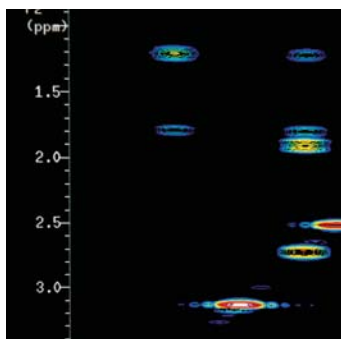


THE DRIVE TO DISCOVER.  
THE EXPERIENCE TO DELIVER.



Annual Report 2006



“With six INDs filed in the last 15 months, we have the potential for multiple clinical proof-of-concept results in 2007.”

**Richard Levy, M.D.**, Senior Vice President, Drug Development, Incyte

**Incyte’s vision** is to become a leading drug discovery and development company by building a proprietary product pipeline of novel small molecule drugs. We have an experienced team with prior success in bringing important new drugs to market. We believe we have the resources, experience and drive to improve the lives of patients and build sustainable value for our shareholders.

INCYTE PIPELINE		Preclinical	Phase I	Phase II
HIV	<b>CCR5 Antagonists</b> INCB9471 INCB15050			
Diabetes	<b>11beta-HSD1</b> INCB13739			
Oncology	<b>Sheddase Inhibitor</b> INCB7839: Solid Tumors <b>JAK2</b>			
Inflammation	<b>CCR2 Antagonists</b> INCB8696: MS/Lupus Nephritis Pfizer Collaboration (as of 11/2005) <b>JAK2</b>			

In 2002, we set out to develop a broad pipeline of potential new therapeutics by:

#### Building a powerful discovery research team

- ✓ 120 biologists and chemists, supported by a core team of clinical and regulatory professionals, working seamlessly to advance multiple programs.

#### Identifying and validating promising drug targets

- ✓ Programs focused on some of the most promising new mechanisms in their therapeutic area: CCR5 for HIV, 11beta-HSD1 for diabetes, sheddase for oncology and JAK for inflammation and oncology.

#### Moving rapidly into lead optimization and preclinical development

- ✓ 8 INDs filed to date; several more expected in 2007.

#### Creating a diversified portfolio of high-quality drug candidates for important medical markets

- ✓ Working in four therapeutic areas: HIV, diabetes, oncology and inflammation. Clinical trials in 2007 expected to generate multiple proof-of-concept results.

#### Pursuing partnerships and acquisitions to accelerate pipeline growth

- ✓ Pfizer collaboration in CCR2 antagonist program.

## To Our Shareholders:

We are working intensively to build a diverse pipeline of products capable of creating significant and sustainable value. With encouraging Phase IIa clinical data for our HIV and diabetes compounds, and with excellent progress in new programs for inflammatory diseases and oncology, we moved closer to this goal in 2006.

## 2006 Accomplishments

Important measures of our success in 2006 were the filings of Investigational New Drug (IND) applications for four novel compounds:

- Our lead CCR5 antagonist for HIV, INCB9471, now in Phase IIa clinical trials. In the first seven HIV patients treated, the compound was well-tolerated and achieved a mean 1.9 log viral load reduction by day 14 of therapy.
- Our lead 11-beta hydroxysteroid dehydrogenase type 1 (11beta-HSD1) inhibitor, INCB13739, for type 2 diabetes, also in Phase IIa development. Clinical results showed that a single oral dose of INCB13739 completely inhibited 11beta-HSD1 activity in both adipose tissue and liver of obese insulin-resistant individuals over a 24 hour period.
- Our follow-on CCR5 antagonist, INCB15050, for HIV.
- Our CCR2 antagonist, INCB8696, for multiple sclerosis, one of the indications we retained in the CCR2 license agreement with Pfizer established in January 2006.

In refractory cancer patients with solid tumors, we continued the testing of our lead sheddase inhibitor, INCB7839, a compound that interferes with signaling through all four of the epidermal growth factor receptors (HER1, HER2, HER3 and HER4). In 2006, there were an increasing number of scientific publications and presentations indicating the importance, in particular, of HER3-driven signaling in maintaining tumor cell growth in the presence of inhibitors of HER1 and HER2. As INCB7839 can inhibit the production of heregulin, the activating ligand for HER3, these publications further support the rationale for this mechanism.

The discovery team also successfully advanced compounds from a new program involving inhibitors of Janus-associated kinases (JAK) into IND-enabling trials. Several INDs have recently been filed and we expect to begin a series of Phase I clinical trials in the first half of this year. I believe these orally available JAK inhibitors could have significant therapeutic potential in a number of areas including inflammatory diseases, myeloproliferative disorders and certain cancers.

