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George A. Scangos PhD, President and Chief Executive Officer

In these challenging times for the biotechnology industry and for our economy in general, I am pleased to report that Exelixis is in excellent shape. We ended 2008 with close to \$500 million in cash and committed funding. We have controlled our expenses and focused our resources. The result is that we have the ability to move the company forward for a substantial period of time without having to access the capital markets.



Our lead compound XL184 is in a phase 3 trial for medullary thyroid cancer (MTC) and has generated encouraging data in a phase 2 trial for patients with glioblastoma (GBM). Together with our partner Bristol-Myers Squibb Company, we are moving the compound aggressively through clinical development with a plan that fully exploits the potential of this promising compound. We have a multitude of other partnered and proprietary compounds and a deep and diverse pipeline of promising candidates. Through aggressive business development, thoughtful cost-control and careful focus, we expect to have the financial resources to make the most of these opportunities. At a time of unprecedented challenge for the biotechnology industry, Exelixis is uncommonly well positioned for success.

The Right Strategy Since our evolution into a drug discovery and development company several years ago, our strategy has been clear and consistent: To discover and aggressively develop multiple, high-quality compounds that have the potential to improve the treatment of patients with cancer and other chronic diseases; to seek to do so at scale and at a fraction of the cost and time of competitors; to build a pipeline that is competitive with large biotechnology and pharmaceutical companies within the therapeutic area of cancer; and to efficiently finance our enterprise to minimize stockholder dilution and maximize value.

The outcome of that strategy to-date is a diverse pipeline of 14 compounds. We have strategically partnered many of our compounds as a source of immediate cash and clinical bandwidth, and we have retained a meaningful economic stake in all of the compounds as a way of building future value for the company. Our commitment to the highest standards of care and quality is yielding rewards in our current clinical programs and partnerships. As a result, Exelixis is well positioned not only to weather the current economic crisis, but also to make significant progress toward our goal of bringing products to market and creating value for patients and stockholders.

Today, Exelixis has succeeded in building an industry leading pipeline that currently consists of the following compounds:

XL184, an inhibitor of the proteins MET, RET and VEGFR2, has generated encouraging data in trials of patients with MTC and GBM. It is currently in a phase 3 trial for patients with MTC, in a phase 2 trial for patients with GBM, and in a phase 1b/2 trial for patients with non-small cell lung cancer (NSCLC). Additionally, together with our partner Bristol-Myers Squibb Company, we are aggressively exploring the potential of this compound to provide benefit to patients with a variety of other tumor types.

XL147 is a selective inhibitor of phosphoinositide-3 kinase (PI3K). The PI3K pathway is the most frequently dysregulated pathway in human tumors. This compound and XL765 are the most advanced compounds targeting the PI3K pathway. XL147 has shown robust pathway modulation in patient tumors and encouraging signs of anti-tumor activity in a phase 1 trial. In addition to the ongoing single agent phase 1 trial, XL147 is currently being tested in phase 1b/2 trials in combination with either erlotinib or chemotherapy (carboplatin and paclitaxel).

XL765 is a dual inhibitor of PI3K and mTOR. This compound also has shown encouraging pathway modulation in patient tumors as a single agent in a phase 1 trial and the evaluation of the combination of XL765 with erlotinib or temozolomide is ongoing in phase 1b/2 trials.

XL518 is a specific inhibitor of MEK, a key component of the MAP kinase pathway. This compound has reached its maximum tolerated dose in an ongoing phase 1 trial and is being transferred to our partner Genentech for further clinical development.

XL228 is an inhibitor of IGF1R, BCR-ABL and SRC. This compound has shown encouraging early signs of activity and is being tested in patients with chronic myelogenous leukemia, multiple myeloma, and advanced solid tumors. As with all of our compounds, we will determine whether to move this compound into later stage development once we have the data from the ongoing trials, anticipated by the end of 2009.



