Exelixis in 2004 is a dramatically different company from what it was just a few years ago. We have built and mobilized a truly integrated biotechnology company that has excellent capabilities in drug research, discovery and development. We have critical mass, first-rate employees, and a culture of dedication and hard work. We have created an emerging pipeline that we believe will place us in the first rank of biotech companies. We have remained innovative and fast at the same time that we have grown and matured. We have increased the breadth and depth of our capabilities and at the same time streamlined our processes. Through our commitment to execution and quality, and the combined talents and strengths of all our people, we believe that we are building an important and compelling company.
To Our Stockholders:

Every year of a biotechnology company's life is critical, and 2003 was no exception for Exelixis. We had a remarkably productive year in which we achieved our clinical and strategic goals while we maintained a high level of fiscal responsibility and operational efficiency.

- Phase 2 clinical trials of XL119 were concluded successfully, and we are on track to initiate a Phase 3 clinical trial of XL119 as a potential treatment for bile duct tumors in the second quarter of 2004.

- We successfully conducted the Phase 1 trial of XL784. The compound was administered orally to healthy volunteers and was shown to be free of side effects and to have an attractive pharmacokinetic profile. The compound showed good activity in preclinical models of renal and cardiac disease, providing a basis for pursuing development of XL784 as a potential treatment for renal and cardiovascular failure.

- We filed an IND application for XL647 in the first quarter of 2004, and we are on track to file an IND application for XL999 in the second quarter. XL647 and XL999 are Spectrum Selective Kinase Inhibitors™ that target proteins involved in both tumor proliferation and angiogenesis (blood vessel formation). Each compound has a different spectrum of inhibition against receptor tyrosine kinases (RTKs) and each has the potential to maximize efficacy through simultaneous inhibition of multiple RTKs.

- We anticipate filing an IND application for XL844 in early 2005, and we have several additional preclinical programs slated for IND applications in 2005 and beyond.

- We extended and expanded our oncology collaboration with Bristol-Myers Squibb, extended our herbicide collaboration with Dow AgroSciences, and achieved our collaboration goals with Bayer, GlaxoSmithKline and all of our other strategic partners.

- We delivered a strong financial performance and exceeded our cash goal by ending the year with approximately $242 million in cash, cash equivalents, short-term investments and restricted cash.
We have generated a substantial development pipeline of small molecule cancer compounds that we believe have the potential to deliver significant benefit to patients with many different types of cancer. The pipeline is led by XL119, which is entering the final stage of clinical testing, and includes XL784, XL647, XL999, XL844 and additional novel anticancer compounds arising from our gene-to-drug platform. This progress is especially notable given that Exelixis began its platform-to-product transformation about three years ago. To have built to critical mass and excellence, to have rapidly mobilized our discovery and development capabilities, and to have generated what we believe is one of the most interesting collection of anticancer compounds in the industry, all within a short timeframe, are remarkable achievements and are attributable to Exelixis' unique blend of intensity, pragmatism and innovation.

Our strong performance in 2003 has set the stage for what we believe will be a successful 2004. We anticipate advancing multiple development candidates that could lead to additional IND applications in 2005 and 2006, and we have more than 30 other targets in high-throughput screening, representing a broad spectrum of commercially interesting drug target classes including kinases, G-protein coupled receptors (GPCRs), nuclear hormone receptors and phosphatases.

- **XL119** is a small molecule anticancer compound for which Exelixis is currently undertaking activities leading to the planned initiation of a Phase 3 trial as a potential treatment for bile duct tumors. Safety and activity data presented at the 2003 annual meeting of the American Society of Clinical Oncology (ASCO) from a Phase 2 clinical trial in 33 patients with bile duct tumors (gall bladder tumors and cholangiocarcinomas) treated with XL119 showed encouraging results relative to overall survival and progression free survival. In addition, data from a Phase 2 clinical trial in 36 patients with non-small cell lung cancer were also presented and showed encouraging results relative to survival. The Phase 3 trial will be conducted with a comparator arm of 5-FU/leucovorin and with a survival-based endpoint. The company anticipates that the Phase 3 trial will begin in the second quarter of 2004. It is estimated that the incidence of bile duct tumors is approximately 30,000 patients per year, worldwide.
The Exelixis Pipeline