## 2007 Program Objectives

In 2007, we expect to make significant and visible pipeline progress in the following programs:

**HIV:** At a scientific meeting later this year, we plan to present the full viral-load reduction and safety data from the Phase IIa trial of our lead CCR5 antagonist, INCB9471. Once we've completed a series of required drug-interaction studies, we plan to initiate Phase IIb trials. Top-line data from the Phase IIa trial reveal the potential for our compound to be differentiated from others in this important new class of drugs. In particular, its long half-life allows once-daily dosing without boosting with ritonavir; its long half-life could also improve the efficacy and sustainability of combination treatment regimens by maintaining drug levels sufficient to block viral replication even when patients occasionally miss doses.



Every year is important, but 2007 has the potential to be transforming for Incyte.

**Diabetes:** For our lead 11beta-HSD1 inhibitor, INCB13739, we are currently enrolling patients in a 28-day Phase IIa trial in type 2 diabetics. This trial will utilize a sensitive technique to measure the ability of INCB13739 to improve the body's response to insulin. Positive results would constitute proof-of-concept for this compound and for the mechanism itself, and are expected to be predictive of long-term improvements in glycemic control. The next step would be a three-month trial to assess the longer-term effects of INCB13739 using the well established primary endpoint of improvement in hemoglobin A1c levels.

**Oncology:** Once the maximum tolerated dose of our oral sheddase inhibitor, INCB7839, has been defined in the ongoing Phase Ib/IIa dose-escalation trial, we plan to initiate Phase II trials in breast cancer and possibly one other solid tumor type. We also plan to disclose relevant biomarker data generated in the Phase Ib/IIa trial.

**Inflammation:** We intend to begin the development of our lead CCR2 antagonist, INCB8696, as a treatment for multiple sclerosis, with a Phase I trial in healthy volunteers.

We also expect to begin clinical trials in the JAK program this year. Therapeutic areas of interest include chronic inflammation, myeloproliferative disorders and cancer. For competitive reasons, we have not disclosed specific details of our clinical plans; however, we expect to produce proof-of-concept results for at least one indication this year.

Importantly, our year-end 2006 cash position of approximately \$330 million is expected to carry us into 2010, providing a strong foundation to advance our pipeline and build value for our stakeholders.

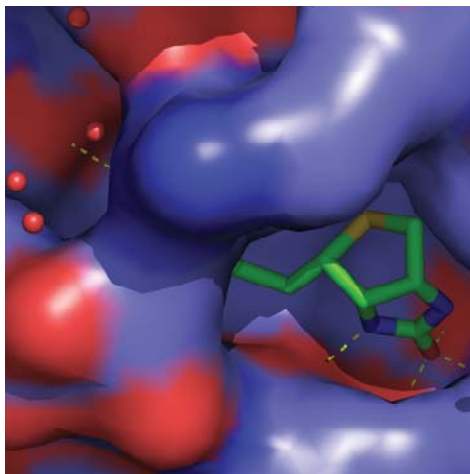
#### Next Steps in Value Creation

Every year is important, but 2007 has the potential to be transforming for Incyte. We anticipate results from clinical proof-of-concept studies with lead compounds from four of our programs: CCR5 antagonists for HIV, 11beta-HSD1 inhibitors for diabetes, sheddase inhibitors for solid cancers, and JAK2 inhibitors. With this high level of clinical activity, driven by our focused and determined team, I remain very optimistic about our prospects for 2007 and beyond.

Sincerely,

Paul A. Friedman, M.D.  
President and Chief Executive Officer  
April 2007





## CCR5 Antagonists: A Next Generation in HIV Therapy

"As part of the original Sustiva team, I was able to see firsthand how a promising product candidate can fundamentally change the treatment of HIV. To once again have the opportunity with INCB9471, which looks like it could be best-in-class among this important new class of CCR5 antagonists, is very exciting."

**Sue Erickson-Viitanen, Ph.D.**

Senior Director, Virology Drug Development, Incyte

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### Mechanism of Action

Human immunodeficiency virus (HIV) enters T-cells by binding to CD4 and one of two obligate co-receptors: CCR5 or CXCR4

- CCR5 antagonists block entry of HIV that binds exclusively to CCR5 (R5 tropic virus).
- Over 85% of patients starting HIV therapy have only R5 tropic virus detectable in blood.
- About 50 to 60% of highly treatment-experienced patients still have only R5 tropic virus detectable in blood.

### Potential Benefits

CCR5 antagonists in HIV regimens may provide

- Substantial benefit in patients with R5 tropic virus.
- Immunologic benefit in all subjects based on increasing CD4 cell counts.

- Safe addition to therapy, complementary to drugs with other modes of action.
- Less risk of developing drug resistance.