(left to right):

Michael M. Morrissey PhD, President of Research and Development
Frances K. Heller JD, Executive Vice President, Business Development
Frank L. Karbe, Executive Vice President and Chief Financial Officer
Gisela M. Schwab MD, Executive Vice President and Chief Medical Officer
Pamela A. Simonton JD, LLM, Executive Vice President and General Counsel
Peter Lamb PhD, Senior Vice President, Discovery Research and Chief Scientific Officer
Lupe M. Rivera SPHR, CCP, Senior Vice President, Operations

XL019 is a selective inhibitor of JAK2. This compound has shown signs of activity in preleukemic myelofibrosis patients but has been associated with low levels of neuropathy at its current dose. We are planning to evaluate XL019 further in patients with preleukemic myelofibrosis or other leukemic conditions where JAK2 activation is thought to be relevant to the disease in order to determine if this compound may provide a therapeutic option for these specific patient populations. We anticipate that we will be able to make a data-driven decision to continue or halt the development of this compound during 2009.

XL139 is an inhibitor of the hedgehog pathway. This pathway is believed to be one of the most important pathways involved in cancer stem cell maintenance and is abnormally activated in many types of cancer. This compound currently is in a phase 1 trial, and our co-development partner Bristol-Myers Squibb Company has primary responsibility for its development and commercialization.

XL413 is a potent, selective, and orally available small molecule inhibitor of the threonine-serine kinase Cdc7, which is an important regulator of cellular DNA synthesis. It is being co-developed with Bristol-Myers Squibb Company, and Bristol-Myers Squibb Company has primary responsibility for its development and commercialization.

XL888 is a novel, synthetic, orally bioavailable inhibitor of HSP90, a chaperone protein that promotes the activity and stability of a range of key regulatory proteins including kinases. It is currently in a phase 1 clinical trial.

XL880 (GSK089) is an inhibitor of MET and VEGFR and is being moved through clinical development by our partner GlaxoSmithKline. Phase 2 clinical trials evaluating XL880 in papillary renal cell carcinoma, gastric cancer, and head and neck cancer are ongoing.

XL281 is a selective inhibitor of the RAF kinase, a member of the MAP kinase pathway that is frequently dysregulated in solid tumors. It has demonstrated on-target activity and substantial pathway inhibition in

patient tumors and is being tested in patients with colorectal cancer, NSCLC, melanoma and papillary thyroid cancer. This compound has been out-licensed to Bristol-Myers Squibb Company.

XL652 is a modulator of the liver X receptor (LXR), a nuclear hormone receptor implicated in a variety of cardiovascular and metabolic disorders. LXR plays a central role in lipid metabolism, and LXR modulators improve lipid profiles and shrink atherosclerotic plaques in preclinical models. XL652 is currently in phase 1 trials, and our partner Bristol-Myers Squibb Company has sole responsibility for the development and commercialization of the compound.

XL550 is a novel small-molecule antagonist the mineralocorticoid receptor (MR), a nuclear hormone receptor implicated in a variety of cardiovascular and metabolic diseases. Preclinical evaluation of XL550 is ongoing with our partner Daiichi-Sankyo, and Daiichi-Sankyo has sole responsibility for its development and commercialization.

The farnesoid X receptor (FXR), a member of the nuclear hormone receptor superfamily, is implicated in a variety of metabolic and liver disorders. Preclinical evaluation of an FXR agonist is ongoing with our partner Wyeth Pharmaceuticals, and Wyeth Pharmaceuticals has sole responsibility for the development and commercialization of the compound.

In addition to these compounds, we have a number of other compounds moving through preclinical development at Exelixis in preparation for potential investigational new drug application filings in 2009 and 2010. Our goal is to continue to replenish our diverse pipeline, as we make tough, data-driven decisions about further investments in specific programs.

Although Exelixis is financially well positioned and has a diverse and valuable pipeline, we are aware of the challenging economic environment in which we find ourselves. We cannot, and will not attempt to independently develop all of the compounds in our pipeline. We have established many



WE ARE CONSTANTLY EVALUATING

successful partnerships with leading biotechnology and pharmaceutical companies. For example, Exelixis and Bristol-Myers Squibb Company are putting substantial resources behind XL184. The data generated by this compound to-date are encouraging, and we believe that this compound merits our continued investment and full support.

