EXELIXIS INC
Form 424B5
September 27, 2006
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Filed pursuant to Rule 424(b)(5)
Registration No. 333-119984

The information in this preliminary prospectus supplement is not complete and may be changed. This preliminary prospectus supplement and the accompanying prospectus are not an offer to sell nor do they seek an offer to buy these securities in any jurisdiction where the offer or sale is not permitted.

Subject to Completion. Dated September 27, 2006.

Prospectus Supplement to Prospectus dated January 12, 2005.

9,000,000 Shares

Common Stock

Exelixis, Inc. is offering 9,000,000 shares to be sold in the offering.

The common stock is quoted on The Nasdaq Global Select Market under the symbol EXEL . The last reported sale price of the common stock on September 26, 2006 was $9.00 per share.

See Risk Factors beginning on page S-8 of this prospectus supplement to read about factors you should consider before buying shares of the common stock.

Neither the Securities and Exchange Commission nor any other regulatory body has approved or disapproved of these securities or passed upon the accuracy or adequacy of this prospectus supplement or the accompanying prospectus. Any representation to the contrary is a criminal offense.

	Per Share	Total
Initial price to public	$	$
Underwriting discount	$	$
Proceeds, before expenses, to Exelixis	$	$

To the extent that the underwriters sell more than 9,000,000 shares of common stock, the underwriters have the option to purchase up to an additional 1,350,000 shares from Exelixis at the initial price to public less the underwriting discount.

The underwriters expect to deliver the shares against payment in New York, New York on , 2006.

Sole Bookrunner

Goldman, Sachs & Co. **Cowen and Company**

Banc of America Securities LLC **Piper Jaffray**

Prospectus Supplement dated , 2006.

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ABOUT THIS PROSPECTUS SUPPLEMENT

This document is in two parts. The first part is this prospectus supplement, which describes the specific terms of the common stock we are offering. The second part, the accompanying prospectus dated January 12, 2005, gives more general information about our common stock. You should read this prospectus supplement and the accompanying prospectus, including the information incorporated by reference and any free writing prospectuses we have authorized for use in connection with this offering, in their entirety before making an investment decision.

You should rely only on the information contained or incorporated by reference in this prospectus supplement and the accompanying prospectus, along with the information contained in any permitted free writing prospectuses we have authorized for use in connection with this offering. If the description of the offering varies between this prospectus supplement and the accompanying prospectus, you should rely on the information in this prospectus supplement. We have not authorized anyone to provide you with different or additional information. Under no circumstances should the delivery to you of this prospectus supplement and the accompanying prospectus or any sale made pursuant to this prospectus supplement create any implication that the information contained in this prospectus supplement or the accompanying prospectus is correct as of any time after the respective dates of such information.

Unless the context requires otherwise, the words Exelixis, we, company, us and our refer to Exelixis, Inc. and its subsidiaries, a the term you refers to a prospective investor.

This prospectus supplement and the accompanying prospectus and the documents incorporated by reference into this prospectus supplement and the accompanying prospectus include trademarks, service marks and trade names owned by us or others. Exelixis, Inc., the Exelixis, Inc. logo, Artemis Pharmaceuticals, ACTTAG, Conditional and all other Exelixis product and service names are trademarks of Exelixis, Inc. in the United States and in other selected countries. All other trademarks, service marks and trade names included or incorporated by reference in this prospectus supplement and the accompanying prospectus are the property of their respective owners.

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PROSPECTUS SUPPLEMENT SUMMARY

This summary highlights selected information appearing elsewhere or incorporated by reference in this prospectus supplement and accompanying prospectus and may not contain all of the information that is important to you. This prospectus supplement and the accompanying prospectus include information about the shares we are offering as well as information regarding our business and financial data. You should read this prospectus supplement and the accompanying prospectus, including the information incorporated by reference and any free writing prospectuses we have authorized for use in connection with this offering, in their entirety.

Business Overview

We are a biotechnology company focused on the discovery and development of novel small molecule therapeutics for cancer and other serious diseases. Utilizing our library of more than four million compounds, we integrate high-throughput processes, medicinal chemistry, bioinformatics, structural biology and early *in vivo* testing in parallel to characterize thousands of compounds. This approach enables us to identify and select from this large pool of compounds those highly qualified drug candidates that meet our stringent list of development criteria. Our broad pipeline consists of product candidates in various stages of development that target cancer, renal disease and various metabolic and cardiovascular disorders. Most of these product candidates are orally administered small molecules and we believe that they offer advantages over currently available therapies.

We currently have a total of 18 compounds in clinical and preclinical development. To date, we have filed nine investigational new drug applications (INDs), eight of which were developed using our internal drug discovery efforts. Four of our lead compounds are currently in Phase 2 trials: XL999 is currently in six separate clinical trials for cancer, XL784 is in a trial for diabetic nephropathy, XL880 is in a trial for papillary renal cell carcinoma and XL647 is in a trial for patients with non-small cell lung cancer. XL820, another anticancer compound, is expected to begin a Phase 2 trial this year. XL119, which has been exclusively licensed to Helsinn Healthcare SA (Helsinn), is currently in a multi-national Phase 3 trial for the treatment of bile duct tumors. Behind these lead compounds are two Phase 1 compounds (XL844 and XL184), one compound for which we filed an IND (XL228), and six anticancer compounds in preclinical development for which we expect to file two INDs by the end of 2006 and additional INDs in 2007. We have an additional three compounds targeting metabolic diseases in preclinical development that we outlicensed. We believe the breadth and quality of our pipeline represents a key strategic asset that diversifies the risk associated with product development and demonstrates the productivity of our drug discovery and development platform.

