we intend to begin a 28-day Phase IIa clinical trial in type 2 diabetics in the first half of 2008.

CCR5 Antagonist Program for HIV

CCR5 is a major chemokine receptor that the HIV virus uses to enter CD4 cells, which are critical to the human immune system. CCR5 antagonists belong to a new class of antiretrovirals known as HIV entry inhibitors. This new class includes various experimental compounds designed to block cell surface receptors, such as CCR5 or CXCR4, as well as other novel compounds that block HIV fusion with the cell surface. Entry inhibitors work by blocking HIV before the virus enters the cell and begins its replication process. In contrast, existing HIV drugs such as nucleoside or nucleotide reverse transcriptase inhibitors (NRTIs), non-nucleoside reverse transcriptase inhibitors (NNRTIs) and protease inhibitors work inside the cell and target the proteins, reverse transcriptases and proteases that are involved in the replication of the virus.

Our CCR5 antagonist program has yielded potent, selective, proprietary compounds with pharmacokinetic properties that have the potential to allow once-daily dosing without use of ritonavir boosting, a key distinction from other CCR5 antagonists. Ritonavir is a protease inhibitor that is often used in combination with other drugs to improve or 'boost' the bioavailability and cellular penetration of other drugs but which is associated with increased cardiovascular risk. This dosing profile is particularly attractive in patients who are in the earlier stages of disease, where CCR5 is most prevalent, where the majority of regimens are once-daily (which improves patient compliance), and where ritonavir, which increases the risk of cardiovascular disease, is less frequently used. Once-a-day dosing also offers the potential for the development of once-daily fixed dose combination formulations with other anti-HIV medications.

We have two CCR5 antagonists in development, INCB9471 and INCB15050. INCB9471 is the most advanced compound in this program. Thus far, from a 14-day Phase IIa clinical trial, we have seen positive results demonstrating that once-daily dosing with INCB9471 offers sustained inhibition of viral replication. This suggests that INCB9471 may provide an advantage over other CCR5 antagonists in development and other antiretroviral drugs that have shorter half-lives, less than 24 hours, especially in patients who are intermittently non-compliant with their medications. Lack of adherence with drugs that have short half lives can lead to insufficient drug levels, which reduces the effectiveness of the drug regimen and allows the virus to replicate. We are conducting several required drug interaction studies and completing longer-term safety studies with INCB9471 to support initiation of two Phase IIb trials in treatment-experienced HIV patients.

Our follow-on CCR5 antagonist, INCB15050, has completed Phase I development. While the results from the Phase I clinical trials suggest that INCB15050 also has the potential to be a potent once-a-day treatment, based on the positive Phase IIa clinical trial data that we have seen with the lead compound, INCB9471, we do not plan to advance INCB15050 beyond Phase I clinical trials at this time.

Sheddase Inhibitor Program for Solid Tumors

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

The signaling pathways that utilize the receptors and ligands of the epidermal growth factor receptor (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. INCB7839, the lead compound from this program, is currently in Phase II development. The first of two Phase II trials has been initiated and is designed to determine the effectiveness of INCB7839 when used in combination with Herceptin. A second Phase II trial in breast cancer patients is planned that will evaluate INCB7839 as a monotherapy.

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 (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. ("Pfizer) 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.

We are pursuing MS first given the preclinical evidence suggesting that selective CCR2 antagonism has therapeutic potential in this disease. We have selected a lead clinical candidate, INCB8696, and initiated a Phase I clinical trial in healthy volunteers in 2007.

Discovery

We have a number of early discovery programs at various stages of preclinical testing, including two lead clinical candidates in oncology. We do not typically disclose these programs and/or targets until we have successfully completed preclinical toxicology tests with the lead clinical candidate.

Commercial Strategy

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 for our CCR2 antagonist program.

Collaborative Research and License Agreement with Pfizer

Effective in January 2006, we entered a collaborative research and license agreement with Pfizer for the pursuit of our CCR2 antagonist program. We received an upfront nonrefundable payment of $40.0 million in January 2006. In addition, we received an aggregate of $20.0 million through the purchase of convertible subordinated notes, $10.0 million in February 2006 and $10.0 million in October 2007, and we are eligible to receive additional future development and milestone payments of up to $740.0 million for the successful development and commercialization of CCR2 antagonists in multiple indications, as well as royalties on worldwide sales. We received a $3.0 million milestone payment from Pfizer in 2007. Pfizer gained worldwide development and commercialization rights to our portfolio of CCR2 antagonist compounds, the most advanced of which was in Phase IIa clinical trials in rheumatoid arthritis and insulin-resistant obese patients at the time the agreement became effective in January 2006. Pfizer's rights extend to the full scope of potential indications, with the exception of multiple sclerosis and lupus nephritis and other autoimmune nephritides, for which we retained worldwide rights, along with certain compounds. We do not have obligations to Pfizer on preclinical development candidates we select for pursuit in these indications.

