2005 ANNUAL REPORT

A BETTER WAY TO BETTER MEDICINE

EXELIXIS™

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

THROUGH FOCUSED SCIENCE

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.

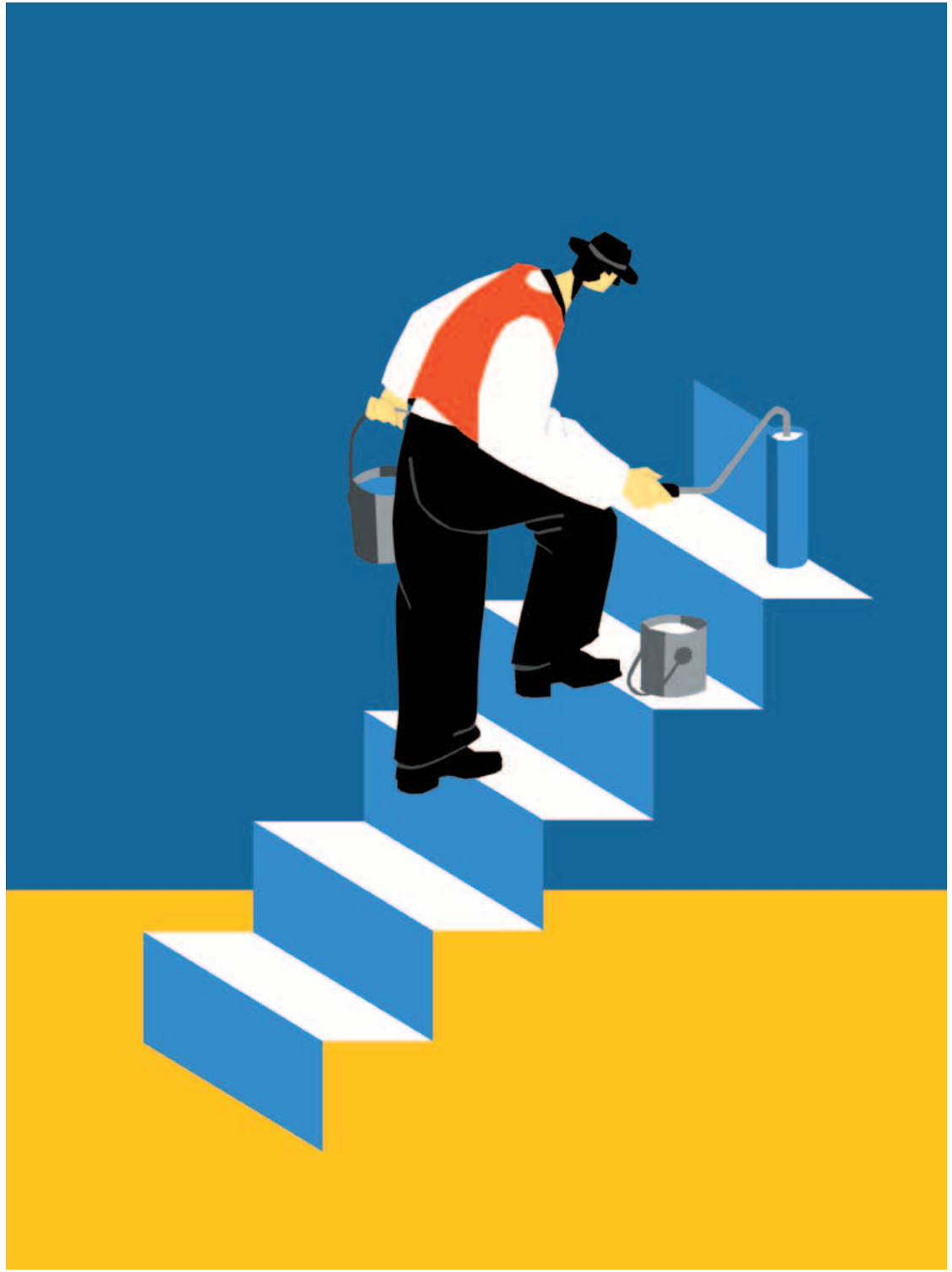
THROUGH ROBUST DEVELOPMENT AND CLINICAL DATA

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.