Our business strategy is to become a fully integrated biotechnology company by leveraging our broad pipeline of diverse compounds with first-in-class or best-in-class potential that fulfill unmet medical needs in the treatment of cancer and other serious diseases. To execute our strategy we intend to continue to establish strategic alliances with world-class pharmaceutical and biotechnology companies that generate near-term revenues, reduce our risk of product failure and allow us to retain meaningful long-term value.

Product Candidates

We currently have nine product candidates in clinical development. We expect to have Phase 2 data on at least four of these compounds and to report initial Phase 1 data on another four of these compounds within the next twelve months.

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We are evaluating XL999 in Phase 2 trials for renal cell, colorectal, ovarian and non-small cell lung cancer as well as multiple myeloma and acute myelogenous leukemia (AML). Preclinically, XL999 is a potent inhibitor of key receptor tyrosine kinases (RTKs) implicated in the development and maintenance of tumor vasculature and in the proliferation of some tumor cells. XL999 potently inhibited FGFR, VEGFR2 PDGFR and FLT3 in preclinical studies. In a Phase 1 trial, XL999 demonstrated that it had an acceptable safety profile and was well tolerated at 2.4 mg/kg dosed once weekly. Of 37 patients dosed at various levels and schedules for whom data were presented by investigators at the annual meeting of the American Society for Clinical Oncology (ASCO) held from June 2-6, 2006, there have been three partial responses in patients and eight patients with prolonged stable disease (3 to 11 months). References to partial or confirmed responses as well as to stable disease throughout this prospectus supplement are in accordance with the Response Evaluation Criteria in Solid Tumors (RECIST).

XL784 is currently in Phase 2 trials for the treatment of diabetic nephropathy, an area of significant unmet medical need. Preclinically, XL784 is a potent inhibitor of ADAM-10 and MMP2, matrix metalloprotease enzymes. XL784 has been specifically optimized to be MMP1 sparing, potentially improving its safety profile significantly and enabling higher dosing compared with other previously studied MMP inhibitors. Results of single and repeat-dose Phase 1 clinical trials of XL784 administered orally to healthy volunteers demonstrated that XL784 has acceptable safety and pharmacokinetic profiles.

XL647 is currently in a Phase 2 clinical trial for patients with non-small cell lung cancer. Preclinically, XL647 demonstrated potent inhibition of the EGFR, VEGFR2 and HER2 RTKs, all validated therapeutic targets of currently approved cancer therapies. We anticipate initiating three additional Phase 2 clinical trials for XL647 in the first quarter of 2007 (two in non-small cell lung cancer and one in metastatic breast cancer). In 40 patients in a Phase 1 trial for whom data were presented by investigators at ASCO 2006, XL647 was generally well tolerated and demonstrated favorable pharmacokinetic characteristics. Of these patients, one patient with non-small cell lung cancer treated at the lowest dose had a partial response and twelve others had prolonged stable disease (>3.5 months), including three with non-small cell lung cancer.

XL880 is currently in a Phase 2 clinical trial for patients with papillary renal cell carcinoma. Preclinically, XL880 targets Met and VEGFR2, which play synergistic roles in promoting tumor growth and angiogenesis. Met has been documented as a key driver of tumor cell growth, motility, invasion, metastasis and angiogenesis. Activation or overexpression of Met is implicated in various carcinomas, and in patients with multiple myeloma, glioma, and other solid tumors. We anticipate initiating three additional Phase 2 clinical trials for XL880 in the first quarter of 2007 (one in head and neck cancer and two in gastric cancer). Of 25 patients in a Phase 1 trial for whom data were presented by investigators at ASCO 2006, the two patients with papillary renal cell carcinoma experienced a partial response. There were also seven patients with various tumors achieving stable disease.

XL820 targets VEGFR2, PDGFR and c-KIT, which have been implicated in a variety of cancers. A Phase 1 trial of XL820 administered orally to patients with solid tumors is ongoing and we expect to start a Phase 2 program later this year.

Our most advanced product candidate, XL119, was in-licensed from Bristol-Myers Squibb. We licensed the worldwide commercialization rights for XL119 to Helsinn Healthcare S.A. on an exclusive basis in 2005. XL119 is currently in a multi-national Phase 3 clinical trial for the treatment of bile duct tumors.

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Beyond the lead product candidates discussed above, we have two additional candidates (XL844 and XL184) that are in Phase I clinical trials and one compound (XL228) for which we filed an IND. We also expect to file two additional INDs by the end of 2006, which would result in a total of 11 candidates in clinical trials. A summary of our current product pipeline is presented below:

Research and Development Platform

The basis for our broad pipeline and continued productivity is a drug discovery platform that combines advanced capabilities in target identification and drug discovery. Our approach, which is designed to operate in an integrated, high-throughput manner, allows us to move from high-throughput screening lead to highly characterized development candidate in as little as 12 months. Our most advanced internally generated anticancer compounds in our clinical pipeline, which include XL999, XL647, XL880, XL820 and XL184, are Spectrum Selective Kinase Inhibitors, or SSKIs, which are designed to target multiple RTKs in a concerted manner. We believe SSKIs may provide more effective treatment than compounds that target only one RTK, or multiple unrelated RTKs, because interactions

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among multiple RTKs contribute to the progression of a variety of diseases. In addition, we believe SSKIs may provide enhanced safety profiles compared to the use of multiple single-target drugs that have not been optimized for use together. Our second generation of cancer compounds, which include XL281, XL418 and XL228, focus on intracellular pathways, which are known to regulate growth, proliferation and survival of cancer cells. Signals from RTKs converge on several critical intracellular signaling pathways and mutational activation of these pathways is common in tumors. This activation leads to tumor progression and also represents an important mechanism of resistance to both targeted drugs and chemotherapy. We are developing multiple inhibitors of these important intracellular signaling cascades.