We are performing limited studies for our proprietary compounds XL228, XL019 and XL888 with the goal of making “go/no go” decisions later this year. We are paying 35% of the development costs for XL139 and XL413, while Bristol-Myers Squibb Company pays the remaining development costs. Our decision to continue to fund these programs into later stage development is contingent on the data generated in phase 1.

We have no financial commitment for XL281, XL518, and XL652; costs for these programs are paid by our partners. We expect to partner XL147 and XL765 in the near future. Success of one or more of these compounds will provide substantial benefit to us, while we have limited our risk in the event of failure.

We are striving to continue our company's development and growth through good decision making.

Substantial Clinical Productivity In 2008, we made substantial progress in our clinical pipeline. A key achievement was the initiation of a phase 3 pivotal trial for XL184 in MTC. XL184 is the first compound discovered and developed at Exelixis to advance to pivotal trials and we have advanced the compound to this stage in less than three years after it entered clinical development. This progress is the result of our robust discovery and early development processes and our strategy for identifying time- and cost-effective paths to potential approval.

In an earlier-stage trial, XL184 demonstrated a 55% response rate and an 84% disease control rate in MTC and we believe that the strength of the data may provide a clear and rapid pathway to the market. Additional

clinical data suggest that XL184 may have potential in diverse cancers, including NSCLC, colorectal cancer, GBM, melanoma and other solid tumors. Thus, while approval in MTC may provide the most time- and cost-effective indication to pursue for initial approval of XL184, subsequent approval in other indications would allow for significant expansion of the compound's market potential.

Toward this end, we are evaluating XL184 in a phase 2 trial in patients with relapsed or recurrent GBM. We rapidly completed accrual in this trial, enrolling more than 40 patients in less than three months. The rapid enrollment reflects both the critical need for new GBM therapies as well as the enthusiasm for XL184 among oncologists. Preliminary data from this trial have been accepted for presentation at the American Society of Clinical Oncology (ASCO) annual meeting, which will take place at the end of May. If the phase 2 results in GBM continue to be positive, we intend to advance this program rapidly to pivotal trials for this indication.

In collaboration with Bristol-Myers Squibb Company, we have completed our initial planning phase of the full development program for XL184 in a variety of oncology indications, including potential pivotal trials that we expect to initiate in 2009, as well as a broad phase 2 “signal search” trial that we plan to initiate this year to identify other potential indications. We have staffed the XL184 development program in a fashion that is competitive with other clinically active agents at this stage of development and, together with Bristol-Myers Squibb Company, have critical mass and expertise in clinical, regulatory, manufacturing and commercial to extend the sizable lead we have with XL184 as the most advanced MET inhibitor in clinical testing.

Over the course of 2008, we presented data from several ongoing clinical development programs at leading medical conferences. We presented data from XL765 and XL147, each of which targets PI3K. Data from phase 1 trials of XL147 and XL765 have shown encouraging pathway inhibition in human tumors and surrogate tissues such as hair and skin. Early signs

OUR STRATEGIES AND STRENGTHS.

of clinical anti-tumor activity have been observed. Importantly, the pharmacodynamic pathway inhibition and early signs of clinical benefit have been achieved with a favorable safety and tolerability profile at or below the maximum tolerated dose.

Encouraging phase 1 data also were reported for XL281, an inhibitor of wild-type and mutant RAF kinases implicated in a variety of human cancers. Of 29 patients in this ongoing dose-escalation trial, one has had a partial response and 12 others have had stable disease for more than three months. This includes stable disease for more than one year in four patients. Substantial modulation of RAF signaling, reduction in proliferation and increased cell death were observed in pharmacodynamic analyses of tumor samples. This trial is ongoing and is part of our development partnership with Bristol-Myers Squibb Company.

Leveraging Our Partnership Potential The encouraging preclinical and clinical data generated from the compounds in our pipeline continue to be validated by success in establishing multiple partnerships with leading biotechnology and pharmaceutical companies. The depth, breadth and continued replenishment of our pipeline gives us flexibility in establishing partnerships and licensing agreements that balance near-, mid- and long-term financial and commercial needs and objectives. To-date, Exelixis has successfully entered into co-development agreements and out-licensing agreements while retaining a number of exciting candidates to develop as proprietary programs. This asset allocation paradigm allows us to diversify the risks of product development while increasing the likelihood for success.