PUSHING AHEAD ON OUR OWN PATH

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.



left to right: Lupe M. Rivera, CCP, Vice President, Human Resources / Ian D. Malcolm, Vice President, Strategic Marketing / Jeffrey R. Latts, MD, Executive Vice President and Chief Medical Officer / Frank Karbe, Senior Vice President and Chief Financial Officer / George A. Scangos, PhD, President and Chief Executive Officer / Pamela A. Simonton, JD, LLM, Senior Vice President, Patents and Licensing / Michael Morrissey, PhD, Executive Vice President, Discovery / Christoph Pereira, Vice President, Legal Affairs and Secretary

TO OUR SHAREHOLDERS

Why do we need better medicines to treat cancer? Because more than 1,500 people die each day of cancer in the United States alone. Because standard cancer therapies are associated with significant toxicities, some of which are treatment limiting or even life threatening. And because many of those patients who initially beat their disease will eventually suffer a relapse and progression of their disease.

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 platform, 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.

A BETTER WAY

For the second consecutive year, we filed three investigational new drug applications (IND) with the US Food and Drug Administration and now have eight compounds in clinical development. We also advanced five additional compounds to development candidate status, bringing our total number of internally discovered pipeline programs to 13. While the size and diversity of our pipeline underscores our high degree of productivity, clinical data presented in 2005 provided clear evidence that we can advance compounds that meet the highest standards of quality even as we move so quickly.

In November, data were presented from Phase I trials of XL999, XL647 and XL880 at the AACR-NCI-EORTC International Conference on Molecular Targets and Cancer Therapeutics. These are the first data presented on compounds identified through our internal drug discovery efforts and they demonstrate that each compound has favorable safety and pharmacokinetic profiles. Significantly, objective disease responses were observed in all three trials, even though the patients in the studies had very advanced disease, were refractory to standard chemotherapy and had limited treatment options.

In the XL999 trial, of 22 evaluable patients with advanced solid tumors, 3 had objective responses and additional 4 patients had stable disease with duration of 3-7 months. These results provided a compelling rationale to advance XL999 to Phase II development. Encouraging results were also observed in the Phase I trials of XL647 and XL880. The data from these initial Phase I trials validate the quality of the compounds that we are bringing into the clinic and underscore the value of our programs even at early stages of the development process.

We plan to undertake comprehensive Phase II trial programs for XL999, XL784, XL647, XL880 and XL820. A multi-trial Phase II clinical development program for XL999, initiated in December 2005, comprises six trials that evaluate XL999 in colon, ovarian and non-small cell lung cancer, renal cell carcinoma, acute myelogenous leukemia and multiple myeloma. The Phase II trial for XL784 was initiated in the first quarter of 2006 and is being conducted in patients with proteinuria associated with diabetic nephropathy. In 2006, the XL647 trials are expected to be conducted in patients with tumors where the kinases inhibited by XL647 are known to play a role and XL880 is expected to enter clinical trials for the treatment of papillary renal cell carcinoma and other solid tumors. For each of these cancer compounds, we have identified potential fast development routes as well as potential broad indications.

A key challenge for Exelixis is to fund and manage rigorous development programs for the large number of compounds emerging from our discovery group. Throughout 2005, we demonstrated our ability to forge partnerships and execute financial transactions that generate near- and mid-term funding for our most advanced product candidates, reduce our

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 XL999, XL784 and XL647. 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 GlaxoSmithKline (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 case 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 XL844, for which Phase I 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 (becatecarin) to Helsinn Healthcare SA. Under the terms of the agreement, Helsinn will assume financial and managerial responsibility for the future development of XL119, now in Phase III trials in patients with bile duct tumors. The transaction generated $4 million in upfront payments and provides 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 for atherosclerosis. 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.