Our lead compound: INCB9471

- Potential to be best-in-class.
- Potent antiviral compound with excellent pharmacokinetics.
- Allows for once daily use without boosting with ritonavir, a compound associated with cardiovascular risk.
- Potential for use in first and second line regimens.
- Long half-life expected to provide more effective anti-viral activity even if doses are occasionally missed.

### Clinical Status

10-Day Phase I studies in healthy volunteers completed

- Single doses of INCB9471 studied up to 300 mg.

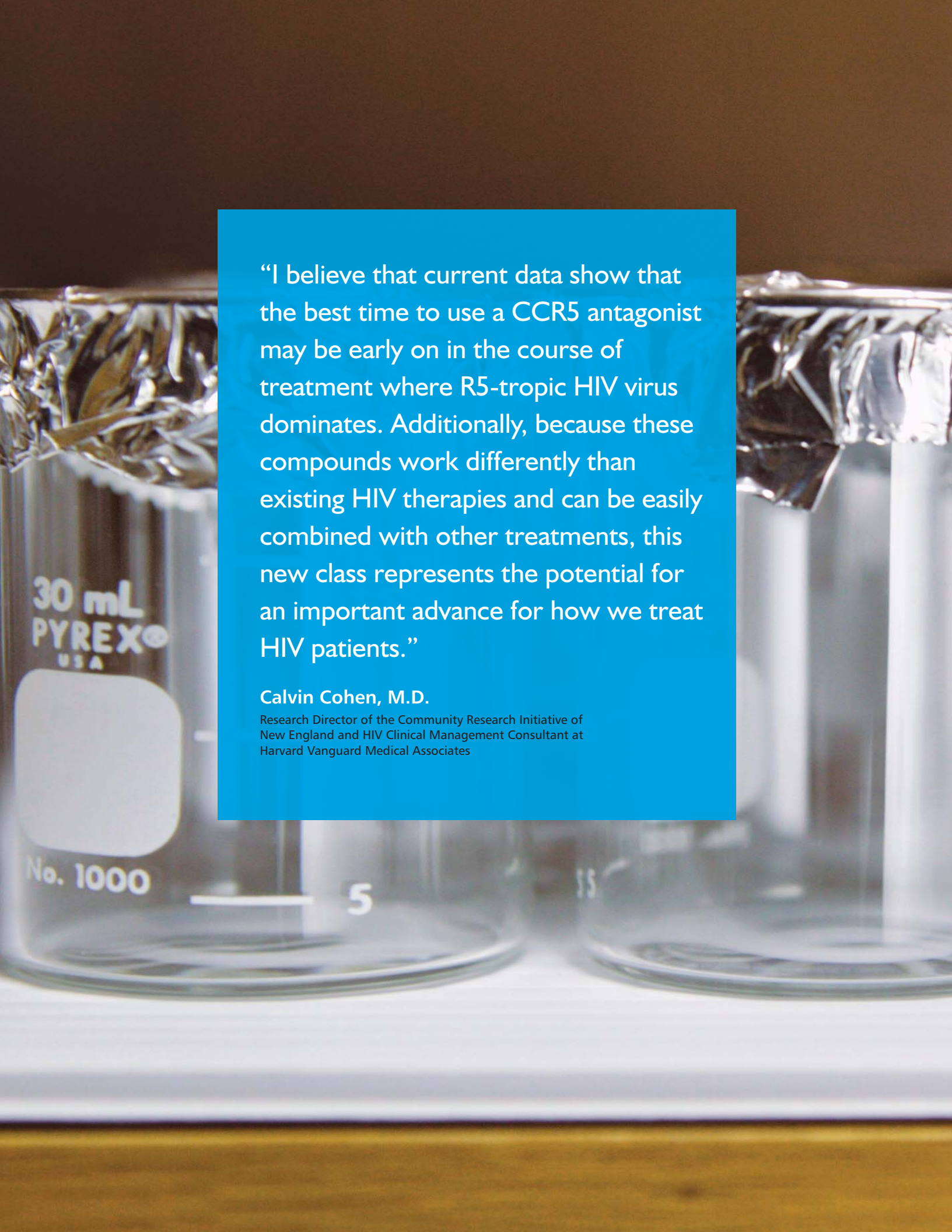
- Multiple doses up to 200 mg once daily for 10 days of dosing.
- Very well-tolerated with no dose-limiting toxicity identified.

14-Day Phase IIa study ongoing

- Includes treatment-naïve and treatment-experienced patients not currently on HIV therapy.
- R5 tropic HIV/naïve to CCR5 antagonists with viral load > 10,000 copies/ml.
- Impressive and sustained antiviral effect demonstrated with 200 mg once daily dose of INCB9471 as monotherapy.
- Additional cohorts planned to examine higher and lower doses.
- Full results expected to be presented at scientific meetings this year.

