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.
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.
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.
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 Ila 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.
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.

In 2005, we expect to advance 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.

**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, mTOR and IGFR, 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 Mineralocorticoid Receptor (MR).
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 (bacecatatin). 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-Fluorouracil 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.

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 Mineralocorticoid 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 continue 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 Ia 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 expect 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 stakeholders, 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