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<thead>
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<th>COMPOUND</th>
<th>Lead Optimization / Candidate Selection</th>
<th>Development Candidate</th>
<th>IND</th>
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XL784 is a potent inhibitor of the ADAM-10 metalloprotease (MP) enzyme, a target of significant interest because of its important role in blood vessel formation and cell proliferation. XL784 was specifically optimized to be MMP1-sparing, thus potentially significantly improving its safety profile and enabling higher dosing in comparison to MMP inhibitors. In preclinical studies, XL784 dosed orally demonstrated significant inhibition of human tumor xenografts derived from a variety of human carcinoma cell lines, and excellent activity in rat models of renal and cardiac failure. Data from a Phase 1 clinical trial of orally administered XL784 in healthy volunteers showed single doses of the compound to be free of side effects and to have an attractive pharmacokinetic profile. In 2004, Exelixis plans to pursue a development path in renal and cardiovascular disease. The company plans to develop a new formulation suitable for chronic administration in patients with renal and cardiac failure with the intention of aggressively moving the compound through development. It is estimated that there are more than three million patients in the U.S. with diabetic nephropathy, a large and currently underserved market. Scientists at Exelixis use high intensity X-ray light to probe the atomic details of human proteins implicated in serious diseases. These studies facilitate the rational design of new therapeutics that specifically interact with and modulate the activity of the protein target.
• XL647 is a potent inhibitor of RTKs that are implicated in driving tumor proliferation and vascularization. XL647 simultaneously inhibits the EGFR, HER2, VEGFR and EphB4 RTKs with high potency and demonstrates excellent activity in target-specific cellular functional assays. XL647 has good oral bioavailability and shows sustained inhibition of target RTKs in vivo following a single oral dose. In preclinical models of major tumor types, including human breast, lung, colon and prostate cancer, XL647 demonstrates potent inhibition of tumor growth and has been shown to cause tumor regression in one model. Consistent with its spectrum of activity, analysis of tumors from XL647-treated animals show significant decreases in both tumor vascularity and tumor cell proliferation and an increase in tumor cell death. We filed an IND application for XL647 in the first quarter of 2004.
• **XL999** is a potent inhibitor of key RTKs that are implicated in the development and maintenance of tumor vasculature. XL999 simultaneously inhibits the FGFR, VEGFR, PDGFR and Flt3 RTKs with high levels of potency and demonstrates excellent activity in target-specific cellular functional assays. In preclinical models of major tumor types, including human breast, lung, colon and prostate cancer, XL999 demonstrates potent inhibition of tumor growth and has been shown to cause tumor regression. XL999 shows rapid onset of action in vivo with significant tumor apoptosis/necrosis and vascular disruption observed after a single oral dose in two different cancer models. XL999 is suitable for both oral and intravenous dosing and shows sustained inhibition of target RTKs in vivo following a single oral dose. In addition, XL999 is a potent inhibitor of Flt3, which is an important driver of cell proliferation in many patients with acute myelogenous leukemia, and demonstrates remarkable potency in a Flt3-driven model of leukemia. Exelixis anticipates filing an IND for XL999 in the second quarter of 2004.

• **XL844** is a potent, selective inhibitor of Chk1 & 2, protein kinases that induce cell cycle arrest in response to a variety of DNA damaging agents. The company believes that XL844 is the first potent, selective Chk inhibitor to advance toward the clinic. In preclinical studies, XL844 has demonstrated significant potency in biochemical and cellular assays, good oral bioavailability and an attractive pharmacokinetic profile. XL844 potentiates the efficacy of chemotherapeutic agents in preclinical tumor models without a concomitant increase in systemic toxicity by exploiting genetic liabilities that arise during tumor cell expansion. Exelixis will continue to evaluate the synergistic effects of XL844 in combination with a variety of DNA damaging agents in different cell lines, both in vitro and in vivo, and to explore the compound’s potential as a radiation sensitizer. It is estimated that close to two million patients worldwide currently receive cancer chemotherapy and 750,000 patients worldwide currently receive radiation therapy for cancer, suggesting that XL844 could have significant therapeutic and commercial potential as a potentiating agent. The company anticipates filing an IND application for XL844 in early 2005.

• **Other Preclinical Programs:** Exelixis has a broad portfolio of compounds in lead discovery and optimization and anticipates advancing several additional compounds toward potential IND applications in 2005. These compounds have demonstrated high levels of potency in biochemical assays as well as excellent cellular and pharmacokinetic properties. Key targets in these ongoing efforts include:

• **KIT**, a RTK that is mutated in a number of human cancers, including gastrointestinal stromal tumors, and is expressed at higher than normal levels in cancers such as small cell lung and ovarian carcinoma. EXEL-9820 is the company’s lead compound active against this target.

• **MET**, a RTK that is over-expressed in the majority of human tumors, including all the major solid tumor classes, and contributes to the growth, survival and invasive properties of tumor cells. EXEL-2880 is the company’s lead compound active against this target.

• **ALK**, a RTK normally expressed in the developing nervous system that becomes inappropriately activated via chromosomal translocations in a subset of non-Hodgkin’s lymphoma patients. EXEL-6109 is the company’s lead compound active against this target.