Required drug interaction studies to be completed in 2007

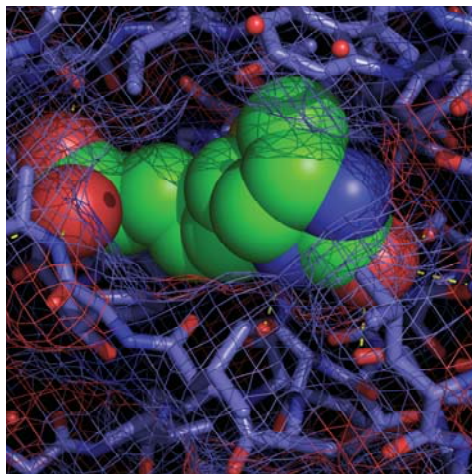
Phase IIb clinical studies expected to follow in late 2007 and early 2008

A background image of a laboratory setting featuring several glass beakers. The beakers are labeled '30 mL PYREX USA' and 'No. 1000'. They are filled with a clear liquid and have aluminum foil wrapped around their necks. The beakers are sitting on a white surface, and the background is a warm, brownish-gold color.

“I believe that current data show that the best time to use a CCR5 antagonist may be early on in the course of treatment where R5-tropic HIV virus dominates. Additionally, because these compounds work differently than existing HIV therapies and can be easily combined with other treatments, this new class represents the potential for an important advance for how we treat HIV patients.”

**Calvin Cohen, M.D.**

Research Director of the Community Research Initiative of  
New England and HIV Clinical Management Consultant at  
Harvard Vanguard Medical Associates



# 11beta-HSD1 Inhibitors: An Emerging New Class of Drugs for Metabolic Disease

“While other companies are pursuing this target, Incyte may well be the first to confirm the clinical relevance of 11beta-HSD1. The fact that our chemists have built such a broad and diverse portfolio of proprietary oral HSD1 inhibitors puts us in an ideal position to generate significant value from this program.”

**Reid Huber, Ph.D.**

Project Leader 11beta-HSD1/Director, Applied Technology, Incyte

## Mechanism of Action

11beta-HSD1 is an enzyme that converts the biologically inactive steroid cortisone into the potent biologically active hormone cortisol, which is known to act as a functional antagonist of insulin action in multiple target tissues

- Liver: cortisol reduces insulin's ability to suppress glucose production.
- Muscle: cortisol reduces insulin's ability to promote glucose uptake.
- Adipose: cortisol blocks insulin's ability to suppress free fatty acid release.

Several additional lines of evidence implicate 11beta-HSD1 activity as a primary driver of insulin resistance and a critical point for disease intervention

- 11beta-HSD1 is upregulated 3-5 fold in obese humans.
- Adipose-specific overexpression of 11beta-HSD1 by 2-3 fold in transgenic mice produces a phenotype closely resembling human type 2 diabetes.

- Reduction of intracellular cortisol levels in the rodent as a result of pharmacologic inhibition of 11beta-HSD1 can reverse manifestations of the metabolic syndrome including obesity, diabetes, dyslipidemia and atherosclerosis.

## Potential Benefits

By reducing the insulin resistance caused by intracellular cortisol, an 11beta-HSD1 inhibitor may be useful as a treatment for type 2 diabetes and also in allied conditions such as dyslipidemia, cardiovascular disease, obesity and hypertension.

Our lead compound: INCB13739

- Potent, selective oral compound with excellent pharmacokinetic profile.
- Completely inhibits the production of intra-adipose and intra-hepatic cortisol by 11beta-HSD1, while maintaining normal systemic cortisol levels, which are essential for immune function and response to stress.

## Clinical Status

Very well-tolerated in single- and multiple-dose-ranging Phase I studies

Phase IIa adipose and liver pharmacodynamic activity study in obese/insulin resistant subjects completed

