At Exelixis, we are transforming the challenges of our industry into opportunities for success. Our pragmatic approach of building critical mass, making data-driven decisions and integrating diverse areas of science, coupled with our commitment to execution makes it possible to combine remarkable productivity with an unwavering commitment to quality. We believe that our unique strategy allows us to increase our chances for success and ensures a steady stream of high-quality compounds to sustain our growth. We are charting an ambitious path toward our goal of making a positive impact on the lives of patients with cancer because we believe there is **A BETTER WAY TO BETTER MEDICINE**
At Exelixis, our commitment to improving the treatment of cancer has driven us to pursue an uncommon path and a different approach to developing drugs. Recognizing the risks inherent in the innovation of novel therapies, we devised a strategy to mitigate those risks and increase our ability to achieve success by combining high-throughput processes with focused rational science, working with stringent quality standards and focusing on execution. These factors allow us to achieve uncommon productivity and enable development of multiple first-in-class or best-in-class compounds. We have made significant investments to enable this strategy and now we are seeing significant returns in the form of promising clinical data, valuable partnerships and continued advancement of our pipeline.

AN UNCOMMON PATH ONE GOAL
In the age of high-throughput drug discovery, generating data is easy. Rapidly transforming experimental data into insights and knowledge that can catalyze the discovery of innovative new therapies is the challenge of the day. At Exelixis, we are leveraging our fundamental biological expertise to evaluate potential targets and compounds in the context of how diseases such as cancer develop, progress and spread. This approach allows us to assess the value of targeting specific gene products individually and in combination with each other and to rapidly transform the knowledge we gain into compounds engineered specifically to match the biology of the disease. Our deep understanding of how individual targets interact with each other and with numerous disease-related pathways is a lens that brings our wealth of data into focus on developing novel therapies that have the potential to improve patient outcomes.
Execution is an essential part of our business strategy and pursuing the highest quality compounds remains our top priority. Our development group has the expertise to move our development candidates from preclinical testing through all phases of clinical development. Our integrated strategy supports advancement of compounds from development candidate status to investigational new drug status in as little as 12 months. We possess critical expertise in the areas of chemistry, manufacturing and controls, preclinical testing, clinical trial design, management and analysis and regulatory affairs. Our team’s proficiency and productivity is a remarkable asset that has enabled us to advance seven compounds from development candidate status to the clinic in two years.

Ultimately, the value of these compounds will be determined in the clinic. After moving quickly to demonstrate safety in Phase I trials, our strategy is to conduct comprehensive Phase II programs in both targeted and broad fashions based on the genetics of individual tumor types and the pharmacology of our compounds. We believe this approach will drive our efforts to rapidly move toward commercialization along a clearly defined regulatory path.
THROUGH PIONEERING BUSINESS STRATEGIES

We believe that better medicines require a better approach to drug development. Our thoughtful approach to discovery and development allows us to generate data that drives our decisions, attracts valuable partnerships and enables innovative financing strategies. We have implemented a number of creative and high-value partnerships that enhances our productivity, diversifies our risk and potentially increases our chances of success. We believe that the value of our partnerships, the strength of our financing strategy and our success to date in the clinic are evidence that we have found a better way. In this manner, we are transcending the “high-risk” biotechnology business paradigm to create better medicines that will benefit patients, our shareholders and our company.
Our uncommon ability to combine quality and productivity has generated significant momentum in the lab and the clinic. We have filed seven investigational new drug applications (IND) in the last two years and are on track to maintain this rate of progress for the foreseeable future. We are keenly aware of the challenges ahead of us, but believe that we have the resources, insight and commitment to transform those challenges into opportunities for success. As we mature as a product development company and move toward commercialization, we remain grounded in science as we advance toward our goal of making a positive impact in the lives of patients with cancer.
How do we create better medicines? At Exelixis, we set out to build an innovative drug discovery and development company that combines the critical mass and resources of a large pharmaceutical company with the speed and agility more typical of the biotechnology industry. In the process, we let data rather than dogma guide our strategies. When others were taking a correlative approach to identifying and sequencing potential disease-related genes, we were leveraging our expertise in biology to study the actual cause and effect of various genes and pathways on the development and progression of disease. At a time when conventional wisdom said that chemical libraries of 200-300,000 compounds were sufficient, we believed that the data said otherwise. Today, our library of over 4 million compounds is a critical factor in our ability to start the development process with higher-quality compounds, reducing time spent on optimization and increasing our productivity. While most biotech companies have either high-throughput screening or structural biology as the foundation of their discovery platforms, we have integrated excellent capabilities in both areas to expedite the identification and optimization of new development candidates.