Our integrated drug discovery platform has allowed us to move compounds rapidly into the clinic and is responsible for our high success rate to date in advancing our compounds into Phase 2 clinical trials. In 2005, we filed three INDs, and we also expect to file a total of three INDs in 2006.

Our ability to generate a large number of preclinical compounds allows us to select for clinical development only those compounds that we believe have both clinical and commercial potential and enables us to diversify our product risk. We intend to commit resources to develop only those compounds that we believe are commercially viable and have the potential to be first-in-class or best-in-class therapeutics. Our broad pipeline also creates additional opportunities for partnerships and collaborations that can help fund further research and development efforts.

Collaborations and Partnerships

In October 2002, we entered into a broad development and commercialization collaboration with GlaxoSmithKline to discover and develop small molecule drugs in the areas of cancer, vascular biology and inflammatory disease. The collaboration, which was amended in January 2005, currently relates to 12 internal programs at various stages of development (XL784, XL647, XL999, XL880, XL184, XL820, XL844, XL281, XL418, XL228 and two earlier stage oncology programs, which do not include XL518, XL147 and XL765). Each program centers on compounds that are directed at one or more targets identified in the collaboration. GlaxoSmithKline has the right to select from these programs up to two compounds at clinical proof-of-concept or three compounds if GlaxoSmithKline extends the collaboration. If GlaxoSmithKline selects a compound, we could receive substantial acceptance milestones. To date, we have received $65.0 million in upfront and milestone payments, $50.0 million in research and development funding, and loans in the principal amount of $85.0 million. We may receive additional development-related milestones and GlaxoSmithKline has agreed to provide additional research funding over the remaining term of the collaboration as well as double digit royalties on product sales and co-promotion rights to products in North America.

More recently, we have executed several additional collaboration and licensing agreements with other world-class pharmaceutical companies that have generated over $80.0 million in committed cash with the potential for significant milestones and royalties:

- In May 2005, we established a collaboration with Genentech to discover and develop therapeutics for the treatment of cancer, inflammatory diseases, and tissue growth and repair.

- In December 2005, we entered into a collaboration agreement with Bristol-Myers Squibb for the discovery, development and commercialization of novel therapies targeted against the Liver X Receptor (LXR), a nuclear hormone receptor implicated in a variety of cardiovascular and metabolic disorders.

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In December 2005, we entered into a license agreement with Wyeth Pharmaceuticals Division related to compounds targeting the Farnesoid X Receptor (FXR), a nuclear hormone receptor implicated in a variety of metabolic and liver disorders.

In March 2006, we entered into a collaboration agreement with Sankyo Company, a wholly owned subsidiary of Daiichi Sankyo Company, Limited, for the discovery, development and commercialization of novel therapies targeted against the Mineralocorticoid Receptor (MR), a nuclear hormone receptor implicated in a variety of cardiovascular and metabolic diseases.

We expect to continue to execute collaboration agreements that provide funding along with development and commercial infrastructure.

In addition to our strategic collaborations, we entered into a series of agreements for the financing of the clinical development of XL999, XL784 and XL647 in June 2005. Under the terms of these agreements, Symphony Evolution, Inc. (SEI) has invested $80.0 million, provided by the parent of SEI, Symphony Evolution Holdings LLC, to fund these programs. In return, we have licensed to SEI our intellectual property rights relating to these compounds and issued warrants to purchase 1,500,000 shares of our common stock at $8.90 per share. Under these agreements we have exclusive options to repurchase one or all of the compounds at specified exercise prices. See Business Corporate Collaborations Pharmaceutical Collaborations Symphony Evolution . We have determined that SEI is a variable interest entity of which we are the primary beneficiary and, accordingly, we include the financial condition and results of operations of SEI in our consolidated financial statements.

Corporate Information

We were incorporated in Delaware in November 1994 as Exelixis Pharmaceuticals, Inc. and we changed our name to Exelixis, Inc. in February 2000. Our principal executive offices are located at 170 Harbor Way, P.O. Box 511, South San Francisco, California 94083. Our telephone number is (650) 837-7000 and our website is http://www.exelixis.com. We have not incorporated by reference into this prospectus supplement or the accompanying prospectus the information on our website, and you should not consider it to be a part of this document. Our website address is included in this document as an inactive textual reference only.

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The Offering

Common stock offered by Exelixis	9,000,000 shares
Common stock to be outstanding after the offering	93,148,243 shares
Use of proceeds	To fund clinical development of product candidates and for working capital and general corporate purposes.
Risk factors	See Risk Factors beginning on page S-8 for a discussion of factors you should consider before buying shares of our common stock.
Nasdaq Global Select Market Symbol	EXEL

The number of shares of common stock to be outstanding after the offering is based on the number of shares outstanding as of June 30, 2006. As of that date, we had 84,148,243 shares of common stock outstanding, excluding:

- 17,695,763 shares of common stock underlying options and warrants outstanding as of June 30, 2006 at a weighted average exercise price of $10.28 per share;
- 6,134,376 shares available for future issuance under our 2000 Equity Incentive Plan, 1,428,798 shares available for future issuance under our 2000 Employee Stock Purchase Plan and 1,259,696 shares available for future issuance under our 2000 Non-Employee Directors Stock Option Plan, all as of June 30, 2006; and
- 9,184,341 shares issuable upon conversion of our convertible debt (assuming that the debt had been converted as of June 30, 2006).

Unless we specifically state otherwise, the information in this prospectus supplement assumes that the underwriters do not exercise their option to purchase up to 1,350,000 additional shares of our common stock.

