Incyte is a drug discovery and development company with a growing pipeline of novel small molecule drugs to treat HIV, inflammation, cancer and diabetes. The company’s most advanced product candidate, Reverset®, is an oral, once-a-day therapy in Phase II clinical trials to treat patients with HIV infections. Currently, Incyte has four drug discovery programs underway, the most advanced of which, CCR2, is expected to enter the clinic in the first half of 2004.

Pictured here is Chu-Diao Xue, Ph.D., an executive director in Incyte’s chemistry group and project leader for the CCR2 receptor antagonist program.
We began 2003 determined to make meaningful progress in building a leading drug discovery and development company and I am pleased to report that the last 15 months have proven extremely successful in that regard. We have had to make some difficult decisions along the way, particularly with respect to our information products line, but we believe that those decisions are clearly in the best interests of the company and our shareholders. During the first quarter of 2004, we concluded that the extensive changes that have taken place in the market for genomic research products and services have made the continuation of our information products line too uncertain and too costly. With that determination, shortly after year end, we announced that we would close our Palo Alto facility, which housed Incyte’s information products line, on April 2, 2004. This decision has allowed us to focus our resources and talent on building a pipeline of novel, orally available, small molecule therapeutics for the treatment of human immunodeficiency virus (HIV) infection, inflammation, cancer and diabetes.

The talented team at Incyte has accomplished a great deal in a very short period of time. When I joined the organization in 2001, we were an information products business with a diminishing revenue stream and a vision to build a pharmaceutical company. Today, Incyte has approximately 140 scientists dedicated to discovery biology and medicinal chemistry, as well as scientific management with extensive experience in successfully discovering, developing and commercializing pharmaceutical products. During the last 15 months, we have strengthened our balance sheet, expanded and advanced our drug pipeline, and assembled an experienced leadership team to drive our company’s drug discovery and development efforts forward.

Measure Our Success by the Strength of Our Pipeline

I believe that the most important ongoing measure of success for our company will be the advancement of our pipeline and our ability to fuel that pipeline with high-quality clinical candidates. Incyte’s pipeline now contains exciting clinical and preclinical programs including Reverset, our Phase II compound for the treatment of HIV, a CCR2 receptor antagonist, for treating chronic inflammation, that is poised to enter the clinic in the first half of 2004, and preclinical programs including inhibitors of sheddase, a novel target for cancer treatment (formerly referred to as our cancer protease program) and inhibitors of a specific protein phosphatase.
We have built this pipeline through both internal discovery and in-licensing of a clinical-stage product candidate. Our HIV program is a demonstration of our ability to identify and in-license promising new product candidates, while our CCR2 receptor antagonist program is a testament to our ability to take an internal discovery through preclinical testing and into IND-enabling development. Remarkably, in this instance, all of this was accomplished in less than two years.

Let me now provide some further detail on our current programs, our progress in 2003, and our development plans for 2004.

**Reverset – Demonstrated Positive Phase IIa Results**

Our lead HIV product candidate, Reverset, is a reverse transcriptase inhibitor being developed as a once-daily, oral therapy. We formed a collaborative licensing agreement with Pharmasset for Reverset in September 2003, and recently reported positive results from a 10-day, dose-escalating, placebo-controlled trial designed to evaluate Reverset as a single therapy in 30 treatment-naive HIV infected patients. The patients in the trial received 50, 100, or 200 milligrams of Reverset once a day for 10 days. Reverset was well-tolerated at all doses and effective at reducing the viral load in all treated patients, with the amount of HIV in the patients' blood being reduced by an average of approximately 98%.

Based on the current data, we believe that Reverset has the potential to be a very potent drug for treating HIV. Furthermore, we believe it has the potential to inhibit many clinically prevalent mutant strains of HIV that show resistance to currently approved therapies. We will begin testing the potential of Reverset against resistant strains of HIV this year as we begin our second Phase II trial and expect that we will initiate pivotal Phase III testing in 2005. There is a serious need for new HIV therapies that are effective against these mutant strains and that are well-tolerated and easy to use. We believe that Reverset can address these issues.

