Forward-looking Statements

Except for the historical information contained herein, the statements contained in this letter, including statements relating to expectations about the value produced by our discovery and development efforts, the timing of the Phase I clinical trials for our CCR5 and CCR2 antagonist compounds, the completion of IND-enabling studies for development candidates from our new inflammation and cancer programs, the timing and focus of clinical trials for our oral sheddase inhibitor, the timing of the initiation of clinical testing for our lead compound in our diabetes program, partnering our diabetes program, our positioning and our strategies toward alliances and future commercial plans, are forward-looking statements that involve risks and uncertainties. These risks and uncertainties may cause actual results to differ materially, and include the high degree of risk associated with drug development and clinical trials, results of further research and development, the impact of competition and of technological advances and our ability to compete against parties with greater financial or other resources, unanticipated delays, our ability to enroll a sufficient number of patients for our clinical trials, and other risks detailed from time to time in our filings with the Securities Exchange Commission, including our Annual Report on Form 10-K for the year ended December 31, 2005. We disclaim any intent or obligation to update these forward-looking statements.
DEAR SHAREHOLDERS:

We made excellent progress advancing and expanding our pipeline in 2005. Therefore, it was disappointing that it was necessary to discontinue development of DFC (dexelvucitabine, formerly Reverset), our Phase II compound for HIV.

We reached this decision because the frequency of grade 4 hyperlipasemia, a marker of pancreatic inflammation, was, in Incyte’s view, unacceptably high in patients taking 200 mg DFC in the manner in which we envisioned it would be used -- in drug combinations without 3TC or FTC. While DFC was our most advanced product candidate and its approval and commercialization had the potential to expedite our growth, I believe it is in the best interests of our shareholders to redirect our resources to our other programs, the lead compounds for which currently all come from internally developed compounds. As we look forward to the next 12 to 18 months, I expect that the value produced by our discovery and development efforts will become increasingly visible as these compounds continue to advance and new ones are added to the current pipeline.

Despite the recent news on DFC, a series of significant achievements occurred in 2005 including:

> Signing a collaborative research and license agreement with Pfizer worth up to $803 million for CCR2 antagonists, our first internally-generated program;

> Advancing our first oncology compound into clinical development; and

> Selecting development candidates from new programs in HIV and diabetes.

Before commenting more broadly on our future plans, I will review in greater detail our achievements in 2005 and the progress we expect to make in 2006.

HIV

DFC: As previously mentioned, because of recently observed increases in the frequency of grade 4 hyperlipasemia, a marker of pancreatic inflammation, in patients receiving the 200 mg dose of DFC and not receiving 3TC or FTC, we announced that the clinical development of DFC in treatment-experienced HIV patients has been discontinued. This outcome is unfortunate given that we had seen potent antiviral effects of DFC in prior studies, but we believe discontinuing the development of DFC is in the best interests of patients. With this decision, our focus in HIV drug development has shifted to a currently promising new class of compounds called CCR5 antagonists.

CCR5 antagonists block the virus from entering and infecting healthy cells, and, because this is a new mechanism, they are active against strains of the virus that are resistant to currently used anti-HIV drugs.

During 2005, we selected an internally discovered oral CCR5 antagonist for clinical development. We filed an IND in March 2006 for the lead compound, INCB9471,
and expect to begin Phase I testing in the first half of this year.

Inflammation Portfolio
CCR2: In November 2005, we established a major alliance with Pfizer for our CCR2 antagonist program, which provides up to $803 million in potential payments, including $40 million upfront and $10 million received from the issuance of a convertible subordinated note to Pfizer. In 2005, prior to establishing this alliance, we advanced the lead compound, INCB3284, into two Phase IIa studies, one in patients with rheumatoid arthritis and one in obese subjects with insulin resistance. The alliance with Pfizer allows us to retain exclusive rights to pursue development in multiple sclerosis and an additional high-value specialty indication, along with certain compounds for our independent pursuit in these indications. We expect to initiate Phase I testing for one of our compounds in the second half of this year.

New Program: We have also identified a development candidate from a new inflammation program, and expect to complete IND-enabling studies for this compound by year-end.

Oncology Portfolio
Sheddase: In 2005, we initiated and completed a Phase I study in healthy volunteers with our oral sheddase inhibitor, INCB7839. Currently, we are conducting a Phase I/II trial in cancer patients who have solid tumors, and we expect to complete this study in the second half of 2006. We then intend to initiate one or more Phase II studies in 2006 to assess the efficacy of this compound against specific solid tumors. These studies could include, for example, breast and/or non-small cell lung cancers.

New Program: We expect to complete IND-enabling studies by the end of 2006 for a compound from a new cancer program with a target distinct from sheddase.