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Summary Consolidated Financial Data

We derived the following information from our audited consolidated financial statements for each of the three years ended December 31, 2003, 2004 and 2005, our unaudited condensed consolidated balance sheet as of June 30, 2006 and our unaudited condensed consolidated statements of operations for the six months ended June 30, 2005 and 2006. In the opinion of our management, our unaudited condensed consolidated financial statements include all adjustments, consisting only of normal and recurring adjustments, considered necessary for a fair presentation of the financial information. The following information should be read in conjunction with our consolidated financial statements and related notes incorporated by reference in this prospectus supplement and the accompanying prospectus.

Operating results for the six months ended June 30, 2006 are not necessarily indicative of the results that may be expected for the year ending December 31, 2006. For more details on how you can obtain our SEC reports and other information, you should read the section of the accompanying prospectus entitled Where You Can Find More Information .

	Year Ended December 31,			Six Months Ended June 30,	
	2003	2004	2005	2005	2006
				(unaudited)	
	(in thousands, except per share data)				
Consolidated Statement of Operations Data					
Total revenues	$ 51,540	$ 52,857	$ 75,961	$ 47,184	$ 45,359
Total operating expenses	$ 147,799	$ 188,059	$ 169,952	$ 83,787	$ 106,799
Net loss	$ (94,774)	$ (137,245)	$ (84,404)	$ (37,107)	$ (51,113)
Net loss per share, basic and diluted	$ (1.45)	$ (1.89)	$ (1.07)	$ (0.49)	$ (0.61)
Shares used in computing basic and diluted net loss per share	65,387	72,504	78,810	76,162	83,867

	As of June 30, 2006	
	Actual	As Adjusted(1)(2)
	(unaudited)	
	(in thousands)	
Consolidated Balance Sheet Data		
Cash, cash equivalents and marketable securities (including investments held by Symphony Evolution, Inc. of $65.0 million and restricted cash and investments of $11.0 million)	$ 192,202	$ 268,082
Working capital	$ 102,271	$ 178,151
Total assets	$ 306,477	$ 382,357
Long-term obligations, less current portion	$ 121,156	$ 121,156
Accumulated deficit	$ (654,890)	$ (654,890)
Total stockholders equity	$ 984	$ 76,864

(1) As adjusted to give effect to the sale of 9.0 million shares of common stock we are offering pursuant to this prospectus supplement and the accompanying prospectus at an assumed public offering price of $9.00 per share, after deducting the estimated underwriting discount and estimated offering expenses payable by us.

(2) Each $1.00 increase (decrease) in the assumed public offering price of $9.00 per share would increase (decrease) each of cash, cash equivalents and marketable securities, working capital, total assets and total stockholders equity by $8.5 million, assuming that the number of shares offered by us, as set forth on the cover page of this prospectus supplement, remains the same, and after deducting the estimated underwriting discount and estimated offering expenses payable by us. We may also increase or decrease the number of shares we are offering. An increase of 1.0 million shares in the number of shares offered by us, to a total of 10.0 million shares, together with a concomitant $1.00 increase in the assumed public offering price of $9.00 per share, would increase each of cash, cash equivalents and marketable securities, working capital, total assets and stockholders equity by $17.9 million. Similarly, a decrease of 1.0 million shares in the number of shares offered by us, to a total of 8.0 million shares, together with a concomitant $1.00 decrease in the assumed public offering price of $9.00 per share, would decrease each of cash, cash equivalents and marketable securities, working capital, total assets and total stockholders equity by $16.0 million. The as adjusted information discussed above is illustrative only and will be adjusted based on the actual public offering price and other terms of this offering determined at pricing.

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RISK FACTORS

Investing in our common stock involves a high degree of risk. You should consider carefully the risk factors described below and all other information contained in or incorporated by reference in this prospectus supplement and the accompanying prospectus before deciding to invest in our common stock. If any of the following risks actually occur, they may materially harm our business, financial condition, operating results and cash flow. As a result, the market price of our common stock could decline, and you could lose all or part of your investment. Additional risks and uncertainties that are not yet identified or that we think are immaterial may also materially harm our business, operating results and financial condition and could result in a complete loss of your investment.

Risks Related to Our Need for Additional Financing and Our Financial Results

If additional capital is not available to us, we would be forced to delay, reduce or eliminate our product development programs or commercialization efforts and we may breach our financial covenants.

We will need to raise additional capital to:

- fund our operations and clinical trials;
- continue our research and development efforts; and
- commercialize our product candidates, if any such candidates receive regulatory approval for commercial sale.

As of June 30, 2006, we had $192.2 million in cash and cash equivalents and marketable securities, which included restricted cash and investments of $11.0 million and investments held by Symphony Evolution, Inc. (SEI) of $65.0 million. We anticipate that the anticipated net proceeds of this offering and our current cash and cash equivalents, marketable securities, investments held by SEI and other funding that we expect to receive from collaborators, which assumes a moderate level of business development activity, will enable us to maintain our operations for at least the next 12 months. However, our future capital requirements will be substantial and will depend on many factors that may require us to consume available capital resources significantly sooner than we anticipate. These factors include:

- the level of payments received under existing collaboration agreements, licensing agreements and other arrangements as well as our ability to enter into new collaboration agreements, licensing agreements and other arrangements that provide for additional payments;
- our ability to remain in compliance with, or amend or cause to be waived, financial covenants contained in agreements with third parties;
- the progress and scope of our collaborative and independent clinical trials and other research and development projects;

the timing and progress of the clinical development of our outlicensed product candidates XL647, XL999 and XL784, which will determine if and when we exercise our program and/or purchase options to reacquire these product candidates from SEI;

whether and when GlaxoSmithKline selects at proof-of-concept for further development one or more of the product candidates licensed to SEI, which would require us to repurchase the selected candidate or candidates through the exercise of our purchase option or program option, and the amount of any selection milestones received from GlaxoSmithKline compared to the amount we are required to pay to exercise the purchase option or program option;

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- the relative timing of the exercise of our options to repurchase candidates from SEI and GSK s selection, or decision not to select, product candidates for further development and the possibility that we repurchase one or all of the compounds in anticipation of one or more milestones from GSK that are ultimately not received in the anticipated time frame or at all;

- future clinical trial results;

- our need to expand our product and clinical development efforts;

- our ability to share the costs of our clinical development efforts with third parties;

- the cost and timing of regulatory approvals;

- the cost of clinical and research supplies of our product candidates;

- the effect of competing technological and market developments;

- the filing, maintenance, prosecution, defense and enforcement of patent claims and other intellectual property rights;

- the cost of any acquisitions of or investments in businesses, products and technologies; and

- the cost and timing of establishing or contracting for sales, marketing and distribution capabilities.