From a financial standpoint, we entered 2006 with $350 million in cash and committed funding over the next several years, which will support our aggressive discovery and development efforts. We have achieved this success by pursuing a four-pillar financing strategy of partnering assets, delivering on milestones, seeking non-dilutive financing opportunities and opportunistically accessing the capital markets.

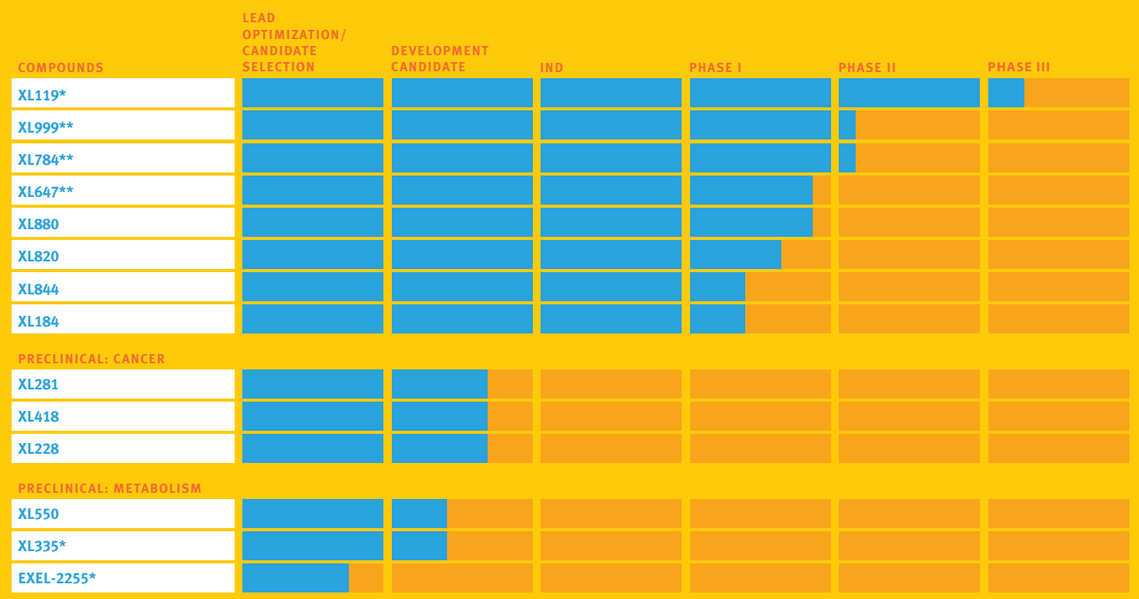
I believe that 2005 was a defining year in our history, one that transformed Exelixis into a development stage company and provided the clinical data to show that we have the capacity for unprecedented levels of productivity and quality. Over the course of 2006, we hope to initiate Phase II trials for XL647, XL880 and XL820, report Phase I data for XL820, XL844 and XL184 and present data from multiple programs at major medical conferences throughout the year. We also expect to advance three or four additional compounds to development candidate status.

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

PIPELINE

We believe that the best way to successfully develop better medicines is to start with a broad portfolio of compounds that have first-in-class or best-in-class potential. At Exelixis, we currently have eight compounds in clinical development. Phase II trials are ongoing for XL999 and XL784 and a Phase II trial for XL647 is expected to be initiated mid-year. Phase I trials of XL880, XL820, XL844 and XL184 were initiated in 2005 and we anticipate data will be presented from these ongoing studies and initiate Phase II trials of XL880 and XL820 in 2006. XL119, which was exclusively licensed to Helsinn Healthcare SA in June 2005, is in a multinational randomized Phase III clinical trial in patients with bile duct tumors.



*XL119, XL335 and EXEL-2255 are out-licensed to Helsinn, Wyeth and BMS, respectively as described in this report.

**Out-licensed to Symphony Evolution, Inc. subject to a repurchase option. We have retained exclusive options to reacquire the compounds at a specified price. We continue to be primarily responsible for the development of these product candidates in accordance with a specified development plan and related development budget.