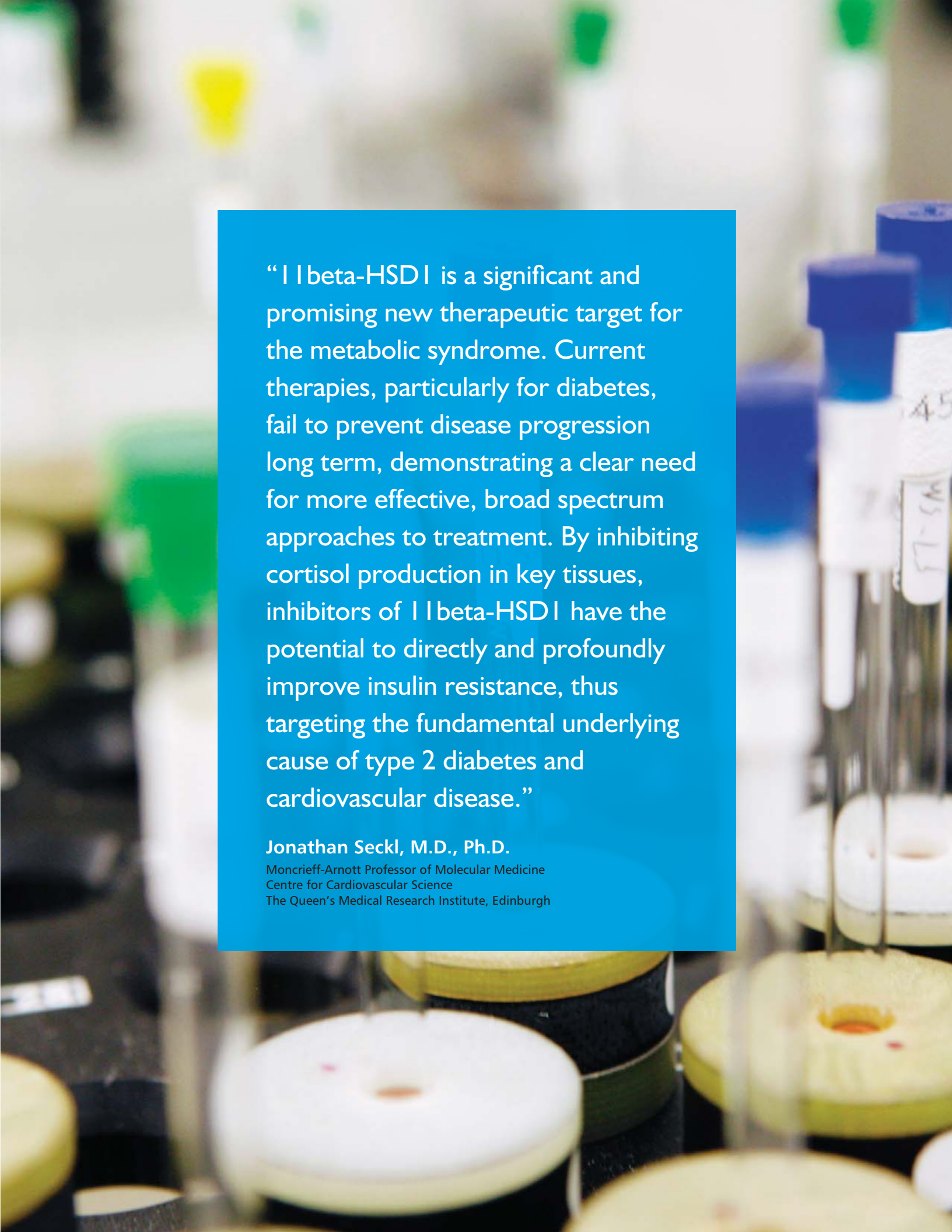
- First compound publicly shown to completely inhibit 11beta-HSD1 activity in both adipose tissue and liver; a required characteristic to truly test the clinical value of 11beta-HSD1 inhibition.

Twenty-eight day study including two-step insulin clamp in type 2 diabetics initiated 1Q2007

- Sensitive and accurate measure of hepatic and peripheral insulin sensitivity; expected to be predictive of long-term improvements in insulin resistance and glycemic control.

Three-month efficacy study in patients with Type 2 diabetes expected to follow

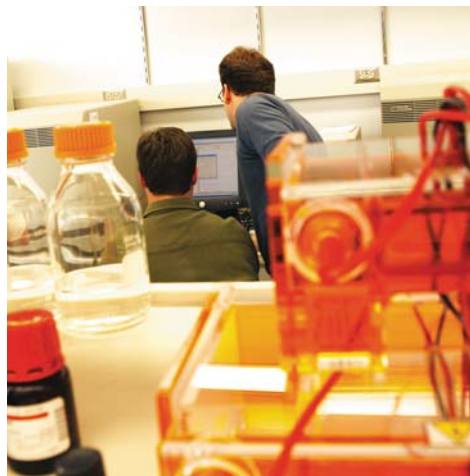




“11beta-HSD1 is a significant and promising new therapeutic target for the metabolic syndrome. Current therapies, particularly for diabetes, fail to prevent disease progression long term, demonstrating a clear need for more effective, broad spectrum approaches to treatment. By inhibiting cortisol production in key tissues, inhibitors of 11beta-HSD1 have the potential to directly and profoundly improve insulin resistance, thus targeting the fundamental underlying cause of type 2 diabetes and cardiovascular disease.”