One or more of these factors or changes to our current operating plan may require us to consume available capital resources significantly sooner than we expect. If our capital resources are insufficient to meet future capital requirements, we will have to raise additional funds. We may be unable to raise sufficient additional capital when we need it, on favorable terms or at all. The sale of equity or convertible debt securities in the future may be dilutive to our existing stockholders, and debt-financing arrangements may require us to pledge certain assets and enter into covenants that would restrict certain business activities or our ability to incur further indebtedness and may contain other terms that are unfavorable to our stockholders or us. If we are unable to obtain adequate funds on reasonable terms, we may be required to curtail operations significantly or obtain funds by entering into financing, supply or collaboration agreements on unattractive terms. If we raise additional funds through collaboration arrangements with third parties, it will be necessary to relinquish some rights to our technologies or product candidates, or we may be required to grant licenses on terms that are unfavorable to us.

In addition, we will have to obtain additional funding in order to stay in compliance with financial covenants contained in agreements with third parties. For example, as part of our collaboration with GlaxoSmithKline, we entered into a loan and security agreement, dated October 28, 2002, which, as amended, contains financial covenants pursuant to which our working capital (the amount by which our current assets exceed our current liabilities as defined by the agreement) must not be less than $25.0 million and our cash and investments (total cash, cash equivalents and investments as defined by the agreement, which excludes restricted cash) must not be less than $50.0 million. As of June 30, 2006, our working capital was $102.3 million and our cash and investments were $181.2 million. Unless we obtain adequate additional funding either through this offering or other equity or long-term debt financings, collaboration agreements, licensing agreements or other arrangements, we will likely not be in compliance with the working capital covenant in the loan and security agreement following the fourth quarter of 2006. If we were to default on the financial covenants under the loan and security agreement, GlaxoSmithKline may, among other remedies, declare

immediately due and payable all obligations under the loan and security agreement. Outstanding borrowings and accrued interest under the loan and security agreement totaled $93.5 million at June 30, 2006.

If we cannot raise additional capital in order to remain in compliance with our financial covenants or if we are unable to renegotiate such covenants and the lender exercises its remedies under the agreement, we would not be able to operate under our current operating plan.

We have a history of net losses. We expect to continue to incur net losses, and we may not achieve or maintain profitability.

We have incurred net losses each year since our inception, including a net loss of $51.1 million for the six-month period ended June 30, 2006 and a net loss of $84.4 million for the year ended

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December 31, 2005. As of June 30, 2006, we had an accumulated deficit of $654.9 million. We expect these losses to continue and anticipate negative operating cash flow for the foreseeable future. We have not yet completed the development, including obtaining regulatory approval, of any of our pharmaceutical product candidates and, consequently, have not generated revenues from the sale of pharmaceutical products. Except for revenues associated with the transgenic mouse business of our German subsidiary, Artemis, our only revenues to date are license revenues and revenues under contracts with our partners. The size of our net losses will depend, in part, on the rate of growth, if any, in our license and contract revenues and on the level of our expenses. These losses have had and will continue to have an adverse effect on our stockholders equity and working capital. Our research and development expenditures and general and administrative expenses have exceeded our revenues to date, and we expect to spend significant additional amounts to fund research and development in order to enhance our technologies and undertake product development. We currently have numerous product candidates in various stages of clinical development and we anticipate filing three additional IND applications for additional product candidates by the end of 2006. As a result, we expect that our operations will continue to increase, and, consequently, we will need to generate significant additional revenues to achieve profitability. Because of the numerous risks and uncertainties associated with developing drugs, we are unable to predict the extent of any future losses or when we will become profitable, if at all. Even if we do increase our revenues and achieve profitability, we may not be able to maintain or increase profitability.

We have licensed the intellectual property, including commercialization rights, to our product candidates XL647, XL999 and XL784 to SEI and will not receive any future royalties or revenues with respect to these product candidates unless we exercise our options to acquire one or all of these product candidates in the future. We may not have the financial resources to exercise these options or sufficient clinical data in order to determine whether we should exercise these options.

We have licensed to SEI our intellectual property rights, including commercialization rights, to our product candidates XL647, XL999 and XL784 in exchange for SEI s investment of $80.0 million to advance the clinical development of XL647, XL999 and XL784. In exchange for this investment and for five-year warrants to purchase shares of our common stock, we received an exclusive purchase option to acquire all of the equity of SEI, thereby allowing us to reacquire the product candidates, including any associated intellectual property rights and commercialization rights. We may, at our sole discretion, exercise this purchase option at any time until the earlier of June 9, 2009 or the 90th day after the date that SEI provides us with financial statements showing cash and cash equivalents of less than $5.0 million. The purchase option exercise price is equal to the sum of: (i) the total amount of capital invested in SEI by its investors and (ii) an amount equal to 25% per year on such funded capital, subject to specified adjustments. The exercise price will also be subject to a premium if we exercise the purchase option before December 11, 2006. The option exercise price may be paid in cash or a combination of cash and our common stock, at our sole discretion, provided that the common stock portion may not exceed 33% of the purchase option exercise price.

