
momentum

Thinking larger. Moving faster.

Creating the ***momentum*** to reach our goal.

Momentum is defined as the energy of a moving body measured by its mass and speed. At Exelixis, we have combined extensive capabilities across all areas of drug discovery and development with an ability to move with remarkable speed and accuracy. In doing so, we have created significant momentum. We are focusing that energy on a singular objective: developing innovative and superior therapies that enhance the care and lives of patients with serious diseases.

an ambitious strategy

While there is no defined path to success for a biopharmaceutical company, we firmly believe that there are certain principles that are essential: put the patient first, let the data be your guide, do the job right the first time and never allow conventional wisdom to stand in the way of innovation.

At Exelixis, we live these ideals daily, and we are committed to making our company one of the top in our industry. Our strategy for attaining this level of success, while ambitious, is simple: commercialize novel therapies that are first-in-class or best-in-class treatments for major illnesses such as cancer.

Simple, however, does not mean easy, and we understand the challenges that are ahead of us. Since our inception, we have worked diligently to assemble the team and technology we need to address those challenges and maintain our momentum. We have integrated our unique strengths in biology with an exceptional drug discovery and development capability.

The output of our processes is extraordinary: the sustained ability to move multiple candidates from screening to the clinic in less than two years. Thinking large, moving fast and focusing on patients' needs defines our path for success and puts us well on our way to reaching our ambitious goal.

unwavering execution

We recognize that our ability to achieve our objectives is only as strong as our ability to execute our strategy. Our accomplishments thus far are the result of a commitment to execution, and are a reminder to every member of the Exelixis team that we can achieve great things when we demand excellence from ourselves.

We believe that any activity worth undertaking is worth doing to the best of our ability. By deploying the resources we need to do the job right the first time, we can provide greater return on our investment than could be achieved working on a more limited scale. On this philosophy, we have assembled one of the largest compound libraries in our industry, developed the ability to screen that library rapidly, and move the most interesting compounds aggressively forward.

In 2004, we filed three investigational new drug applications (INDs) and are on track to file three more in 2005, exceeding our aggressive goal of filing two new INDs each year. Importantly, we have achieved this level of output while maintaining stringent quality criteria for the compounds. All of these INDs are for compounds that have a chance to be first-in-class or best-in-class therapies. This diverse and growing pipeline provides significant opportunities for success over the near-, mid- and long-term.

targeting multiple pathways

Our unique strengths in biology enable us to evaluate the role of specific genes and pathway interactions in the development, progression and treatment of cancer and other diseases. We believe that the most effective therapies for cancer will target multiple pathways, simultaneously shutting off growth signals, increasing rates of programmed cell death and reducing the growth of blood vessels necessary to support tumor growth.

At Exelixis, our focus has been on developing Spectrum Selective Kinase Inhibitors™ (SSKIs), which are specifically optimized to inhibit a unique combination of receptor tyrosine kinase (RTK) activities. RTKs are proteins that play an essential role in mediating many cancer-related pathways. These compounds have the ability to target simultaneously multiple pathways involved in tumor growth and angiogenesis, thereby providing the potential for more potent therapeutic effects. Our broad portfolio of SSKIs enables us to match the specific inhibition profile of each compound with the complex biology of a particular type of cancer. We believe these compounds have the potential for greater potency and efficacy than most currently available cancer therapies.

We are leveraging our unique biology capabilities and discovery infrastructure to expand our pipeline into additional therapeutic areas, including metabolic and cardiovascular diseases. In these areas, we are targeting nuclear hormone receptors (NHRs) and G-protein coupled receptors (GPCRs), target classes that are amenable to our high throughput screening and drug discovery processes.

an absolute commitment to quality

At Exelixis, we have rapidly generated a robust and growing pipeline of compounds. However, we believe that quantity is only one aspect of the story, and we are firmly committed to undertaking everything we do with the highest quality. We believe that quality starts with people. We have built departments with critical mass and expertise in all areas of drug discovery. We have hired people at the top of their fields because we have made an organizational commitment to critical mass and excellence. We have developed a culture of aggressive hard work.