Each step we have taken to build a sustainable, integrated drug discovery and development company has advanced us further down a unique path toward improving the outcomes for patients with cancer. I believe that our achievements in 2005 demonstrate clearly that the uncommon path we have chosen is, in fact, a better way to better medicine. Each step we have taken to build a sustainable, integrated drug discovery and development company has advanced us further down a unique path toward improving the outcomes for patients with cancer. I believe that our achievements in 2005 demonstrate clearly that the uncommon path we have chosen is, in fact, a better way to better medicine.
exposure to product failure, enable us to capture long-term value from non-cancer programs and provide attractive economics for our company and our shareholders.

A key example of our ability to access capital through innovative transactions was the establishment of Symphony Evolution, Inc. in June 2005. This transaction will provide up to $80 million to fund comprehensive Phase II programs for XL335, XL228 and XL418. These funds allow us to pursue aggressive clinical programs for all of these programs while eliminating the financial risk of compound failure, since we have no obligation to repay Symphony if the compounds fail. Since these compounds are part of our collaboration with GleeceSmithKline (GSK) and are subject to significant selection payments if GSK elects to take one or more of them forward in clinical development, we can use the milestone payments to provide all or most of the funds that we will provide to Symphony investors in the cause of success.

Additional validation for our productivity and ability to advance compounds quickly through early development was provided by an amendment in January 2005 to our GSK collaboration and by the receipt of $35 million in milestone payments under the collaboration. A total of $30 million was achieved as a result of submitting the INDs for XL880, XL820, and XL44A, for which Phase Ia trials are now ongoing. A second milestone payment, totaling $5 million, was triggered by progress made in several earlier-stage programs.

Throughout the year, we took a number of steps to prioritize our pipeline to focus on our internally developed cancer compounds while retaining the potential long-term value of our other product opportunities. We exclusively licensed XL119 (b catercarin) to Helios Healthcare SA. Under the terms of the agreement, Helios will assume financial and managerial responsibility for the future development of XL119, now in Phase II trials in patients with bile duct tumors. The transaction generated $4 million in upfront payments and provides us up to $21 million in milestones and royalties on sales. Significantly, we have an option of reacquiring commercial rights to XL119 in North America.

Similarly, we licensed our preclinical farnesoid X receptor (FXR) program (XL335) to Wyeth Pharmaceuticals, a division of Wyeth. FXR is a nuclear hormone receptor implicated in a variety of metabolic and liver disorders. We also established a collaboration with Bristol-Myers Squibb Company to advance our liver X receptor (LXR) program (EXEL-2255) that is focused on developing novel therapies fortherosclerosis. In preclinical models, these compounds shrink the size of existing atherosclerotic plaques. If we were to achieve the same results in humans, the potential benefits are obvious. We are very enthusiastic about working with BMS on this extremely exciting project.

TO BETTER MEDICINE

We also initiated a collaboration with Genentech in the areas of oncology, inflammation and tissue growth and repair, amended and terminated on favorable terms the joint venture with Bayer to develop insecticides and nematicides for crop protection, Genoptera LLC and raised net proceeds of $49.6 million through an offering of common stock.

We believe that the key to successfully develop better medicines is to start with a broad portfolio of compounds that have potential for multiple indications. At Exelixis, we currently have eight compounds in clinical development. Phase II trials are ongoing for XL999 and XL2354 and a Phase II trial for XL247 is expected to be initiated next year. Phase I trials of XL1005, XL550, XL44A and XL2354 were initiated in 2005 and we anticipate data will be presented from these ongoing studies and initiate Phase II trials of XL1005 and XL550 in 2006. XL119, which was exclusively licensed to Helios Healthcare SA in June 2005, is in a multinational randomized Phase III trial in patients with bile duct tumors.