In December 2008, Exelixis entered into a global collaboration with Bristol-Myers Squibb Company covering XL184 and XL281. The terms of the agreement provide Exelixis with \$240 million in upfront and license fees, with \$195 million received upfront and \$45 million in additional license payments payable in 2009. Exelixis and Bristol-Myers Squibb Company have agreed to

co-develop XL184, which is currently in a pivotal phase 3 trial for MTC and in phase 2 and phase 1b/2 trials for GBM and NSCLC, respectively. Exelixis will share U.S. commercial profits 50/50 with Bristol-Myers Squibb Company and has the option to co-promote XL184 in the United States. Exelixis also is eligible to receive sales performance milestones of up to \$150 million and double-digit royalties on sales outside the United States. Exelixis and Bristol-Myers Squibb Company will share worldwide (except for Japan) development costs, 35% (Exelixis) and 65% (Bristol-Myers Squibb Company)¹.

Bristol-Myers Squibb Company has an exclusive worldwide license to develop and commercialize XL281, currently in a phase 1 trial in patients with advanced solid tumors, and will be responsible for funding all future development of the compound. Exelixis is eligible for development and regulatory milestones of up to \$315 million, sales performance milestones of up to \$150 million and double-digit royalties on worldwide sales of XL281.

These favorable economic terms reflect the substantial clinical and commercial potential of XL184 and XL281 in diverse cancers and our ability to work effectively with our partners. We have worked with Bristol-Myers Squibb Company for nearly a decade on multiple collaborations and we are excited about the opportunity to co-develop XL184.

In 2008, our partnerships with leading oncology companies progressed as planned. GlaxoSmithKline is conducting phase 2 trials of XL880 in papillary renal cell carcinoma, gastric cancer and head and neck cancer. Bristol-Myers Squibb Company is conducting phase 1 trials of XL652 in cardiovascular disease and XL139 and XL413 in various cancers. XL518, which Genentech selected for development in 2008, is in phase 1 trials in solid tumors and the maximum tolerated dose has been defined. The selection triggered a \$3 million milestone payment and Exelixis is entitled to receive another \$7 million after Genentech initiates phase 2 trials.

¹ We will be responsible to fund the initial \$100 million of such costs. We will have the option to defer payments for development, early commercialization and other costs above certain thresholds.

Going forward, we will continue to allocate compounds to co-development partnerships, licensing arrangements, and our own proprietary pipeline based on the time and resources needed to bring specific compounds to the market, the risk, and the ability of a partner to enhance the size of the market opportunity or shorten the time to market. Regardless of the pathway to which individual compounds are allocated, our goal is to bring first- or best-in-class medicines to patients with unmet medical need. We believe that our partnerships can result in shorter development times and/or approval for a broader array of indications. Success of the partnerships, and of our partners, benefits patients and Exelixis' stockholders.

Combined, the cash and clinical progress generated by our partnerships help to keep our balance sheet strong.

A Focused Organization with Healthy Productivity In 2008, we streamlined our operations through a 10% reduction in head count. While there is always reluctance to lose people who have contributed to our organization, this reduction was necessary to bring our operations in-line with our financial resources. Being tightly focused and productive is a priority for everyone at Exelixis and we continue to strengthen the necessary areas of our organization to ensure that our compounds advance.

Continuing on a Better Path to Better Medicines Although I am pleased with our accomplishments over the past year, we are keenly focused on our goals and are determined to remain on course despite the turmoil of the financial markets. Moving into 2009, we are focused on continued execution of multiple clinical development programs and disciplined and pragmatic use of our financial assets. A top priority is the successful execution of the clinical development plan for XL184, and we are pleased to be in partnership with Bristol-Myers Squibb Company to expedite this effort.

Seven abstracts have been accepted for presentation at ASCO, including data from the phase 2 GBM trial for XL184 and phase 1 trials of XL765,

XL147, XL228 and XL281. As in recent years, we expect that the conference will afford us the opportunity to garner additional enthusiasm for our pipeline within the oncology community.