**Jonathan Seckl, M.D., Ph.D.**

Moncrieff-Arnott Professor of Molecular Medicine  
Centre for Cardiovascular Science  
The Queen's Medical Research Institute, Edinburgh



# Sheddase Inhibitors: Novel Intervention in a Proven Pathway

"There is compelling evidence suggesting that elevated levels of EGFR/HER ligands as well as increased levels of circulating HER2 extracellular domain (ECD) correlate with poor patient outcomes. As early pharmacodynamic data clearly demonstrate that INCB7839 is impacting both ligand and HER2 shedding, we remain confident that sheddase inhibition could well represent an important and novel approach to treating cancers."

**Steve Friedman, M.D.**

Senior Vice President, Drug Discovery, Incyte

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## Mechanism of Action

Epidermal growth factor receptor (EGFR) signaling pathways consist of four known cellular receptors: HER1 (also known as EGFR), HER2, HER3, and HER4. Normally, these HER pathways are tightly regulated. In cancer, signaling through these pathways can increase, resulting in growth, proliferation, migration, and survival of cancer cells. This correlates with disease progression and poor prognosis.

Sheddases are enzymes, specifically ADAM enzymes 10 and 17, that promote growth activity through all four HER pathways. Several marketed therapies that target individual EGFR family members have demonstrated that inhibition of HER signaling is an effective mechanism for treating certain solid tumors.

## Potential Benefits

Sheddase inhibition blocks two different pro-oncogenic mechanisms, generation of active EGFR ligands and generation of a constitutively active HER2 kinase.

- Inhibition of additional and/or common HER pathways is expected to be synergistic with currently approved EGFR inhibitors and improve patient outcomes.
- Sheddase can activate HER3 through generation of the HER3 ligand, heregulin. As this pathway is involved in resistance to current EGFR targeted therapies, decreasing the activity of this pathway with inhibitors of sheddase may be beneficial.

Our lead compound: INCB7839

- Novel, potent, orally bioavailable.

- In preclinical models: single agent efficacy; synergistic with other EGFR therapies; and synergistic with chemotherapy.

## Clinical Status

Phase I completed in healthy volunteers

- INCB7839 was well-tolerated.
- In a dose-dependent manner, INCB7839 decreased HER2 ECD levels, a clinically relevant biomarker.

Phase Ib/IIa trial in refractory cancer patients (breast, colorectal, head and neck, prostate, non-small cell lung) is ongoing

Phase II trials in HER2+ breast cancer planned for the second half of 2007

Phase II trial in an additional solid tumor expected to follow in late 2007 or early 2008

F2  
(ppm)

1.5

2.0

2.5

3.0

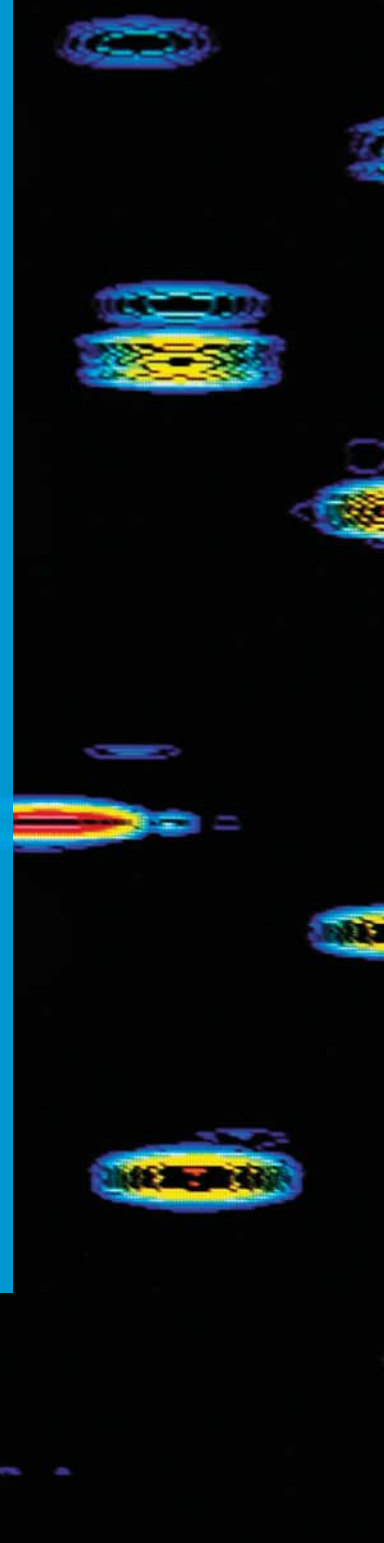
3.5

4.0

“Currently approved agents that target the EGFR/HER pathway have shown limited activity in treating solid tumors. While the reasons for this are still emerging, this limited efficacy in metastatic disease may relate to the fact that existing treatments inhibit only one or two of the HER pathways. I believe new agents in development that target multiple HER pathways or target these pathways through novel mechanisms such as inhibition of ligand shedding and receptor cleavage are likely to lead to superior clinical outcomes, especially when used in combination with current therapies.”