Diabetes
Our program in diabetes focuses on a very interesting emerging target — 11 beta-hydroxy sterol dehydrogenase 1, or 11ßHSD1. This enzyme is responsible for the conversion of cortisone to the hormone cortisol, which, when formed in metabolically important tissues such as fat, muscle, and liver, essentially counteracts the function of insulin. The lead compound, INCB13739, is scheduled to enter clinical testing in the first half of 2006.

Building a Solid Foundation for the Future
We have made substantial progress over the past year and are well-positioned to address the key challenges
faced by companies of our size and stage of development, specifically:

- Establishing the basis for sustainable growth
- Managing the uncertainties of the capital markets
- Maximizing shareholder value

I believe it is timely to review our approaches to address these issues.

**Establishing the Basis for Sustainable Growth**

Our decision to discontinue the development of DFC is a reminder that long-term success requires us to build a deep and sustainable pipeline in our areas of therapeutic focus. As you can see from what we have done in 2005 and what we expect to achieve in 2006, we are making solid progress in that regard.

In addition to creating continuous value from our pipeline and maintaining a state-of-the-art R&D organization, we are planning a future in which Incyte will have commercial capabilities in the U.S. for specialty indications, such as oncology, multiple sclerosis and/or HIV. The exact composition and size of this commercial arm will obviously be determined by our levels of success in bringing drugs to market for these specialty indications. In primary care areas, such as diabetes, where development and commercialization requirements exceed what we can reasonably establish, we will seek high-value alliances.

**Managing the Uncertainties of the Capital Markets**

We are fortunate to have started 2006 with a strong cash position of approximately $395 million (including the proceeds from initial payments under the Pfizer collaboration). This provides us with the resources to expand and advance our pipeline without the constant pressure and distraction of seeking access to new capital. We are confident that progress in our drug development programs will provide the value-creation events necessary to efficiently raise additional funds to support the anticipated growth of our pipeline.

**Maximizing Shareholder Value**

Our experienced scientific team remains one of our most important competitive advantages; with the expansion of our internally generated pipeline, the results of their productivity are becoming increasingly visible.

**Drugs that target certain epidermal growth factor signaling pathways, such as Herceptin®, Erbitux®, and Tarceva®, have already established themselves as effective cancer therapies. Our oral sheddase inhibitors, which target these pathways in a distinct fashion, are effective as monotherapy and synergistic with other anti-cancer agents in preclinical models.**

In addition, we will continue to selectively seek high-quality in-licensing opportunities to bolster our late-phase portfolio. We will also seek to establish additional strategic alliances to maximize the value and reduce the resource requirements of those programs which exceed...
HSD1 addresses a major medical need -- diabetes -- that lies outside our areas of therapeutic focus but which our medicinal chemists were able to approach effectively. We would expect to partner the program at an appropriate value-creation point, as we did with our CCR2 program.

our current or anticipated internal capabilities. With these assets and strategies in place, I believe Incyte is in a strong position to bring important new medicines to market and to create significant and sustainable value for our shareholders.

In closing, I would like to thank Fred Craves, Ph.D., who is retiring from our board of directors, for his many years of service. Fred, who has a scientific background in pharmacology and is as well a very successful and experienced venture capitalist, has consistently provided Incyte with invaluable direction and support. We are fortunate that John Niblack, Ph.D., former vice chairman and director of Pfizer Inc., has agreed to stand for election at our 2006 annual stockholders’ meeting and, if elected, to join our board. John’s 35-year tenure at Pfizer included a succession of scientific positions of increasing responsibility in the areas of virology, cancer and autoimmune disorders, culminating in his serving as the president of Pfizer Global Research and Development. We are also fortunate that Matthew Emmens, chief executive officer and chairman of the executive committee of Shire Pharmaceuticals Group plc, has also agreed to stand for election and join the board. Before joining Shire in 2003, Matt held a number of high level management positions at leading pharmaceutical firms including: president of Merck KGaA’s global prescription pharmaceuticals business, president and chief executive officer of EMD Pharmaceuticals, Merck KGaA’s U.S. prescription pharmaceutical business, chief executive officer of Astra Merck, Inc., and various positions at Merck and Co., Inc. Both Matt and John bring a wealth of expertise and relevant experience to our board; their addition reflects our commitment to building a world-class drug discovery and development company.

I truly appreciate your support and look forward to keeping you updated on our progress.

Sincerely,

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

April 2006
Company Profile
Incyte is a Wilmington, Delaware based drug discovery and development company with a growing pipeline of compounds to treat oncology, inflammation, HIV and diabetes.

Incyte Pipeline

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