The Exelixis pipeline is the foundation of our clinical and financial success to-date and we intend to continue to replenish it with compelling new development candidates. We will continue to critically prioritize compounds in the clinical pipeline, retaining those with clear clinical and commercial potential, or halting development of programs that we believe have a low probability of success and seeking partnerships for programs with complex, lengthy or costly clinical trajectories.

Our continued commitment to rationalize our pipeline is intended to keep our clinical expenses in-line with our financial resources. In the months ahead, we expect to further enhance our financial resources – already close to \$500 million in cash and committed funding as of the end of 2008 – through additional partnerships. And we will continue to focus on prudent use of our financial and intellectual assets so that we have the resources and flexibility to make ongoing progress in a dynamic environment.

I want to thank all of you for your support and confidence in Exelixis. I look forward to sharing our progress with you in the months ahead.

Sincerely,



George A. Scangos, PhD
President and Chief Executive Officer

The Exelixis pipeline is the foundation of our clinical and financial success to-date and we intend to continue to replenish it with compelling new development candidates.

The following table shows our clinical-stage compounds that we are developing internally or are co-developing with a partner:

COMPOUND	PARTNER	PRINCIPAL TARGETS	INDICATION	STAGE OF DEVELOPMENT
XL184	Bristol-Myers Squibb	MET, RET, VEGFR2	MTC	Phase 3
			GBM	Phase 2
			NSCLC+erlotinib	Phase 1b/2
XL147	Unpartnered	PI3K	NSCLC+erlotinib	Phase 1b/2
			NSCLC+paclitaxel/carboplatin	Phase 1b/2
			Solid Tumors	Phase 1
XL765	Unpartnered	PI3K, mTOR	GBM+temozolomide	Phase 1b/2
			NSCLC+erlotinib	Phase 1b/2
			Solid Tumors	Phase 1
XL518	Genentech	MEK	Cancer	Phase 1
XL228	Unpartnered	IGF1R, BCR-ABL, SRC	Resistant CML	Phase 1
			Advanced Malignancies	Phase 1
XL019	Unpartnered	JAK2	Hematological Malignancies	Phase 1
XL139	Bristol-Myers Squibb	Hedgehog	Cancer	Phase 1
XL413	Bristol-Myers Squibb	Cdc7	Cancer	Phase 1
XL888	Unpartnered	HSP90	Cancer	Phase 1

The following table shows our preclinical and clinical-stage compounds that we have out-licensed to third parties for further development and commercialization:

COMPOUND	PARTNER	PRINCIPAL TARGETS	INDICATION	STAGE OF DEVELOPMENT
XL880	GlaxoSmithKline	MET, VEGFR2	Renal Cell Carcinoma	Phase 2
			Gastric Cancer	Phase 2
			Head and Neck Cancer	Phase 2
XL281	Bristol-Myers Squibb	RAF	Cancer	Phase 1
XL652	Bristol-Myers Squibb	LXR	Metabolic and Cardiovascular Disease	Phase 1
XL550	Daiichi-Sankyo	MR	Metabolic and Cardiovascular Disease	Preclinical
FXR	Wyeth	FXR	Metabolic and Liver Disorders	Preclinical

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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 Corporate Communications Department by calling 650.837.7012.

Stock Information

The common stock of the company has traded on the Nasdaq Global Select Market under the symbol "EXEL" since April 11, 2000. No dividends have been paid on the common stock since the company's inception.

Common Stock

The following table sets forth, for the periods indicated, the high and low intraday sales prices for the company's common stock as reported by the Nasdaq Global Select Market:

Quarter Ended	High	Low
January 2, 2009	\$6.30	\$2.11
September 26, 2008	\$7.35	\$4.64
June 27, 2008	\$8.15	\$5.00
March 28, 2008	\$8.95	\$4.81

Board of Directors

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Professor of Tumor Biology and Cancer
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George Poste, DVM, PhD

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George A. Scangos, PhD

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Lupe M. Rivera, SPHR, CCP

Senior Vice President, Operations

D. Ry Wagner, PhD

Vice President, Plant Biotechnology,
Exelixis Plant Sciences, Inc.