We have also received an exclusive program option from SEI allowing us under certain conditions to separately reacquire from SEI one of the three product candidates licensed to SEI. The program option is exercisable at any time, at our sole discretion, until December 9, 2006 at an exercise price equal to that portion of the funded capital expended on the development of the applicable product candidate being repurchased, plus a specified premium. The program option exercise price may be paid in cash only.

If we elect to exercise either one of the options, we will be required to make a substantial cash payment and/or to issue a substantial number of shares of our common stock, or enter into a financing arrangement or license arrangement with one or more third parties, or some combination of the

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foregoing. A payment in cash would reduce our capital resources. A payment in shares of our common stock could result in dilution to our stockholders at that time. Other financing or licensing alternatives may be expensive or impossible to obtain. If we do not exercise the purchase options prior to their expiration, our rights in and to SEI with respect to XL647, XL999 and XL784 will terminate. We may not have the financial resources to exercise the options, which may result in our loss of these rights. Additionally, we may not have sufficient clinical data in order to determine whether we should exercise the options.

In addition, under our collaboration with GlaxoSmithKline, GlaxoSmithKline may continue to select at proof-of-concept for further development one or more of the product candidates licensed to SEI, in which case we would have to repurchase the selected candidate or candidates through the exercise of our purchase option or program option. If, after receiving any selection milestones from GlaxoSmithKline, we do not have sufficient resources to exercise the purchase option or program option following a product candidate selection by GlaxoSmithKline, we could be in breach of our collaboration agreement with GlaxoSmithKline. In the event of such breach, GlaxoSmithKline could terminate the collaboration and, among other remedies, declare all amounts under our loan facility with GlaxoSmithKline immediately due and payable, which would harm our business.

Risks Related to Development of Product Candidates

Clinical testing of our product candidates is a lengthy, costly and uncertain process and may fail to demonstrate safety and efficacy, which could prevent or significantly delay regulatory approval.

Clinical trials are inherently risky and may reveal that our product candidates are ineffective or have unacceptable toxicity or other side effects that may significantly decrease the likelihood of regulatory approval. The results of preliminary studies do not necessarily predict clinical or commercial success, and later-stage clinical trials may fail to confirm the results observed in earlier-stage trials or preliminary studies. Although we have established timelines for manufacturing and clinical development based on existing knowledge of our compounds in development and industry metrics, we may not be able to meet those timelines.

We may experience numerous unforeseen events during, or as a result of, clinical testing that could delay or prevent commercialization of our product candidates, including:

- our product candidates may not prove to be efficacious or may cause harmful side effects;
- negative or inconclusive clinical trial results may require us to conduct further testing or to abandon projects that we had expected to be promising;
- patient registration or enrollment in our clinical testing may be lower than we anticipate, resulting in the delay or cancellation of clinical testing; and
- regulators or institutional review boards may not authorize, delay, suspend or terminate clinical research for various reasons, including noncompliance with regulatory requirements or their determination that participating patients are being exposed to unacceptable health risks.

If any of these events were to occur and, as a result, we were to have significant delays in or termination of our clinical testing, our expenses could increase and our ability to generate revenue from the affected product candidates could be impaired, which would adversely impact our financial results.

We have limited experience in conducting clinical trials and may not be able to rapidly or effectively continue the further development of our compounds or meet current or future requirements identified based on our discussions with the FDA. We do not know whether our planned clinical trials will begin on time, will be completed on schedule, or at all, will be sufficient for registration of these compounds or will result in approvable products.

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Completion of clinical trials may take several years or more, but the length of time generally varies substantially according to the type, complexity, novelty and intended use of a product candidate. The duration and the cost of clinical trials may vary significantly over the life of a project as a result of factors relating to the clinical trial, including, among others:

- the number of patients that ultimately participate in the clinical trial;
- the duration of patient follow-up that is appropriate in view of the results;
- the number of clinical sites included in the trials; and
- the length of time required to enroll suitable patient subjects.

Our research and clinical testing may be delayed or abandoned if we or our competitors subsequently discover other compounds that we believe show significantly improved safety or efficacy compared to our product candidates, which could limit our ability to generate revenues, cause us to incur additional expense and cause the market price of our common stock to decline significantly.

Risks Related to Our Relationships with Third Parties

We depend on our exclusive licensee, Helsinn, for the completion of the XL119 clinical program and the commercialization of XL119.

Under an exclusive license agreement with us, Helsinn is responsible for all aspects of clinical development of XL119. If XL119 receives regulatory approval, Helsinn will be responsible for the marketing and sale of the commercial product worldwide unless we reacquire the commercialization rights for North America. Because Helsinn is responsible for these functions, we have no control over the development schedule or, if XL119 receives regulatory approval, the marketing plan for XL119. If the clinical trials for XL119 are not successful, XL119 will not be commercialized. Moreover, Helsinn may relinquish all rights and the license granted to it under the license agreement and thereby terminate the license agreement on at least six months prior written notice, if in Helsinn s reasonable business judgment based on scientific or economic evidence, it is impossible for Helsinn to carry out further development or marketing of XL119. If the rights to develop and market XL119 revert to us, we will have to fund the clinical programs for XL119 on our own, seek a strategic partner to fund the further development, which may not be available on favorable terms, or at all, or outlicense or abandon XL119.