Drug research and discovery is a process and we believe that there is substantial room for improvement in the quality of that process as it has been carried out over the past few years within our industry. We have designed our processes from the bottom up, going back to first principles to design approaches that take advantage of our strengths and overcome possible competitive disadvantages. The result is that we have repeatedly gone from screen to IND in two years or less. This is a remarkably short period of time that reflects both the design of the processes and the quality of the people carrying them out.

Most importantly, the quality of our compounds is paramount. Our goal is to discover and develop compounds that will provide therapeutic value and improve the lives of patients with cancer and other serious diseases. Therefore, it is imperative that we put our resources behind compounds that are of the highest quality and that meet stringent criteria.

By doing so, we may minimize the risks of clinical failure. Each of our compounds has the potential to be first-in-class or best-in-class, and we will continue to put our resources behind such projects.

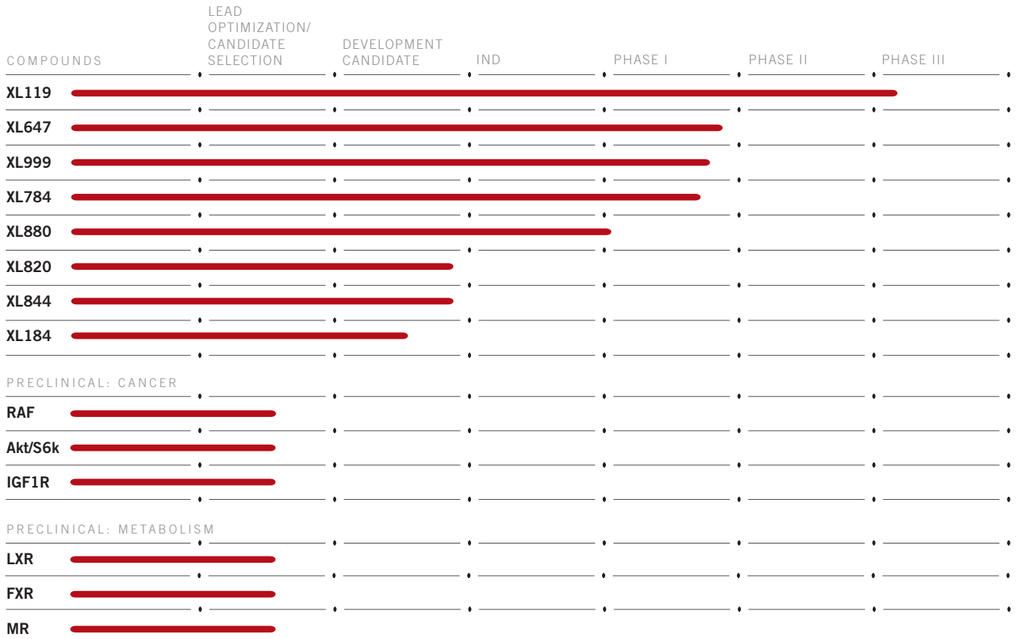
innovative partnerships

The power of our drug discovery engine has supported deal structures that allow Exelixis to retain a significant portion of the downstream value of any products developed through these partnerships, as exemplified by our partnerships with Bristol-Myers Squibb (BMS) and GlaxoSmithKline (GSK).

In our BMS collaboration, we are using our understanding of cancer biology to discover novel targets. Targets discovered under the collaboration are divided equally between the companies for further development and will support the development of novel cancer therapies providing the foundation for the growth of our cancer franchise. Additionally, through an earlier collaboration with BMS we obtained a clinical-stage compound (XL119) and other technology that we have used to advance our programs.

Our collaboration with GSK was established to discover and develop novel therapeutics. This partnership provides significant funding to advance our broad pipeline while enabling us to potentially retain ownership of a majority of our compounds. GSK has the option to select two or three of our current pipeline programs for continued development following Phase IIa trials, while the remainder of the compounds will be owned by Exelixis. Compounds covered by the collaboration include our current development pipeline (except for XL119) and five early stage programs. For those compounds selected by GSK, Exelixis will receive significant milestone payments, double-digit royalties on product sales and certain rights to co-promote products in North America.

building a pipeline with significant potential



In 2004, we leveraged the momentum generated by our powerful drug discovery engine. We filed three investigational new drug applications (INDs) and made substantial progress moving forward other compounds in our pipeline. Each compound in the pipeline has demonstrated first-in-class or best-in-class potential in a variety of preclinical studies. The quality, diversity and depth of the Exelixis pipeline provide significant opportunities to benefit patients, our shareholders and our company.