Pursuant to a product development and commercialization agreement between Exelixis and GlaxoSmithKline, GlaxoSmithKline has the option, after completion of clinical proof-of-concept by Exelixis, to elect to develop up to three compounds in Exelixis' product pipeline, which may include XL784 and the cancer compounds identified in the table above (other than XL119).

XL119 (becatecarin) is a small molecule anticancer compound, for which a multinational Phase III clinical trial in bile duct tumors is ongoing. The Phase III trial includes approximately 60 centers in the United States, Canada and Europe and is designed to enroll up to 600 patients with inoperable bile duct tumors. The primary endpoint of the trial is survival and the two-arm trial is designed to compare patients treated with XL119 to patients treated with 5-FU/leucovorin. Exelixis exclusively licensed XL119 to Helsinn Healthcare SA in June of 2005 and retains rights to reacquire commercial rights to the compound in North America.

XL999 is a potent inhibitor of key receptor tyrosine kinases (RTKs) implicated in the development and maintenance of tumor vasculature and in the proliferation of some tumor cells. It inhibits the FGFR, VEGFR and PDGFR RTKs and also is a potent inhibitor of FLT3, an important driver of leukemia cell proliferation in some patients with acute myelogenous leukemia (AML).

Data from the Phase I trial of XL999 in patients with advanced solid tumors were presented in November 2005. Of 22 patients who had been followed for 8 weeks, there were 3 partial responses (liver, thyroid, renal cell), and 4 patients with stable disease for 3-7 months (thyroid [n=2], renal cell [n=2]). The results of the dose-escalation study also identified a dose that will be used for the Phase II clinical trials.

A multi-trial Phase II clinical development program for XL999 was initiated in December of 2005. The Phase II program is composed of six trials that will evaluate XL999 in colon, ovarian and non-small cell lung cancer (NSCLC), renal cell carcinoma, AML and multiple myeloma. These trials will evaluate XL999 as a single agent, looking for responses in patients who have failed prior therapies. Some of the studies are also designed to evaluate single-agent activity of XL999 in previously untreated patients for whom conventional therapy is not appropriate. The trials will be conducted at multiple centers throughout the United States. In addition we are also considering combination trials of XL999 with other targeted compounds or with cytotoxic chemotherapy.

XL784 was the first small molecule compound developed using our proprietary drug discovery engine. The compound is a potent inhibitor of the ADAM-10 metalloprotease enzyme, a target of significant interest because of its important role in blood vessel formation and cell proliferation. XL784 was specifically optimized to be matrix metalloprotease-1 (MMP-1) sparing, thus potentially significantly enhancing its safety profile and enabling higher dosing compared with other previously studied metalloprotease 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 EGFR, HER2 and 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], chordoma [n=2], adenoid cystic carcinoma, adrenocortical carcinoma, colorectal) have had prolonged stable disease (>3 months). 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 combination trials of XL647 with other anticancer treatments to test the ability of the combination therapy to prolong progression free survival.

XL880 inhibits Met and VEGFR2, which play synergistic roles in promoting tumor growth and angiogenesis. Activation or overexpression of Met is a prevalent feature of a wide spectrum of human tumors and is a negative prognostic indicator in patients with multiple myeloma, glioma and certain solid tumors. XL880 is the first small molecule Met inhibitor to enter the clinic. Interim data from an ongoing Phase I study of XL880 were presented in November 2005. In 13 patients evaluable at the time of the presentation, XL880 demonstrated favorable safety and pharmacokinetic profiles. At that time, one patient with papillary renal cell carcinoma, a tumor driven by mutational activation of Met, experienced a 15 percent reduction in tumor volume after failing multiple other therapies. Since that presentation, the investigators have reported that the patient continued to receive XL880 and subsequently achieved a partial response. Additional data from this trial are anticipated in 2006.