This annual report and the accompanying letter to stockholders contain statements that are forward-looking, including, without limitation, statements relating to: Exelixis' ability to move the company forward for a substantial period of time without having to access the capital markets; Exelixis' expectation that it will have the financial resources to capitalize on the company's diverse pipeline of promising candidates; Exelixis' belief that the company is uncommonly well positioned for success; Exelixis' belief that the company is well positioned to weather the current economic crisis and that the company will make significant progress toward its goal of bringing products to market and creating value for patients and stockholders; the future development and therapeutic and commercial potential of XL184, XL147, XL765, XL518, XL228, XL019, XL139, XL413, XL888, XL880, XL281, XL652, XL550, FXR and Exelixis' other compounds; Exelixis' goal to continue to replenish the company's diverse pipeline, as it makes decisions about further investments in specific programs; the availability of data related to XL228, XL019, XL888, XL184 and Exelixis' other compounds; the timing for go/no go decisions with respect to XL228, XL019 and XL888; Exelixis' expectations to partner XL147 and XL765 in the near future and the benefits and impact thereof; the continued development and growth of the company; Exelixis' expectations and plans for the development of XL184, including the initiation a broad phase 2 "signal searching" trial for XL184 in 2009 and other clinical trials; Exelixis' and Bristol-Myers Squibb's plans to share costs, profits and losses with respect to XL184; Exelixis' potential receipt of milestones and royalties on sales of XL184 outside the United States; Exelixis' potential receipt of milestones and royalties on worldwide sales of XL281; Exelixis' expectation that it will receive a \$7 milestone from Genentech for XL518; Exelixis' plan to continue to allocate compounds to co-development partnerships, licensing arrangements, and its own proprietary pipeline; Exelixis' belief that partnerships can result in shorter development times and/or approval for a broader array of indications and that successful partnerships benefit patients and Exelixis stockholders; Exelixis' plan to continue to strengthen the necessary areas of the company to ensure that its compounds advance; Exelixis' expectation that ASCO will afford the company the opportunity to garner additional enthusiasm for its pipeline within the oncology community; Exelixis' plan to keep the company's clinical expenses in line with its financial resources; Exelixis' expectations to further enhance the company's financial resources through additional partnerships; and Exelixis' continued focus on prudent use of the company's financial and intellectual assets. Words such as "plan," "goal," "may," "would," "will," "could," "expect," "should," "anticipate," "suggest," "intend," "potential," "encouraging," "promising," "continue," "well positioned" and similar expressions are intended to identify forward-looking statements. These statements are only predictions and are based upon Exelixis' current plans, assumptions, beliefs and 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, risks related to: the potential failure of XL647, XL184, XL880, XL019, XL147, XL765, XL281, XL518, XL228, XL820, XL844, XL139 and other Exelixis compounds to demonstrate safety and efficacy in clinical testing; the therapeutic and commercial value of XL647, XL184, XL880, XL019, XL147, XL765, XL281, XL518, XL228, XL820, XL844, XL139 and other Exelixis compounds; Exelixis' ability to initiate clinical trials at the referenced times; the ability to conduct clinical trials for Exelixis' compounds sufficient to achieve a positive completion; the timing and level of expenses associated with the advancement and maturation of the Exelixis pipeline; Exelixis' ability to control its costs; Exelixis' dependence on its relationship with Bristol-Myers Squibb Company; Exelixis' ability to enter into new collaborations; Exelixis' ability to execute upon its objectives; the timely receipt of potential license payments, research funding, milestones and royalties under Exelixis' collaborative agreements; the uncertainty of the FDA approval process; market competition; and changes in economic and business conditions. These and other risk factors are discussed under "Risk Factors" and elsewhere in Exelixis' Annual Report on Form 10-K for the fiscal year ended January 2, 2009 and Exelixis' other reports filed with the Securities and Exchange Commission. Exelixis expressly disclaims any duty, obligation or undertaking to release publicly any updates or revisions to any forward-looking statements made in this discussion to reflect any change in Exelixis' expectations with regard thereto or any changes in events, conditions or circumstances on which any such statements are based.

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