CLINICAL PROGRAMS

XL119 (becatecarin) is an anticancer compound that we are developing as the first potential treatment indicated for bile duct tumors. In a Phase II clinical trial, patients with bile duct tumors who received XL119 showed encouraging results relative to overall survival. The ongoing Phase III trial, initiated in June of 2004, is designed to compare patients treated with XL119 to patients treated with 5-FU/leucovorin.

The two-arm 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.

XL647, Exelixis' first Spectrum Selective Kinase Inhibitor™ (SSKI), has been designed to inhibit targets that are involved in the proliferation of tumor cells, and to simultaneously inhibit targets involved in bringing a blood supply into the tumor. This strategy is realized through simultaneous inhibition of EGFR, and HER2, which are involved in tumor cell growth, and VEGFR, which is a potent driver of tumor vascularization. Each of these molecules is a target for currently approved cancer therapies, but they have not been previously combined into one molecule. In preclinical models of major tumor types, including human breast, lung, colon and prostate cancer, XL647 demonstrated potent inhibition of tumor growth and caused tumor regression in one model. In our studies, XL647 demonstrated more potency than other EGFR inhibitors, including two inhibitors currently approved for treating cancer.

An IND was filed for XL647 in February of 2004 and initial results of an ongoing Phase I dose-escalation trial suggest that the compound is orally bioavailable, well absorbed, and has an excellent half-life. We anticipate reporting results from this trial in 2005.

XL999 Angiogenesis, the process by which new blood vessels form, plays an important role in supporting tumor growth. Drugs that target VEGF, a molecule which attracts blood vessels into tumors, have been shown to provide effective therapy for certain types of tumors. FGF and PDGF are two additional molecules that also are potent stimulators of angiogenesis, and XL999 is a SSKI that is designed to simultaneously inhibit receptors for VEGF, FGF and PDGF. XL999 also potently inhibits Flt3, an important driver of cell proliferation in many patients with acute myelogenous leukemia (AML).

In preclinical models of major tumor types, including human breast, lung, colon and prostate cancer, XL999 demonstrated potent inhibition of tumor growth and induced tumor regression. Potent activity also has been observed in an Flt3-driven model of leukemia. 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.

An IND was filed for XL999 in June of 2004. A Phase I trial of XL999 is ongoing and we anticipate reporting results from this trial in 2005.

XL784 is a potent inhibitor of ADAM-10, a metalloprotease enzyme that plays an important role in blood vessel formation and cell proliferation. XL784 showed good activity in a rat model of renal failure. Data from a Phase I trial of orally administered XL784 in 70 healthy volunteers showed that single doses of the compound had favorable safety and pharmacokinetic profiles. Efforts by other groups to develop metalloprotease inhibitors have failed largely due to unfavorable toxicology in joints, which potentially result from inhibition of another metalloprotease enzyme, MMP-1. We addressed this issue by optimizing XL784 to avoid inhibition of MMP-1, potentially improving its safety profile and enabling higher dosing in comparison to other metalloprotease inhibitors.

Throughout 2004, we made progress in developing an XL784 formulation suitable for chronic administration to patients with renal failure. We successfully concluded long-term toxicology studies, and we generated additional pharmacology data. We anticipate initiating additional clinical studies for this indication in 2005.

XL880 is the most advanced compound of which we know that targets an important driver of tumor cell proliferation and angiogenesis called Met, while simultaneously inhibiting VEGFR2 (KDR) also involved in angiogenesis, and Flt3, involved in certain leukemias. Activation or overexpression of Met has been implicated in a wide variety of solid tumors, multiple myeloma, glioma and hereditary and sporadic papillary renal carcinomas. XL880 is a SSKI that has demonstrated dose-dependent growth inhibition of tumor models for breast, colon and small cell lung cancer and glioblastoma and has been shown to cause tumor regression in many models. Significantly, in one of these models a single dose of XL880 completely inhibited tumor growth for 21 days.

The IND for XL880 was filed in December 2004, and we initiated the Phase I trial in early 2005.

