



THE DRIVE TO DISCOVER. THE EXPERIENCE TO DELIVER.



## INCYTE PIPELINE

### Growing Pipeline of Novel Orally-Available Compounds



#### About the structures on the front and back cover

On the front cover is a computer generated model of Reverset™, Incyte's once-daily nucleoside analog reverse transcriptase inhibitor for treatment of HIV infection that is in Phase II development. The model shows Reverset (in green) bound to the HIV reverse transcriptase molecule.

The back cover is a computer generated model of an Incyte oral sheddase inhibitor (INCB7839, shown as a dotted mesh outline) bound to its cancer protease target (in green). Non-sheddase proteases, to which INCB7839 does not bind, are also shown (yellow, red and blue). We believe selective inhibition of sheddase has the potential to slow the growth of proliferating tumor cells while maintaining a favorable tolerability profile. INCB7839 is in Phase I development as a treatment for solid tumors.



**Incyte Corporation**  
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[www.incyte.com](http://www.incyte.com)

Dear Shareholder:

In 2004, we completed Incyte's transition into drug discovery and development, allowing us to dedicate our resources to creating much needed medicines that should also provide us significant commercial opportunities. We are working on a variety of novel oral therapeutics for the treatment of human immunodeficiency virus (HIV), inflammation, cancer and diabetes, and, I believe, in 2005 Incyte is poised to make substantial clinical progress so that all of our stakeholders—patients, physicians, employees and investors—will benefit.

We strengthened our financial position in 2004, ending the year with approximately \$470 million in cash and marketable securities giving us the ability to advance our programs on our own or, as appropriate, with strategic partners.

With the truly exceptional and experienced scientific team we have assembled at Incyte, our progress in drug discovery and development has been quite rapid.

### **Our Lead Drug Discovery Programs Made Substantial Progress in 2004**

Reverset™, an in-licensed compound and our lead product, and our two lead internal programs (CCR2 antagonists for inflammatory diseases and sheddase inhibitors, a novel approach to cancer treatment) have made important progress in 2004.

### **Reverset Continues to Demonstrate the Potential to Benefit Treatment-Experienced HIV Patients**

Reverset, an oral nucleoside analogue reverse transcriptase inhibitor (NRTI) licensed from Pharmasset, Inc. completed Phase IIa clinical testing and is now in a Phase IIb study designed to support the initiation of pivotal Phase III trials.

- Results to date suggest Reverset has the potential to become a preferred second-line therapy for treatment-experienced HIV patients.
- Study 203, the Phase IIb trial which involves 180 treatment-experienced patients evaluated over 24 weeks, is fully enrolled.

- Interim analysis of 140 patients who have already been in Study 203 for at least 30 days showed that Reverset was generally well-tolerated at all doses studied for as long as 24 weeks.
- Topline results from the interim analysis suggest that Reverset also can provide sustained antiviral activity in treatment-experienced HIV patients who have multiple resistance mutations.
- A higher than expected incidence of asymptomatic hyperlipasemia, a marker of pancreatic inflammation, in patients who are also receiving the drug didanosine (ddl, or Videx®) has been the only adverse event of note in Study 203 so far. This condition has also occurred when didanosine was combined with certain other NRTIs.

### **CCR2 Continues to be a Promising Approach to Treating Chronic Inflammation**

Our chemokine receptor antagonist, INCB3284, now in Phase IIa development, is one of a new class of drugs with potential to treat chronic inflammation associated with diseases such as rheumatoid arthritis, diabetes, multiple sclerosis and atherosclerosis.

- The role of CCR2 is to control the migration of cells called monocytes from the blood into tissue compartments that are sites of incipient or chronic inflammation. The monocytes then evolve into cells called macrophages which produce substances (e.g., proinflammatory cytokines) that orchestrate and perpetuate the inflammatory state. Blocking monocyte migration with a CCR2 antagonist in a variety of animal models has reduced or prevented this chronic inflammation.
- In 2004, Phase I trials for INCB3284 were completed. We also developed a tablet formulation for use in Phase IIb and beyond. Discussions with prospective partners were initiated and continue, as the breadth of this program makes clear that optimal development requires that, at some point prior to Phase III, we enter into a collaboration with a larger company having the resources to maximize the potential of CCR2 antagonists both expeditiously and in multiple indications.