XL820 has demonstrated potent inhibitory activity in preclinical models against KIT, VEGFR and PDGFR, clinically validated targets implicated in a variety of human cancers. In cellular models, XL820 is a potent inhibitor of mutationally activated forms of KIT found in human cancers. In tumor models of breast carcinoma, glioma and leukemia the compound exhibited dose-dependent growth inhibition and has been shown to cause tumor regression. A Phase I clinical trial of XL820 was initiated in July of 2005 in patients with solid tumors for whom there are no available therapies known to prolong survival and data from this study are expected 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 XL844 is the first selective small molecule Chk inhibitor to advance into the clinic.

XL184 inhibits VEGFR2 and Met, key drivers for tumor formation and growth. The compelling preclinical efficacy of XL880, our first VEGFR2/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/S6k (XL418) and IGF1R/Src/Abl (XL228), kinases that are implicated in various cancers. All of these 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 X receptor (EXEL-2255*) in advanced lead optimization, and farnesoid X receptor (XL335**) and mineralocortiocoid receptor (XL550) for which drug candidates have been identified. The compounds in these programs modulate nuclear hormone receptors implicated in various metabolic and cardiovascular disorders.

*Exclusively out-licensed to Bristol-Myers Squibb
**Exclusively out-licensed to Wyeth Pharmaceuticals

Design: Hane Chow, Inc., Oakland, California / Illustrations: Craig Frazier / Photography: Jim Karageorge

Corporate Headquarters
Exelixis, Inc.
210 East Grand Ave.
South San Francisco, CA
94083-0511
650.837.7000 tel
650.837.8300 fax
http://www.exelixis.com

Corporate Counsel
Cooley Godward LLP
Palo Alto, California

Transfer Agent
Mellon Investor Services
480 Washington Blvd.
Jersey City, NJ 07310
800.356.2017 tel
Foreign Shareholders:
+1 201.329.8660
http://www.melloninvestor.com

Independent Registered Public Accountants
Ernst & Young LLP
Palo Alto, California

SEC Form 10-K
A copy of the Exelixis annual report on Form 10-K filed with the Securities and Exchange Commission is available free of charge from the company's Investor Relations Department at Exelixis by calling 650.837.7277.

Stock Information
The common stock of the company is traded on the NASDAQ National Market System under the symbol EXEL.
No dividends have been paid on the common stock since the company's inception.

Quarter Ending	High	Low
03.31.05	$ 9.69	$ 6.02
06.30.05	8.57	6.51
09.30.05	9.37	7.10
12.31.05	9.96	6.57

This annual report contains forward-looking statements, including without limitation all statements related to plans to advance and derive milestones from compounds in clinical and preclinical development, including XL119, XL999, XL647, XL784, XL880, XL820, XL844, XL184 and other early-stage compounds, as well as the therapeutic and commercial potential of these compounds, and all statements related to Exelixis' strategic objectives. Words such as "believes," "anticipates," "plans," "expects," "intends," "will," "slated," "goal" and similar expressions are intended to identify forward-looking statements. These forward-looking statements are based upon Exelixis' current expectations. Forward-looking statements involve risks and uncertainties. Exelixis' actual results and the timing of events could differ materially from those anticipated in such forward-looking statements as a result of these risks and uncertainties, which include, without limitation, the potential failure of product candidates to demonstrate safety and efficacy in clinical testing; the ability of Helsinn Healthcare S.A. to conduct the Phase III clinical trial of XL119 sufficient to achieve FDA approval; the ability to complete and initiate trials at the referenced times; the ability to conduct clinical trials sufficient to achieve a positive completion; the ability to file INDs at the referenced times; the ability of Exelixis to advance additional preclinical compounds into clinical development; and the uncertainty of the FDA approval process. These and other risk factors are discussed under "Risk Factors" and elsewhere in our annual report on Form 10-K for the year ended December 31, 2005 and other filings with the Securities and Exchange Commission. The company expressly disclaims any obligation or undertaking to release publicly any updates or revisions to any forward-looking statements contained herein to reflect any change in the company's expectations with regard thereto or any change in events, conditions or circumstances on which any such statements are based.

EXELIXIS™

www.exelixis.com

210 East Grand Avenue
South San Francisco, CA
94083-0511
650.837.7000 main
650.837.8300 fax