Our reliance on Helsinn poses a number of risks, including the following:

- potential disputes regarding milestone payments may arise in the future, which may postpone or disrupt payments under the license agreement;

if Helsinn fails to successfully advance XL119 in clinical development or fails to obtain regulatory approvals for XL119, we will not be able to generate revenues from milestones or the commercialization of XL119;

we cannot control whether Helsinn will devote sufficient resources to the clinical program and, if XL119 is approved by the FDA or other regulatory agencies, the marketing plan for the commercialization of the drug product in countries where we do not hold commercialization rights;

although we have no history of royalty payment disputes, even if XL119 is approved and commercialized, disputes may arise in the future with respect to the calculation of royalty payments based on net sales related to XL119; and

if Helsinn perceives that the market opportunity for XL119 or its profit margin from the sale of XL119 is too small to justify commercialization, the interests and motivations of Helsinn may not be, or may not remain, aligned with ours.

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Disagreements between SEI and us regarding the development of our product candidates XL647, XL999 and XL784 may cause significant delays and other impediments in the development of these product candidates, which could negatively affect the value of these product candidates.

We have licensed to SEI our intellectual property rights, including commercialization rights, to our product candidates XL647, XL999 and XL784 in exchange for SEI s investment of $80.0 million to advance the clinical development of XL647, XL999 and XL784. We are responsible for developing XL647, XL999 and XL784 in accordance with a specified development plan and related development budget. Our development activities will be supervised by SEI s development committee, which is comprised of an equal number of representatives from Exelixis and SEI. If the development committee cannot resolve a particular development issue, the issue will be referred to the chief executive officers of Exelixis and SEI. Any disagreements between SEI and Exelixis regarding a development decision may cause significant delays in the development and commercialization of our product candidates XL647, XL999 and XL784 as well as lead to development decisions that do not reflect our interests. Any such delays or development decisions not in our interest could negatively affect the value of XL647, XL999 and XL784.

We are dependent upon our collaborations with major companies. If we are unable to achieve milestones, develop products or renew or enter into new collaborations, our revenues may decrease and our activities may fail to lead to commercialized products.

We have derived substantially all of our revenues to date from collaborative research and development agreements. Revenues from research and development collaborations depend upon continuation of the collaborations, the achievement of milestones and royalties we earn from any future products developed from the collaborative research. If we are unable to successfully achieve milestones or our collaborators fail to develop successful products, we will not earn the revenues contemplated under such collaborative agreements. In addition, some of our collaborations are exclusive and preclude us from entering into additional collaboration arrangements with other parties in the area or field of exclusivity. Future collaborations may require us to relinquish some important rights, such as marketing and distribution rights.

If these agreements or agreements with other partners are not renewed or are terminated early, whether unilaterally or by mutual agreement, or if we are unable to enter into new collaboration agreements on commercially acceptable terms, our revenues and product development efforts could suffer. For example, our agreement with Pharmacia Corporation terminated by mutual agreement in February 2002, which eliminated the opportunity for us to earn approximately $9.0 million in research revenue in 2002 and 2003. Similarly, our collaboration with GlaxoSmithKline is scheduled to expire in October 2008 but became subject to earlier termination at the discretion of GlaxoSmithKline starting in 2005. Our agreements with Bristol-Myers Squibb and Wyeth also contain early termination provisions. In addition, from time to time we review and assess certain aspects of our collaborations, partnerships and agreements and may amend or terminate, either by mutual agreement or pursuant to any applicable early termination provisions, such collaborations, partnerships or agreements if we deem them to be no longer in our economic or strategic interests. For example, in March 2005, we agreed with Bayer CropScience LP to terminate the research term under our collaboration with Bayer CropScience in order to allow us to focus on our core business. We may not be able to enter into new collaboration agreements on similar or superior financial terms to offset the loss of revenue from the termination or expiration of any of our existing arrangements, and the timing of new collaboration agreements may have a material adverse effect on our ability to continue to successfully meet our objectives.

Conflicts with our collaborators could jeopardize the outcome of our collaboration agreements and our ability to commercialize products.

We are conducting proprietary research programs in specific disease, therapeutic modality and agricultural product areas that are not covered by our collaboration agreements. Our pursuit of

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opportunities in pharmaceutical and agricultural markets could result in conflicts with our collaborators in the event that any of our collaborators takes the position that our internal activities overlap with those areas that are exclusive to our collaboration agreements, and we should be precluded from such internal activities. Moreover, disagreements with our collaborators could develop over rights to our intellectual property. In addition, our collaboration agreements may have provisions that give rise to disputes regarding the respective rights and obligations of the parties, including the rights of collaborators with respect to our internal programs and disease area research. Any conflict with or among our collaborators could lead to the termination of our collaborative agreements, delay collaborative activities, impair our ability to renew agreements or obtain future collaboration agreements or result in litigation or arbitration and would negatively impact our relationship with existing collaborators. If our collaborators fail to develop or commercialize any of our compounds or product candidates, we would not receive any future royalties or milestone payments for such compounds or product candidates. We have limited or no control over the resources that our collaborators may choose to devote to our joint efforts. Our collaborators may breach or terminate their agreements with us or fail to perform their contractual obligations. Also, our collaboration agreements may be subject to early termination by mutual agreement. Further, our collaborators may elect not to develop products arising out of our collaboration arrangements, may experience financial difficulties, may undertake business combinations or significant changes in business strategy that adversely affect their willingness or ability to complete their obligations under any arrangement with us or may fail to devote sufficient resources to the development, manufacture, marketing or sale of such products. Certain of our collaborators could also become competitors in the future. If our collaborators develop competing products, preclude us from entering into collaborations with their competitors, fail to obtain necessary regulatory approvals, terminate their agreements with us prematurely or fail to devote sufficient resources to the development and commercialization of our products, our product development efforts could be delayed or otherwise adversely effected and may fail to lead to commercialized products.

If third parties upon which we rely do not perform as contractually required or expected, we may not be able to obtain regulatory approval for or commercialize our product candidates.