Patents and Other Intellectual Property

We regard the protection of patents and other enforceable intellectual property rights that we own or license as critical to our business and competitive position. Accordingly, we rely on patent, trade secret and copyright law, as well as nondisclosure and other contractual arrangements, to protect our intellectual property. We have established a patent portfolio of owned or in-licensed patents and patent applications that cover aspects of all our drug candidates, as well as other patents and patent applications that relate to full-length genes and genomics-related technologies obtained as a result of our past high-throughput gene sequencing efforts. The patents and patent applications relating to our drug candidates generally include claims directed to the drug candidates, methods of using the drug candidates, formulations of the drug candidates, and methods of manufacturing the drug candidates. Our policy is to pursue patent applications on inventions and discoveries we believe that are commercially important to the development and growth of our business.

Patents extend for varying periods according to the date of patent filing or grant and the legal term of patents in the various countries where patent protection is obtained. The actual protection afforded by a patent, which can vary from country to country, depends on the type of patent, the scope of its coverage and the availability of legal remedies in the country.

We have a number of established patent license agreements relating to our gene patent portfolio and our genomics-related technology patent portfolio. We are presently receiving royalties and other payments under certain of our gene and genomics-related patent license agreements. Under our gene patent license agreements, we may in the future receive royalties and other payments if our partners are successful in their efforts to discover drugs and diagnostics under these license agreements.

We may seek to license rights relating to compounds or technologies in connection with our drug discovery and development programs. Under these licenses, we may be required to pay up-front fees, license fees, milestone payments and royalties on sales of future products.

Although we believe our rights under patents and patent applications provide a competitive advantage, the patent positions of pharmaceutical and biotechnology companies are highly uncertain and involve complex legal and factual questions. We may not be able to develop patentable products or processes, and may not be able to obtain patents in the United States or elsewhere from pending applications. Even if patent claims are allowed, the claims may not issue, or in the event of issuance, may not be valid or enforceable or may not be sufficient to protect the technology owned by or licensed to us or provide us with a competitive advantage. Any patent or other intellectual property rights that we own or obtain may be circumvented, challenged or invalidated by our competitors. Others may have patents that relate to our business or technology and that may prevent us from marketing our product candidates unless we are able to obtain a license to those patents. In addition, litigation or other proceedings may be necessary to defend against claims of infringement, to enforce patents, to protect our other intellectual property rights, to determine the scope and validity of the proprietary rights of third parties or to defend ourselves in patent or other intellectual property right suits brought by third parties. We could incur substantial costs in such litigation or other proceedings. An adverse outcome in any such litigation or proceeding could subject us to significant liability.

With respect to proprietary information that is not patentable, and for inventions for which patents are difficult to enforce, we rely on trade secret protection and confidentiality agreements to protect our interests. While we require all employees, consultants and potential business partners to enter into confidentiality agreements, we may not be able to adequately protect our trade secrets or other proprietary information. Others may independently develop substantially equivalent proprietary information and techniques or otherwise gain access to our trade secrets.

Competition

Our drug discovery and development activities face, and will continue to face, intense competition from organizations such as pharmaceutical and biotechnology companies, as well as academic and research institutions and government agencies. Our major competitors include fully integrated pharmaceutical companies that have extensive drug discovery efforts and are developing novel small molecule pharmaceuticals. We face significant competition from organizations that are pursuing pharmaceuticals that are competitive with our potential products.

Many companies and institutions, either alone or together with their collaborative partners, have substantially greater financial resources and larger research and development staffs than we do. In addition, many competitors, either alone or together with their collaborative partners, have significantly greater experience than we do in:

drug discovery;

developing products;

undertaking preclinical testing and clinical trials;

obtaining FDA and other regulatory approvals of products; and

manufacturing, marketing, distributing and selling products.