• **p70S6K**, a serine-threonine kinase that controls cell growth and is at the end of a pathway that is frequently activated through mutation or gene amplification in many human tumors. EXEL-2942 is the company’s lead compound active against this target.
In 2003, Exelixis installed a new, custom-designed high throughput screening assay platform that supports both 384- and 1536-well microtiter plate formats and increases throughput to over 600,000 compounds per day.
We are proud of our company and of our people— their extraordinary talents and will to succeed. Together, we are working toward the day when patients in need can benefit from our efforts and enjoy longer, healthier lives.
THE GENE-TO-DRUG DIFFERENCE

We have combined our unique strengths in biology, drug discovery and development to create a highly integrated, fine-tuned and productive R&D engine that is operating in high gear.

Our strong biology-based research leverages considerable assets in comparative genomics and invertebrate and vertebrate genetics and utilizes state-of-the-art high-content screening to elucidate complex biological pathways and identify and validate key targets of interest. We believe that we possess broad expertise in commercially attractive target classes, including kinases, proteases, GPCRs and ATP-utilizing enzymes.

Our substantial drug discovery capability has gained critical mass in all operational areas. Our screening library today is comprised of greater than three million highly diverse, well-characterized compounds. In 2003, we performed 38 high-throughput screens. We can screen over 600,000 compounds per day, generating highly potent leads (5-10 nanomolar) and, in less than one year, generate optimized lead compounds with full pharmacokinetic, efficacy and toxicological profiles. Our structural biology capability is first-rate: we have crystallized and determined the structures of almost 20 of our protein targets, and we created more than 200 co-crystals of compounds and targets of interest. We have four fully staffed, multi-disciplinary lead optimization teams capable of producing a steady stream of high quality development candidates that represent potential future development programs.

Our development group is comprised of disciplined, experienced professionals with the expertise to quickly move our development candidate compounds from preclinical testing to IND status and through Phase 3 clinical trials.

Working closely together, our research, discovery and development groups are currently operating on a trajectory of advancing a compound from screen to IND in two years or less, filing at least two IND applications per year, and concurrently conducting multiple clinical trials.

The creative process of marrying high-quality biology and drug development began about three years ago at Exelixis, and today represents what we believe is an unusually high level of productivity in the biotechnology arena. Proud as we are of our platform capabilities, the ultimate measure of our value will be therapies that we bring to patients in need. We believe that in 2004 and beyond, we will build on the rapid progress that we have made toward this goal and will continue to advance along the pathway to products.
Exelixis is committed to meeting or exceeding its partners’ expectations. Our integrity and follow-through have engendered a high degree of respect and reciprocity among our corporate collaborators. In the area of oncology, with Bristol-Myers Squibb and with GlaxoSmithKline, we have established broadly enabling, collegial relationships that leverage and add value to our assets, fund our pipeline growth, provide significant revenue and milestones, and provide a pathway to potential commercialization. Our combinatorial chemistry collaborations have been highly productive. Our agricultural collaborations with Bayer, Dow AgroSciences and Renessen also leverage key capabilities. Our Exelixis Plant Sciences subsidiary has delivered many new high quality agricultural leads to these partners while developing a new program in the cell-based production of valuable plant-derived compounds. This program is designed to facilitate the rapid production of a variety of well-defined plant compounds in controlled and contained laboratory environments, and to set the stage for additional partnering opportunities.

Because a lot of what transpires in collaborations is shared only by the parties involved, putting a value on the intangible rewards and acknowledgments that occur in good partnerships is challenging for investors. We believe that our collaborations are models of how pharmaceutical and biotechnology companies can work together successfully to exploit novel insights, defray the risks and share in the rewards of drug discovery and work together to advance compounds towards the market.
In our development collaboration with GlaxoSmithKline, we believe that we are advancing programs that are consistent with our partner’s internal standards of excellence. The productivity of our cancer collaboration with Bristol-Myers Squibb was underscored in their decision at the end of 2003 to extend and significantly expand our relationship for another five years. Our collaboration with Bayer continues to generate interesting and unique assets that may be the basis for novel and environmentally-friendly pesticides. Separately and together, these collaborations capitalize on the innovativeness and professional capabilities of our respective organizations. They provide significant committed funding and performance milestones and are key contributors to our financial performance. Equally important, these relationships help build our asset base, fuel our pipeline, enhance our reputation and enable us to benchmark our performance against highly respected R&D organizations.

In 2004 and beyond, we anticipate cultivating new strategic opportunities that have the potential to leverage our assets in therapeutic areas outside of cancer, broaden the potential of our development pipeline and provide additional funding with which we can advance our proprietary programs. Our goal is to continue to maintain balance in partnered and retained rights to our assets and ensure considerable commercial participation in products emerging from collaborations.
COMMITMENT TO FISCAL RESPONSIBILITY

Exelixis delivered a strong financial performance in 2003. As compared to 2002, we increased revenue by 16.3% and, despite significant expansion in the output of our drug discovery and development programs, were able to keep the increase in operating expenses to just 11.8%.