We will continue to leverage the strength of our pipeline and drug discovery infrastructure to establish new alliances and execute strategic transactions that enhance our ability to move our promising product candidates toward commercialization. I believe that our success to date shows that we have found a better way. In the months to come, I look forward to sharing with you our progress as we follow this unique path to better medicine.

George A. Scangos, PhD
President and Chief Executive Officer
XL784 was the first small molecule compound developed using our proprietary drug discovery engine. The compound is a potent inhibitor of the AOMT, a matrix metalloproteinase enzyme, a target of significant interest because of its important role in blood vessel formation and cell proliferation. XL784 was specifically optimized to be more matrix metalloproteinase-1 (MMP-1) sparing, thus potentially significantly enhancing its safety profile and enabling higher dosing compared with other previously studied metalloproteinase inhibitors. Results of a single dose Phase I clinical trial of XL784 administered orally to 70 healthy volunteers demonstrated that XL784 has attractive safety and pharmacokinetic profiles. A repeat-dose Phase I clinical trial of a capsule formulation of XL784 was completed in healthy volunteers in 2005 and a Phase II double-blind, placebo-controlled trial in patients with proteinuria associated with diabetic kidney disease was initiated in the first quarter of 2006.

XL647 is a potent inhibitor of RTKs that are implicated in driving tumor proliferation and angiogenesis (tumor blood vessel formation). XL647 inhibits the EPR2 and HER2 VEGFR RTKs simultaneously in preclinical studies. Data from a Phase I trial of XL647 were presented in November 2005. In 31 patients evaluable at the time of the presentation, XL647 was generally well tolerated and demonstrated favorable pharmacokinetic characteristics. To date, 1 patient with NSCLC treated at the lowest dose had a partial response and 7 others (NSCLC n=2, choroid n=1, adenoid cystic carcinoma, adenocarcinoma colorectal, colorectal and breast metastases) have had prolonged stable disease (>1 month). The study is ongoing to select the optimum dose and schedule for Phase II trials anticipated in 2006.

XL647 is expected to enter into Phase II trials mid-year in patients with tumors where the kinases inhibited by XL647 are known to play a role. Additionally, we are considering therapies in patients with tumors where the kinases inhibited by XL647 is expected to enter into Phase II trials mid-year in 2006.

XL844 potently inhibits CHK1 & CHK2, kinases that induce cell cycle arrest in response to a variety of DNA damaging agents, allowing repair of damaged DNA and promoting resistance to many standard chemotherapies. In preclinical studies, XL844 significantly enhances the ability of multiple chemotherapeutic agents to kill tumor cells without increasing systemic toxicity. A Phase I clinical trial of XL844 in patients with chronic lymphocytic leukemia was initiated in September 2005 and data from this study are expected in 2006. We believe that XL8X4 is the first selective small molecule CHK inhibitor to advance into the clinic.

XL184 inhibits VEGFR2 and Met, key drivers for tumor growth and formation. The compelling preclinical efficacy of XL800, our first VEGFR/Met inhibitor, increased our interest in inhibitors of these RTKs and resulted in the discovery and development of XL184, a highly potent VEGFR2 inhibitor with nanomolar potency against Met. XL184 has demonstrated potent growth inhibition and tumor regression in a variety of tumor models. A Phase I clinical trial in patients with solid tumors for whom there are no available therapies was initiated in September 2005 and data from this study are expected in 2006.

**Preclinical: Cancer**

Our preclinical oncology pipeline is comprised of three programs focused on the inhibition of RAF (XL281), Akt/Srk (XL418) and IGF/IR/Src/Akt (XL282), kinases that are implicated in various cancers. All of these three compounds have been designated as drug candidates and will potentially support the filing of INDs in 2006.

**Preclinical: Metabolism**

The preclinical metabolism pipeline is comprised of three programs comprising liver receptor (DXL-2255) in advanced lead optimization, and famoxed X receptor (OL3135) and monoclonal receptor (OLX550) for which drug candidates have been identified. The compounds in these programs modulate nuclear hormone receptors implicated in various metabolic and cardiovascular disorders.