Accordingly, our competitors may succeed in obtaining patent protection, receiving FDA approval or commercializing products before we do. If we commence commercial product sales, we will be competing against companies with greater manufacturing, marketing, distributing and selling capabilities, areas in which we have limited or no experience.

In addition, any drug candidate that we successfully develop may compete with existing therapies that have long histories of safe and effective use. Competition may also arise from:

- other drug development technologies and methods of preventing or reducing the incidence of disease;
- new small molecules; or
- other classes of therapeutic agents.

Developments by others may render our drug candidates obsolete or noncompetitive. We face and will continue to face intense competition from other companies for collaborative arrangements with pharmaceutical and biotechnology companies, for establishing relationships with academic and research institutions and for licenses to proprietary technology. These competitors, either alone or with their collaborative partners, may succeed in developing products that are more effective than ours.

Our ability to compete successfully will depend, in part, on our ability to:

- develop proprietary products;
- develop and maintain products that reach the market first, are technologically superior to and/or are of lower cost than other products in the market;
- attract and retain scientific and product development personnel;
- obtain patent or other proprietary protection for our products and technologies;
- obtain required regulatory approvals; and
- manufacture, market, distribute and sell any products that we develop.

In a number of countries, including in particular, developing countries, government officials and other groups have suggested that pharmaceutical companies should make drugs available at a low cost. In some cases, governmental authorities have indicated that where pharmaceutical companies do not do so, their patents might not be enforceable to prevent generic competition. Some major pharmaceutical companies have greatly reduced prices for their drugs in certain developing countries. If certain countries do not permit enforcement of any of our patents, sales of our products in those countries, and in other countries by importation from low-price countries, could be reduced by generic competition or by parallel importation of our product. Alternatively, governments in those countries could require that we grant compulsory licenses to allow competitors to manufacture and sell their own versions of our products in those countries, thereby reducing our product sales, or we could respond to governmental concerns by reducing prices for our products. In all of these situations, our results of operations could be adversely affected.

Government Regulation

Our related ongoing research and development activities and any manufacturing and marketing of our potential small molecule products to treat major medical conditions are subject to extensive regulation by numerous governmental authorities in the United States and other countries. Before marketing in the United States, any drug developed by us must undergo rigorous preclinical testing and clinical trials and an extensive regulatory clearance process implemented by the FDA under the United States Food, Drug and Cosmetic Act. The FDA regulates, among other things, the development, testing, manufacture, safety, efficacy, record-keeping, labeling, storage, approval, advertising, promotion, sale and distribution of these products. None of our drug candidates has, to date, been submitted for approval for sale in the United States or any foreign market. The regulatory review and approval process, which includes preclinical testing and clinical trials of each drug candidate, is lengthy, expensive and uncertain. Securing FDA approval requires the submission of extensive preclinical and

13

clinical data and supporting information to the FDA for each indication to establish a drug candidate's safety and efficacy. The approval process takes many years, requires the expenditure of substantial resources, involves post-marketing surveillance and may involve ongoing requirements for post-marketing studies. Before commencing clinical investigations in humans, we must submit to, and receive approval from, the FDA of an IND application. The steps required before a drug may be marketed in the United States include:

- preclinical laboratory tests, animal studies and formulation studies;
- submission to the FDA of an IND for human clinical testing, which must become effective before human clinical trials may commence;
- adequate and well-controlled clinical trials in three phases, as described below, to establish the safety and efficacy of the drug for each indication;
- submission to the FDA of a new drug application, or NDA, which must become effective before marketing can commence;
- satisfactory completion of an FDA inspection of the manufacturing facility or facilities at which the drug is produced to assess compliance with current good manufacturing practices; and
- FDA review and approval of the NDA.

Similar requirements exist within many foreign agencies as well. The time required to satisfy FDA requirements or similar requirements of foreign regulatory agencies may vary substantially based on the type, complexity and novelty of the product or the targeted disease.

Preclinical testing includes laboratory evaluation of product chemistry, toxicity and formulation, as well as animal studies. The results of the preclinical tests, together with manufacturing information and analytical data, are submitted to the FDA as part of an IND. An IND will automatically become effective 30 days after receipt by the FDA, unless before that time, the FDA raises concerns or questions about issues such as the conduct of the clinical trials as outlined in the IND. In the latter case, the IND sponsor and the FDA must resolve any outstanding FDA concerns or questions before clinical trials can proceed. We cannot be sure that submission of an IND will result in the FDA allowing clinical trials to commence.