We ended the year with approximately $242 million in cash, cash equivalents, short-term investments and restricted cash, a healthy balance sheet and sufficient resources to set and achieve aggressive operating goals in 2004 and beyond.

As our company has matured and our development efforts have intensified, we have restructured the organization as needed to reallocate resources and enhance the efficiency of our operations. We believe that these efforts have strengthened the company by enabling us to achieve an appropriate functional balance within the organization. We have retained our substantial biological capabilities that are at the core of the company, expanded our discovery and development assets and enhanced our ability to aggressively expand our development pipeline. We believe that organizational growth, ambitious performance and fiscal prudence are compatible, and we intend to continue to operate in a highly focused, productive and financially responsible manner.
Exelixis is still a relatively young enterprise: in 2004, we will celebrate the 10-year anniversary of our founding and mark our remarkable evolution from a fly genetics laboratory to a potentially important cancer therapeutics company. We are proud of our company and of our people — their extraordinary talents and will to succeed. Together, we are working toward the day when patients in need can benefit from our efforts and enjoy longer, healthier lives.

Our goals for 2004 are substantial. We intend to file an IND application for XL999, initiate clinical programs for XL647 and XL999, advance XL844 toward IND status in early 2005 and make progress in our other preclinical programs with the goal of filing additional IND applications and initiating additional clinical programs in 2005 and beyond. We anticipate initiating the Phase 3 clinical trial for XL119 in patients with bile duct tumors before the end of the second quarter 2004. We expect to grow our revenue, manage expenses and continue to maintain a healthy cash balance. We expect to continue to use corporate partnering as a strategic tool to monetize our assets and fund our operations, and we plan to expand the therapeutic and commercial potential of our pipeline. In short, we intend to continue to exploit and manage our assets, advance our pipeline and build an important biotechnology company with the potential to improve the lives of patients with serious diseases.

The Exelixis management team and board of directors join me in expressing our appreciation to you, our stockholders, for your ongoing support and confidence.

George A. Scangos, PhD
President and Chief Executive Officer
Exelixis, Inc.
Corporate Information

Corporate Headquarters
Exelixis, Inc.
170 Harbor Way
P.O. Box 511
South San Francisco, CA 94083-0511
650-837-7000 tel
650-837-8300 fax
e-mail: info@exelixis.com
http://www.exelixis.com

Corporate Counsel
Cooley Godward LLP
Palo Alto, California

Transfer Agent
Mellon Investor Services
85 Challenger Road
Overpeck Center
Ridgefield Park, NJ 07660
800-356-2017 tel

Foreign Shareholders:
+1 201-329-8660 tel
http://www.melloninvestor.com

Independent Auditors
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 650-837-7012 or via e-mail: ir@exelixis.com

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 Low High
03.31.03  $6.35  7.29
06.30.03  6.65  7.28
09.30.03  7.00  7.50
12.31.03  6.71  7.12

Management
George A. Scangos, PhD
President and Chief Executive Officer, Exelixis, Inc.

Lance Willsey, MD
Founding Partner, DCF Capital

Frank McCormick, PhD
Director of the University of California, San Francisco
Comprehensive Cancer Center

George A. Scangos, PhD
President and Chief Executive Officer, Exelixis, Inc.

Board of Directors
Stelios Papadopoulos, PhD
Chairman of the Board, Exelixis, Inc.
Managing Director, Investment Banking Healthcare, SG Cowen

Charles Cohen, PhD
Chairman, Supervisory Board, Cellzome GmbH

Jason Fisherman, MD
Managing Director, Advent International Corporation

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Director, Boyer Center for Molecular Medicine and Professor of Pathology and Cell Biology, Yale University

Frank Karbe
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Jeffrey R. Latts, MD
Senior Vice President and Chief Medical Officer

Michael M. Morrissey, PhD
Senior Vice President, Discovery

Gregory D. Plowman, MD, PhD
Senior Vice President, Pharmaceutical Research

Pamela A. Simonton, JD, LLM
Senior Vice President, Patents and Licensing

Jane M. Green, PhD
Vice President, Corporate Communications

D. Ry Wagner, PhD
Vice President, Research, Exelixis Plant Sciences

This annual report contains forward-looking statements, including without limitation all statements related to plans to advance compounds in preclinical and clinical development, including XL119, XL784, XL647, XL999, XL844 and other early-stage compounds, as well as the therapeutic and commercial potential of these compounds, and all statements related to cultivating new strategic opportunities. Words such as “believes,” “anticipates,” “plans,” “expects,” “intends,” “will” 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 are discussed under “Risk Factors” and elsewhere in our annual report on Form 10-K for the year ended December 31, 2003, 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 our expectations with regard thereto or any change in events, conditions or circumstances on which any such statements are based.

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