**Allan Lipton, M.D.**

Medical Oncology and Hematology  
Milton S. Hershey Medical Center  
Penn State University College of Medicine





# JAK Inhibitors: Compelling Approach to Treat Inflammation, Myeloproliferative Disorders and Cancer

“Multiple activating mutations in JAK2 have recently been identified in the majority of myeloproliferative disorders, including polycythemia vera, essential thrombocythemia and primary myelofibrosis. Research results suggesting a causal role for these mutations in the pathogenesis of myeloproliferative disorders strongly support the development of JAK2 inhibitors as targeted drugs for these disorders - many of which can be life threatening and for which we lack effective therapies.”

**Ayalew Tefferi, M.D.**

Professor in Hematology and Internal Medicine  
Mayo Clinic College of Medicine, Division of Hematology in the Department of Medicine

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## Mechanism of Action

Janus-associated kinases (JAK) are enzymes that mediate signaling of several important drivers of inflammatory diseases, myeloproliferative disorders (MPDs) and malignancies. There are four known JAK enzymes: JAK1, 2, 3 and TYK2

- Known inflammatory cytokines, such as IL-6, IL-12, and IL-23, signal through JAKs to promote inflammation.
- Activating mutations of JAK2 are present in >90% of polycythemia vera and ~50% of essential thrombocythemia and myeloid metaplasia with myelofibrosis.
- Aberrant activation of the JAK-STAT pathway has been documented in a variety of cancers.

## Potential Benefits

- Convenient oral dosing - current best-of-care therapies are injectable.
- Expected to be effective in patients refractory to anti-TNF therapies.
- Rapid onset of action based on data from early clinical studies.
- Potential to be first targeted therapy for MPDs.
- Broad applicability in a number of autoimmune diseases and malignant conditions.

## Program Status

Multiple potent, selective, orally bioavailable candidates currently in preclinical development


- >100x selectivity against a broad panel of kinases.
- 10 – 40x selectivity over the JAK3 enzyme.

GLP-safety studies successfully completed

Multiple IND applications expected to be filed in 2007

Multiple clinical trials planned in 2007

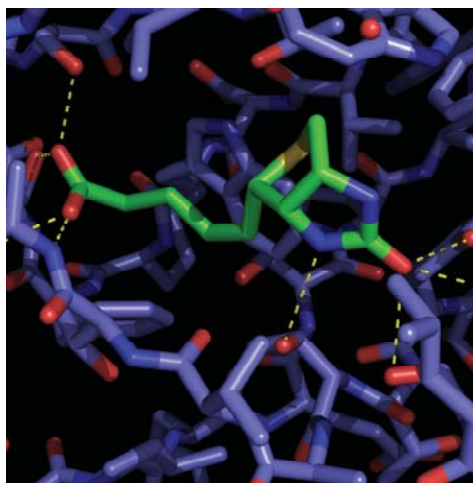




“Recent clinical data with an oral JAK inhibitor demonstrating dramatic efficacy and rapid onset of action in both rheumatoid arthritis and psoriasis represent a significant development in our approach to treat these diseases. While the data are still early, I believe that JAK inhibition is one of the most exciting new therapeutic approaches for chronic inflammatory diseases.”

**Larry Moreland, M.D.**

Professor of Medicine, University of Alabama  
Director of the UAB Arthritis Clinical Intervention Program  
Director of the UAB Pittman General Clinical Research Center



"In preclinical studies, INCB8696 has demonstrated a favorable safety profile at doses sufficient to completely inhibit CCR2 function. Given the critical role the CCR2 chemokine receptor is thought to play in the formation of MS lesions, we believe our CCR2 antagonist could provide a safe and effective approach to treating this chronic and debilitating disease. Preclinical data also suggest that autoimmune nephritides are additional indications for this mechanism."

**William Williams, M.D.**

Vice President, Exploratory Development, Incyte

## CCR2 Antagonists: A Promising Target for Inflammatory Diseases

"CCR2 is a chemokine receptor that is involved in the trafficking of inflammatory monocytes. These monocytes are believed to play critical roles in the pathogenesis of inflammatory diseases, including multiple sclerosis. Based on the published preclinical data on CCR2, an oral CCR2 antagonist may have the potential to provide significant therapeutic effects in MS, and not cause overt immunosuppression."