Clinical trials involve the administration of the investigational drug to human subjects under the supervision of qualified investigators. Clinical trials are conducted under protocols detailing the objectives of the study, the parameters to be used in monitoring safety and the effectiveness criteria to be evaluated. Each protocol must be submitted to the FDA as part of the IND and each trial must be reviewed and approved by an independent ethics committee or institutional review board (IRB) before it can begin.

Clinical trials typically are conducted in three sequential phases, but the phases may overlap or be combined. Phase I usually involves the initial introduction of the investigational drug into healthy volunteers to evaluate its safety, dosage tolerance, absorption, metabolism, distribution and excretion, and, if possible, to gain an early indication of its effectiveness. Phase II usually involves clinical trials in a limited patient population to:

- evaluate dosage tolerance and optimal dosage;
- identify possible adverse effects and safety risks; and
- evaluate and gain preliminary evidence of the efficacy of the drug for specific indications.

Phase III clinical trials usually further evaluate clinical efficacy and safety by testing the drug in its final form in an expanded patient population, providing statistical evidence of efficacy and safety and providing an adequate basis for physician labeling. We cannot guarantee that Phase I, Phase II or

Phase III testing will be completed successfully within any specified period of time, if at all. Furthermore, we or the FDA may suspend clinical trials at any time on various grounds, including a finding that the subjects or patients are being exposed to an unacceptable health risk.

Even after initial FDA approval has been obtained, further studies, including post-approval trials, may be required to provide additional data on safety and will be required to gain approval for the sale of a product as a treatment for clinical indications other than those for which the product was initially tested and approved. Also, the FDA will require post-approval reporting to monitor the side effects of the drug. Results of post-approval programs may limit or expand the indications for which the drug product may be marketed. Further, if there are any requests for modifications to the initial FDA approval for the drug, including changes in indication, manufacturing process, labeling or manufacturing facilities, a supplemental NDA may be required to be submitted to the FDA.

Clinical trials must meet requirements for IRB oversight, informed consent and good clinical practices. Clinical trials must be conducted under FDA oversight. Before receiving FDA clearance to market a product, we must demonstrate that the product is safe and effective for the patient population that will be treated. If regulatory clearance of a product is granted, this clearance will be limited to those disease states and conditions for which the product is safe and effective, as demonstrated through clinical trials. Marketing or promoting a drug for an unapproved indication is prohibited. Furthermore, clearance may entail ongoing requirements for post-marketing studies. Even if this regulatory clearance is obtained, a marketed product, its manufacturer and its manufacturing facilities are subject to continual review and periodic inspections by the FDA. Discovery of previously unknown problems with a product, manufacturer or facility may result in restrictions on this product, manufacturer or facility, including costly recalls or withdrawal of the product from the market.

The length of time and related costs necessary to complete clinical trials varies significantly and may be difficult to predict. Clinical results are frequently susceptible to varying interpretations that may delay, limit or prevent regulatory approvals. Additional factors that can cause delay or termination of our clinical trials, or cause the costs of these clinical trials to increase, include:

- slow patient enrollment due to the nature of the protocol, the proximity of patients to clinical sites, the eligibility criteria for the study, competition with clinical trials for other drug candidates or other factors;
- inadequately trained or insufficient personnel at the study site to assist in overseeing and monitoring clinical trials;
- delays in approvals from a study site's IRB;
- longer than anticipated treatment time required to demonstrate effectiveness or determine the appropriate product dose;
- lack of sufficient supplies of the drug candidate for use in clinical trials;
- adverse medical events or side effects in treated patients; and
- lack of effectiveness of the drug candidate being tested.

Any drug is likely to produce some toxicities or undesirable side effects in animals and in humans when administered at sufficiently high doses and/or for sufficiently long periods of time. Unacceptable toxicities or side effects may occur at any dose level, and at any time in the course of animal studies designed to identify unacceptable effects of a drug candidate, known as toxicological studies, or in clinical trials of our potential products. The appearance of any unacceptable toxicity or side effect could cause us or regulatory authorities to interrupt, limit, delay or abort the development of any of our drug candidates, and could ultimately prevent their marketing clearance by the FDA or foreign regulatory authorities for any or all targeted indications.