PRECLINICAL PROGRAMS

XL820 is a SSKI with demonstrated inhibitory activity against VEGFR, KIT and PDGFR, clinically validated targets implicated in a variety of human cancers. In tumor models of breast carcinomas, gliomas and leukemia, the compound exhibited dose-dependent growth inhibition and has been shown to cause tumor regression. We expect to file an IND for XL820 in the first half of 2005.

XL844 potently inhibits Chk1 & 2, kinases that induce cell cycle arrest in response to a variety of DNA damaging agents. We believe that XL844 is the first Chk inhibitor to advance toward the clinic. In preclinical studies, XL844 has been shown to enhance the efficacy of chemotherapeutic agents in tumor models, without increasing systemic toxicity. We expect to file an IND for XL844 in the first half of 2005.

XL184 inhibits VEGFR2 and Met, previously discussed as key drivers for tumor formation and growth. The compelling preclinical efficacy of XL880 led us to identify XL184 as an additional compound with a potent Met/VEGFR2 inhibitory profile. This SSKI has demonstrated dose-dependent growth inhibition of tumor models for breast, colon and small cell lung cancer and glioblastoma and has been shown in tumor models to cause tumor regression. We expect to file an IND for XL184 in the first half of 2005.

ADVANCED LEAD OPTIMIZATION PROGRAMS

The power of the Exelixis drug discovery engine provides us with a renewable source of promising compounds: we have six programs in advanced lead optimization, three in oncology and three in metabolism. In 2005, we expect to advance compounds from each program to drug candidate status, with IND filings beginning in 2006.

CANCER

We are currently optimizing additional lead compounds against RAF, Akt/S6k and IGF1R, targets with significant potential in the treatment of cancer.

METABOLIC DISORDERS

We are evaluating a variety of innovative compounds with potential utility in cardiovascular disease and metabolic disorders such as dyslipidemia, diabetes and obesity. Targets for these compounds are Liver X Receptor (LXR), Farnesoid X Receptor (FXR) and Mineralocortiocoid Receptor (MR).

letter to our shareholders

It is remarkable to think of the progress that Exelixis has made over the past few years. Two years ago, our only clinical compound was XL119, which we in-licensed from our partner, Bristol-Myers Squibb (BMS) and we had only filed one investigational new drug application (IND) for XL784. Today, we have five compounds post IND that are aggressively advancing in clinical development, and we anticipate bringing another three compounds into the clinic in 2005. It is a remarkable achievement to have generated such a deep pipeline of high-quality compounds, and we feel justifiably proud of our accomplishments.

At the same time, we know that while generating a pipeline and filing INDs are important milestones what truly matters is moving our compounds quickly and intelligently through the clinic and onto the market to provide benefits to patients in need. We are aware of the challenges ahead of us, and I am confident that we are well-positioned to meet those challenges to build a thriving, exciting company. I want to take this opportunity to highlight our key 2004 achievements and briefly discuss our 2005 goals.

PIPELINE AND CLINICAL PROGRAMS

In 2004, we filed INDs with the Food and Drug Administration (FDA) for three Spectrum Selective Kinase Inhibitors™ (SSKIs), XL647, XL999 and XL880. Each of these novel compounds was generated by our internal discovery engine and has significant potential as a first-in-class or best-in-class cancer therapy. Phase I trials for XL647 and XL999 were initiated in 2004, and the Phase I trial for XL880 was initiated in early 2005. Results of the Phase I trials for at least two of these compounds are anticipated in 2005.

Development of XL784 continued as planned in 2004. This compound is a potent inhibitor of the ADAM-10 metalloprotease enzyme. Our intent is to move this compound forward as a potential treatment for chronic renal failure, focusing on diabetic nephropathy. In 2004, we conducted pharmacological studies to further assess the potential of the drug in renal failure, successfully concluded chronic toxicology studies, and developed a formulation for XL784 that is suitable for chronic administration. We anticipate initiating additional clinical studies in 2005.

We achieved two important objectives in our development of XL119 (becatecarin). In March, the FDA granted orphan drug designation to this compound as a treatment for bile duct tumors, and in June we initiated a Phase III trial for XL119 in this indication. The trial will compare survival of patients with inoperable bile duct tumors treated with XL119 to patients treated with 5-FU/leucovorin and is statistically powered to show a two-month increase in survival. The Special Protocol Assessment (SPA), established with the FDA, recognizes this as a clinically meaningful outcome.