### **Sheddase Inhibition is a Novel Approach to Treating Common Cancers**

INCB7839 inhibits the sheddase enzyme, thereby blocking human epidermal growth factor receptor (HER) signaling pathways. Encouraging efficacy, seen in

a variety of animal tumor models, suggests that this approach, either alone or in combination with other blockers of HER pathways and/or cytotoxic agents, has the potential to treat a spectrum of common human solid tumors, including breast, colorectal and non-small cell lung cancers. We look forward to testing the sheddase inhibitor concept in the clinic since the value of blocking HER pathways has already been validated by several approved products including Herceptin<sup>®</sup>, Erbitux<sup>™</sup> and Tarceva<sup>™</sup>.

- INCB7839, which demonstrated a very favorable safety profile in all of our preclinical studies, has received clearance from the U.S. Food and Drug Administration; we began Phase I testing in the first quarter of this year.

### **Successful Fundraising Supports Pipeline Development**

During 2004, Incyte raised net proceeds of approximately \$326 million through both the sale of common stock in a public offering as well as the sale of convertible notes to qualified institutional investors. This successful fundraising, along with careful control of our cash, will allow us to continue to drive our clinical development activities and support our discovery efforts.

### **Incyte's Goals for 2005 Build on Our Accomplishments in 2004**

Our goals for 2005 are ambitious and include:

- completing Reverset Study 203 and presenting these Phase IIb results; provided the data remain consistent with the aforementioned interim analysis, we plan, after reviewing our proposed program with the FDA, to initiate pivotal Phase III trials;
- completing two Phase IIa trials (one in rheumatoid arthritis and a second in obese insulin resistant subjects) with our lead CCR2 antagonist, INCB3284; these studies are intended to allow us to understand better the potential of CCR2 antagonists to treat diseases which appear to be driven by a chronic inflammatory component;
- completing a Phase I study in healthy volunteers with our lead cancer compound, INCB7839, and then beginning a "proof of concept" Phase II trial by year-end; and
- advancing at least one of our early discovery compounds into preclinical toxicology and prepare for human testing.

With a strong balance sheet, a growing pipeline and an outstanding team to advance our programs, I am confident that we can achieve our goals for 2005. I appreciate your continued support and look forward to keeping you informed of our progress.

Sincerely,

A handwritten signature in black ink, reading "Paul A. Friedman". The signature is written in a cursive, flowing style.

Paul A. Friedman, M.D.  
President & Chief Executive Officer

April 2005

#### Forward Looking Statements

Except for the historical information set forth herein, the matters set forth in this letter, including, without limitation, statements regarding our anticipated progress for and ability to fund our drug discovery and development programs, our plans and expected timelines for advancing our drug candidates through preclinical and clinical trials, the potential therapeutic value, including attributes and indications, of our Reverset, CCR2 antagonist and INCB 7839 drug candidates, partnering strategies and plans for our drug candidates, contain predictions, estimates and other forward-looking statements.

These forward-looking statements are subject to risks and uncertainties that may cause actual results to differ materially, including the risk that results of clinical trials may be unsuccessful or insufficient to meet applicable regulatory standards, the high degree of risk associated with drug discovery and development, the ability to enroll sufficient numbers of subjects in clinical trials, the impact of competition and technological advances, the results of further scientific research, unanticipated delays, the ability of Incyte to compete against parties with greater financial or other resources, greater than expected expenses, economic factors, unanticipated or unpredictable expenses relating to litigation or strategic activities, our ability to obtain additional capital when needed, risks related to product candidates that are in-licensed, and other risks detailed from time to time in Incyte's reports filed with the Securities and Exchange Commission, including our Annual Report on Form 10-K for the year ended December 31, 2004.

## BOARD OF DIRECTORS

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Chairman of the Board  
Formerly Chairman  
and Chief Executive Officer  
DuPont Pharmaceuticals Company

### **Paul A. Friedman, M.D.**

President and Chief Executive Officer  
Incyte Corporation

### **Barry M. Ariko**

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Advisory Director, Morgan Stanley  
Venture Partner, MPM Capital

### **Frederick B. Craves, Ph.D.**

Managing Director  
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### **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

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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  
85 Challenger Road  
Ridgefield Park, New Jersey 07660  
Phone: 800/522-6645  
TDD for Hearing Impaired:  
800/231-5469  
Foreign Investors:  
201/329-8660  
TDD for Foreign Investors:  
201/329-8354  
[www.melloninvestor.com](http://www.melloninvestor.com)

### **Annual Meeting**

The Annual Meeting of Stockholders will be held June 1, 2005, at 10:30 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 trades on the NASDAQ Stock 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**

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### **Corporate Headquarters**

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