**Israel F. Charo, M.D., Ph.D.**

Professor of Medicine, University of California, San Francisco

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### Mechanism of Action

CCR2 antagonists prevent blood monocytes from entering tissue and becoming inflammatory macrophages:

- The severity of inflammation in a number of disease states correlates with the number of macrophages in tissue.
- In multiple sclerosis (MS), activated

macrophages accumulate in the lesions and are associated with destruction of the myelin sheath.

- In autoimmune nephritides, macrophages are implicated in lupus renal pathology.

### Potential Benefits

- Novel mechanism.
- Potential for efficacy with minimal immunosuppression.

Our lead compound: INCB8696

- Selective compound with excellent pharmacokinetic properties.
- Convenient oral dosing.

### Clinical Status

- IND filed for MS with Phase I trials in healthy volunteers planned in 2007.

## BOARD OF DIRECTORS

### **Richard U. De Schutter**

Chairman of the Board  
Formerly Chairman  
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DuPont Pharmaceuticals Company

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President and Chief Executive Officer  
Incyte Corporation

### **Barry M. Ariko**

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### **Paul A. Brooke**

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Managing Member, PMSV Holdings, LLC  
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### **Matthew W. Emmens**

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### **John F. Niblack, Ph.D.**

Formerly Vice Chairman  
and President of Global Research  
and Development  
Pfizer Inc.

### **Roy A. Whitfield**

Formerly Chairman of the Board  
and Chief Executive Officer  
Incyte Corporation

## EXECUTIVE MANAGEMENT

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President and Chief Executive Officer

### **David C. Hastings**

Executive Vice President  
and Chief Financial Officer

### **John A. Keller, Ph.D.**

Executive Vice President  
and Chief Business Officer

### **Brian W. Metcalf, Ph.D.**

Executive Vice President  
and Chief Drug Discovery Scientist

### **Patricia A. Schreck**

Executive Vice President  
and General Counsel

### **Paula J. Swain**

Executive Vice President,  
Human Resources

### **Transfer Agent and Registrar**

Mellon Investor Services LLC  
PO Box 3315  
South Hackensack, New Jersey 07606  
or  
480 Washington Boulevard  
Jersey City, New Jersey 07310  
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TDD for Hearing Impaired:  
800/231-5469  
Foreign Shareholders:  
201/680-6610  
TDD Foreign Shareholders:  
201/680-6578  
[www.mellon-investor.com/isd](http://www.mellon-investor.com/isd)

### **Annual Meeting**

The Annual Meeting of Stockholders  
will be held May 22, 2007, at 10:00 a.m.,  
Eastern Daylight Time, at the  
Hotel du Pont, 11th and Market Streets,  
Wilmington, Delaware.

### **Outside Counsel**

Pillsbury Winthrop Shaw Pittman LLP

### **Independent Registered Public Accounting Firm**

Ernst & Young LLP

### **Market Information**

Incyte's Common Stock is listed on  
the NASDAQ Global Market under the  
symbol INCY.

### **Investor Relations**

You can obtain recent press releases  
and other publicly available information  
on Incyte by visiting our web site at  
[www.incyte.com](http://www.incyte.com).

### **Contact**

Pamela Murphy  
Vice President, Investor Relations and  
Corporate Communications  
Email: [pmurphy@incyte.com](mailto:pmurphy@incyte.com)

### **Corporate Headquarters**

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Building E336  
Wilmington, Delaware 19880  
302/498-6700

## Forward-looking Statements

Except for the historical statements contained herein, the statements contained in this annual report, including without limitation, statements as to the anticipated advancement and composition of our pipeline, the expected timing, progress and other information regarding our preclinical and clinical trials, our development plans and goals for 2007 and 2008, plans to present and disclose data from our clinical trials, the potential benefits and effectiveness of our compounds in treating disease, and the ability of our cash position to advance our pipeline and continue our operations for a stated period of time, are forward-looking statements within the meaning of the "safe harbor" provisions of the Private Securities Litigation Reform Act of 1995. The forward-looking statements are based on our current intent, belief and expectations, using information currently available to us, and are therefore subject to certain risks, uncertainties, and assumptions that may cause actual results to differ materially, including the results of further scientific research, the impact of technological advances and competition, unanticipated delays or uses of capital, and other risks discussed in our Annual Report on Form 10-K for the year ended December 31, 2006, which is contained herein, and in our filings with the Securities and Exchange Commission. These forward-looking statements speak only as of the date hereof. Incyte disclaims any intent or obligation to update these forward-looking statements.





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