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

In 2004, we expanded our program in metabolic and cardiovascular diseases through the acquisition of X-Ceptor Therapeutics, Inc. X-Ceptor has developed one of the most sophisticated programs in the biology of a class of proteins called Nuclear Hormone Receptors (NHRs). We believe that these molecules have substantial potential as drug targets to treat cancer, metabolic diseases, cardiovascular diseases, and other indications as well. The expertise represented by X-Ceptor will allow us to attack the biological complexity of this area. More importantly, X-Ceptor had three advanced lead-optimization projects and with our added capabilities, we are confident of moving them into development in 2005 and 2006. These programs target the Liver X Receptor (LXR), Farnesoid X Receptor (FXR), and Mineralocortiocoid Receptor (MR), and could represent important new therapies for metabolic and cardiovascular diseases. These programs provide exciting clinical and commercial opportunities, and we intend to aggressively advance their development.

PARTNERSHIPS AND COLLABORATIONS

We continued to make substantial progress in our partnerships with GlaxoSmithKline (GSK) and BMS. Our collaboration with GSK successfully produced high-quality clinical compounds more quickly than anticipated, which created a short-term imbalance in the payments we were to receive from GSK. To help pay for this success, we amended our agreement with GSK to address this short-term funding issue. Although the amendment to our collaboration was signed in early January of 2005, it was largely negotiated during 2004.

As part of the amendment, GSK agreed to provide $35 million in new milestone payments, which are creditable against downstream milestones. The new $35 million milestones, which we are confident of reaching in 2005, reflects GSK's confidence in our ability to successfully reach additional downstream milestones. Furthermore, we can now obtain independent funding for clinical development of the most advanced compounds in the collaboration under financial terms that can substantially reduce our cost of capital. The new funding will facilitate our ability to aggressively move our compounds forward.

The amendment also defined the scope of the collaboration moving forward. After completion of Phase IIa clinical development, GSK has the option to select two or three compounds from the following: XL647, XL999, XL784, XL880, XL820, XL844, XL184, and five earlier stage programs. The remaining compounds are ours to develop, partner and/or commercialize independently. Upon selection, GSK will pay substantial milestone payments to us and conduct the remaining clinical development. For those compounds selected by GSK, we will receive substantial additional milestones, favorable royalty rates, and certain co-promotion rights in North America. This innovative collaboration is a cornerstone on which we are building a robust proprietary pipeline, while providing GSK with the opportunity to enhance its own pipeline.