The FDA's fast track program is intended to facilitate the development and expedite the review of drug candidates intended for the treatment of serious or life-threatening diseases and that demonstrate the potential to address unmet medical needs for these conditions. Under this program, the FDA can, for example, review portions of an NDA for a fast track product before the entire application is complete, thus potentially beginning the review process at an earlier time.

We cannot guarantee that the FDA will grant any of our requests for fast track designation, that any fast track designation would affect the time of review or that the FDA will approve the NDA submitted for any of our drug candidates, whether or not fast track designation is granted. Additionally, FDA approval of a fast track product can include restrictions on the product's use or distribution (such as permitting use only for specified medical procedures or limiting distribution to physicians or facilities with special training or experience). Approval of fast track products can be conditioned on additional clinical trials after approval.

FDA procedures also provide for priority review of NDAs submitted for drugs that, compared to currently marketed products, offer a significant improvement in the treatment, diagnosis or prevention of a disease. The FDA seeks to review NDAs that are granted priority status more quickly than NDAs given standard status. The FDA's stated policy is to act on 90% of priority NDAs within six months of receipt. Although the FDA historically has not met these goals, the agency has made significant improvements in the timeliness of the review process.

We and any of our contract manufacturers are also required to comply with applicable FDA current good manufacturing practice regulations. Good manufacturing practices include requirements relating to quality control and quality assurance as well as to corresponding maintenance of records and documentation. Manufacturing facilities are subject to inspection by the applicable regulatory authorities. These facilities, whether our own or our contract manufacturers, must be approved before we can use them in commercial manufacturing of our related products. We or our contract manufacturers may not be able to comply with applicable good manufacturing practices and FDA or other regulatory requirements. If we or our contract manufacturers fail to comply, we or our contract manufacturers may be subject to legal or regulatory action, such as suspension of manufacturing, seizure of product, or voluntary recall of product. Furthermore, continued compliance with applicable good manufacturing practices will require continual expenditure of time, money and effort on the part of us or our contract manufacturers in the areas of production and quality control and record keeping and reporting, in order to ensure full compliance.

Outside the United States, our ability to market a product is contingent upon receiving a marketing authorization from the appropriate regulatory authorities. The requirements governing the conduct of clinical trials, marketing authorization, pricing and reimbursement vary widely from country to country. At present, foreign marketing authorizations are applied for at a national level, although within the European Union, or EU, regional registration procedures are available to companies wishing to market a product in more than one EU member state. If the regulatory authority is satisfied that adequate evidence of safety, quality and efficacy has been presented, a marketing authorization may be granted. This foreign regulatory approval process involves all of the risks associated with FDA approval discussed above and may also include additional risks.

Incyte's Transition into Small-Molecule Drug Discovery and Development

Before the completion of our transition into a drug discovery and development company, we marketed and sold access to our genomic information databases. However, in recent years, consolidation within the pharmaceutical and biotechnology sectors and a challenging economic environment led to reduced demand for research tools and services. This trend, together with the public availability of genomic information, significantly reduced the market for and revenues from, our information products.

On February 2, 2004, we announced substantial changes in our information products operations, including the closure of our Palo Alto, California facility and the cessation of development of the information products developed at this facility. In January 2005, we sold certain assets and liabilities related to our Proteome facility based in Beverly, Massachusetts. We no longer have any activities in the information products area. However, we retain certain existing licenses and licensing activities related to the intellectual property portfolio generated prior to the transition.

Research and Development

Since our inception, we have made substantial investments in research and technology development. During 2007, 2006 and 2005, we incurred research and development expenses of $104.9 million, $87.6 million and $95.6 million, respectively.

Human Resources

As of December 31, 2007, we had 196 employees, including 158 in research and development and 38 in operations support, finance and administrative positions. Of these employees, 74 employees have advanced technical degrees including 8 MD's and 66 Ph.D's. None of our employees are covered by collective bargaining agreements, and management considers relations with our employees to be good.

Available Information

We were incorporated in Delaware in 1991 and our website is located at *www.incyte.com*. We make available free of charge on our website our annual reports on Form 10-K, quarterly reports on Form 10-Q, current reports on Form 8-K and amendments to those reports, as soon as reasonably practicable after we electronically file or furnish such materials to the Securities and Exchange Commission. Our website and the information contained therein or connected thereto are not intended to be incorporated into this Annual Report on Form 10-K.

Item 1A. ***Risk Factors***

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.

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 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. 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 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 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 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 termina