**CCR2 Receptor Antagonists – from Discovery to IND in Less than Two Years**

This program is focused on the development of a new class of small-molecule drugs to treat chronic inflammatory diseases, such as rheumatoid arthritis, multiple sclerosis and possibly neuro-pathic pain and atherosclerosis. CCR2 is a receptor that resides on the surface of blood cells.
 ongoing measure of success for our of our pipeline and our ability to clinical candidates.”

called monocytes and controls the migration of these cells into sites of inflammation, where they become macrophages, a cell type critical to the induction and maintenance of an inflammatory response. If monocyte migration is blocked through the administration of a CCR2 receptor antagonist compound, the potential exists to abrogate or significantly diminish the inflammatory response.

Through our internal discovery efforts we have identified a series of orally available CCR2 receptor antagonist compounds and selected a lead candidate to advance into clinical development. We plan to initiate human clinical testing of this compound in the first half of 2004. While we are still in the early stages of development for this new class of drugs, we believe the potential of this type of small molecule anti-inflammatory agent is quite significant.

Sheddase Inhibitor – Our Second Internal Discovery to Advance to Preclinical Development
We have identified several novel, potent and orally available small molecule inhibitors of sheddase – a protease enzyme that is a part of the signaling mechanism critical for the growth and metastasis of breast cancer, and possibly other cancers. We have shown efficacy of our sheddase inhibitors in animal tumor models and have advanced a lead compound into preclinical development. We hope to begin human testing of this compound by the end of 2004.

Fueling the Pipeline – Internal Discovery & In-licensing Opportunities
Incyte will be measured on the strength of our pipeline. Along with the programs mentioned above, we have a number of earlier discovery programs in cancer and diabetes. As the year 2004 unfolds, you can expect to see Incyte further fuel our pipeline by bringing additional internal programs forward into preclinical development, while continuing to pursue the in-licensing of compounds that are either in clinical development or about to enter the clinic.

We Have the Drive to Discover and the Experience to Deliver
In the past two years, we have assembled an exceptional team to drive our business forward. While all of us are fairly recent additions to Incyte, the majority of us have worked together before and successfully developed and commercialized pharmaceutical products.
This year will be remembered as the year Incyte focused its efforts on becoming a leading drug discovery and development company. We have set ambitious, but achievable, goals for 2004. We plan to:

- Initiate and enroll a second Phase II trial for Reverset,
- Advance our first two internally discovered product candidates, a CCR2 receptor antagonist to treat chronic inflammatory diseases and a sheddase inhibitor to treat breast cancer, into human clinical testing, and
- Continue to fuel our pipeline with preclinical candidates from our discovery programs and potentially through the in-licensing of a clinical-stage compound.

Along with scientific prowess and development expertise, in the past year we have added the requisite skills and experience in finance, business development and legal strategy and counsel to our executive team. Our goal is to have every Incyte employee work on a successful pharmaceutical product. I believe this goal is achievable given our organization’s collective experience, tenacity and maturity.

In closing, I would like to thank Jon Saxe, who is retiring from our Board of Directors, for his years of dedicated service, leadership and counsel to our organization.

I appreciate your continued interest and support. I look forward to updating you on our progress throughout 2004, which promises to be an important year for Incyte.

Sincerely,

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

April 2004
Incyte’s CCR2 receptor antagonist program is a new class of drugs with the potential to treat chronic inflammation by interfering with the action of a key inflammatory cell known as the macrophage. Under normal circumstance, macrophage cells clean up damaged, inflamed tissue and then cease their activity. In chronic inflammation, macrophage activity continues inappropriately and the macrophages release molecules toxic to the tissue, including destructive enzymes and pro-inflammatory cytokines, such as TNF, which recruit other inflammatory cells. The severity of inflammation in a number of disease states correlates with the number of macrophages in tissue, and effective anti-inflammatory therapies are associated with a reduction in the number of macrophages.
This image is a model of Reverset (green) binding to the viral polymerase and therefore blocking viral replication of HIV. Reverset is an investigational nucleoside analogue reverse transcriptase inhibitor (NRTI) that is being developed as a once-a-day oral therapy for use in combination with other antiretroviral drugs for patients with HIV infections.