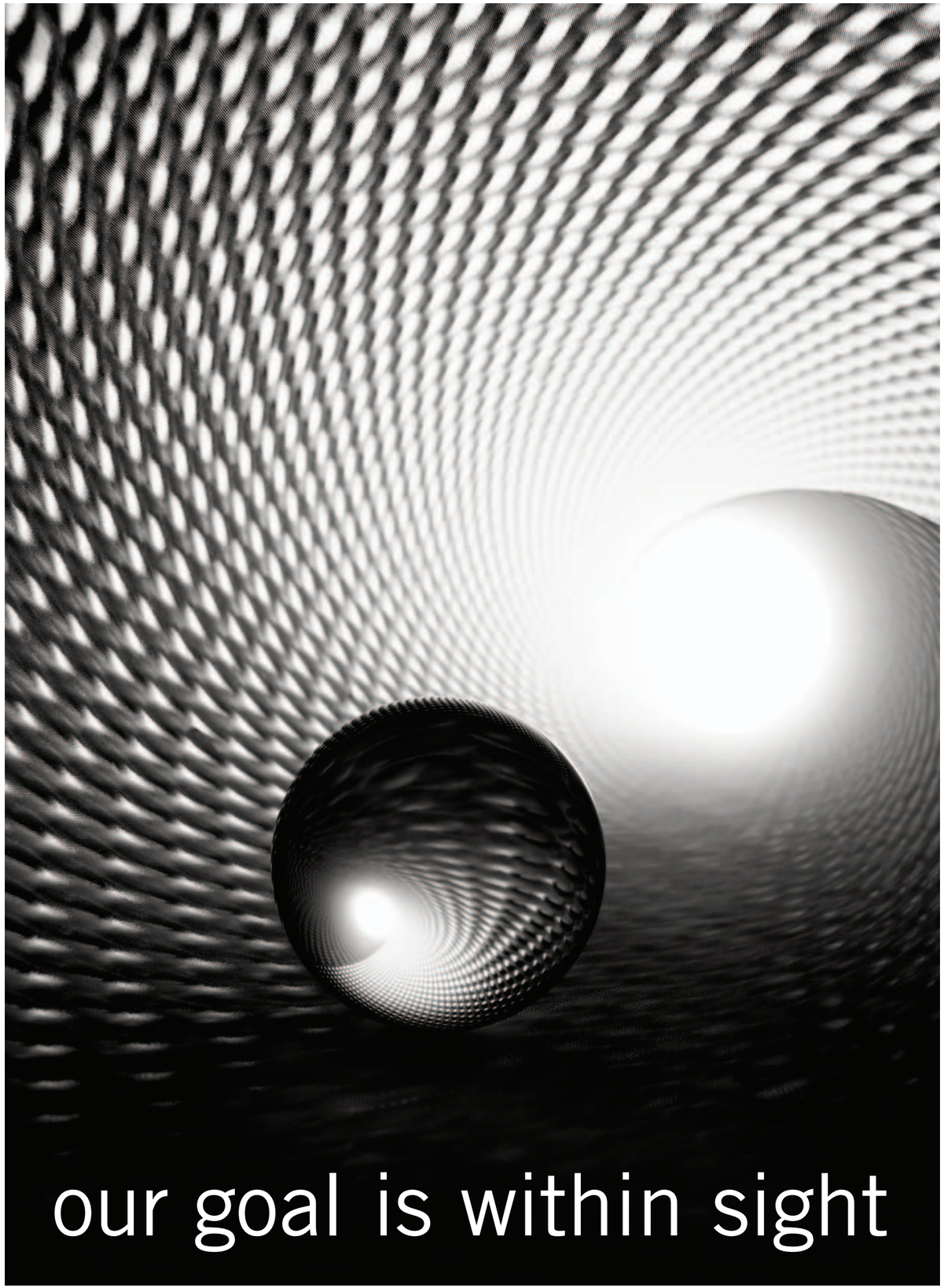
As we leverage the GSK collaboration to advance our pipeline, we also continue to build our future through our partnership with BMS. Capitalizing on our unique biology capabilities, we continued in 2004 to identify and validate a variety of novel cancer targets under this collaboration. These targets are a rich source of discovery and development opportunities that will help to expand our cancer franchise over the long-term. BMS has announced their intent to begin development of compounds against several of these targets in 2005.

OUR ORGANIZATION

Advancing science, expanding our pipeline and moving closer to our goal of treating patients require more than keen intellect and advanced technology. Fiscal discipline and pragmatic allocation of our resources have been key factors in our accomplishments to date and are essential to our success. In June, we consolidated our research and discovery organizations to maximize our ability to generate multiple high-quality INDs each year and rapidly advance these drug candidates through clinical development. This move will enhance the quality and growth of our pipeline and ensure our ability to build a proprietary Exelixis pipeline while fulfilling obligations to corporate partners.

We have an ambitious vision to become a top-five biopharmaceutical company. Our accomplishments in 2004 increased our momentum, and we enter 2005 with tremendous energy and focus to continue on our trajectory toward making this vision a reality. We have an ambitious set of goals for 2005. By year-end we could have up to eight compounds in clinical development, three to four in preclinical development, and several more in lead optimization. We are excited about this pipeline, and we believe that this set of compounds, together with the R&D organization that generated it, provide a powerful engine for the company to grow today and into the future. Much remains to be done to achieve our goal and I thank you, our stockholders, for your continued support of our efforts to build a company from which patients, and each of us, may benefit.

George A. Scangos, PhD
President and Chief Executive Officer
March 2005



our goal is within sight

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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: info@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
03.31.04	$ 6.81	$ 9.50
06.30.04	8.04	10.64
09.30.04	6.11	10.10
12.31.04	8.07	9.79

This annual report contains forward-looking statements, including without limitation all statements related to plans to advance and derive milestones from compounds in preclinical and clinical development, including XL119, XL647, XL999, 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" 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, 2004, 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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