We do not have the ability to independently conduct clinical trials for our product candidates, and we must rely on third parties we do not control such as contract research organizations, medical institutions, clinical investigators and contract laboratories to conduct our clinical trials. If these third parties do not successfully carry out their contractual duties or regulatory obligations or meet expected deadlines, if the third parties need to be replaced or if the quality or accuracy of the data they obtain is compromised due to the failure to adhere to our clinical protocols or regulatory requirements or for other reasons, our preclinical development activities or clinical trials may be extended, delayed, suspended or terminated, and we may not be able to obtain regulatory approval for or successfully commercialize our product candidates.

We lack the capability to manufacture compounds for clinical trials and rely on third parties to manufacture our product candidates, and we may be unable to obtain required material in a timely manner, at an acceptable cost or at a quality level required to receive regulatory approval.

We currently do not have the manufacturing capabilities or experience necessary to enable us to produce materials for our clinical trials. We rely on collaborators and third-party contractors to produce our compounds for preclinical and clinical testing. These suppliers must comply with applicable regulatory requirements, including the FDA s current Good Manufacturing Practices, or GMP. Our current and anticipated future dependence upon these third-party manufacturers may adversely affect our future profit margins and our ability to develop and commercialize product candidates on a timely and competitive basis. These manufacturers may not be able to produce material on a timely basis or

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manufacture material at the quality level or in the quantity required to meet our development timelines and applicable regulatory requirements. We may not be able to maintain or renew our existing third-party manufacturing arrangements, or enter into new arrangements, on acceptable terms, or at all. Our third-party manufacturers could terminate or decline to renew our manufacturing arrangements based on their own business priorities, at a time that is costly or inconvenient for us. If we are unable to contract for the production of materials in sufficient quantity and of sufficient quality on acceptable terms, our clinical trials may be delayed. Delays in preclinical or clinical testing could delay the filing of our INDs and the initiation of clinical trials.

Our third-party manufacturers may not be able to comply with the GMP regulations, other applicable FDA regulatory requirements or similar regulations applicable outside of the United States. Additionally, if we are required to enter into new supply arrangements, we may not be able to obtain approval from the FDA of any alternate supplier in a timely manner, or at all, which could delay or prevent the clinical development and commercialization of any related product candidates. Failure of our third-party manufacturers or us to obtain approval from the FDA or to comply with applicable regulations could result in sanctions being imposed on us, including fines, civil penalties, delays in or failure to grant marketing approval of our product candidates, injunctions, delays, suspension or withdrawal of approvals, license revocation, seizures or recalls of products and compounds, operating restrictions and criminal prosecutions, any of which could significantly and adversely affect our business.

Materials necessary to manufacture some of our compounds currently under development may not be available on commercially reasonable terms, or at all, which may delay our development and commercialization of these compounds.

Some of the materials necessary for the manufacture of our compounds under development may, from time to time, be available either in limited quantities, or from a limited number of manufacturers, or both. Our contract manufacturers need to obtain these materials for our clinical trials and, potentially, for commercial distribution when and if we obtain marketing approval for these compounds. Suppliers may not sell us these materials at the time we need them or on commercially reasonable terms. If we are unable to obtain the materials needed to conduct our clinical trials, product testing and potential regulatory approval could be delayed, adversely affecting our ability to develop the product candidates. Similarly, if we are unable to obtain critical manufacturing materials after regulatory approval has been obtained for a product candidate, the commercial launch of that product candidate could be delayed or there could be a shortage in supply, which could materially affect our ability to generate revenues from that product candidate. If suppliers increase the price of manufacturing materials, the price for one or more of our products may increase, which may make our products less competitive in the marketplace. If it becomes necessary to change suppliers for any of these materials or if any of our suppliers experience a shutdown or disruption at the facilities used to produce these materials, due to technical, regulatory or other reasons, it could harm our ability to manufacture our products.

Risks Related to Regulatory Approval of Our Product Candidates

Our product candidates are subject to a lengthy and uncertain regulatory process that may not result in the necessary regulatory approvals, which could adversely affect our ability to commercialize products.

Our product candidates, as well as the activities associated with their research, development and commercialization, are subject to extensive regulation by the FDA and other regulatory agencies in the United States and by comparable authorities in other countries. Failure to obtain regulatory approval for a product candidate would prevent us from commercializing that product candidate. We have not received regulatory approval to market any of our product candidates in any jurisdiction and have only

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limited experience in preparing and filing the applications necessary to gain regulatory approvals. The process of obtaining regulatory approvals is expensive, and often takes many years, if approval is obtained at all, and can vary substantially based upon the type, complexity and novelty of the product candidates involved. Before a new drug application can be filed with the FDA, the product candidate must undergo extensive clinical trials, which can take many years and may require substantial expenditures. Any clinical trial may fail to produce results satisfactory to the FDA. For example, the FDA could determine that the design of a clinical trial is inadequate to produce reliable results. The regulatory process also requires preclinical testing, and data obtained from preclinical and clinical activities are susceptible to varying interpretations, which could delay, limit or prevent regulatory approval. In addition, delays or rejections may be encountered based upon changes in regulatory policy for product approval during the period of product development and regulatory agency review. Changes in regulatory approval policy, regulations or statutes or the process for regulatory review during the development or approval periods of our product candidates may cause delays in the approval or rejection of an application. Even if the FDA or a comparable authority in another country approves a product candidate, the approval may impose significant restrictions on the indicated uses, conditions for use, labeling, advertising, promotion, marketing and/or production of such product and may impose ongoing requirements for post-approval studies, including additional research and development and clinical trials. These agencies also may impose various civil or criminal sanctions for failure to comply with regulatory requirements, including withdrawal of product approval.

Risks Related to Commercialization of Products

The commercial success of any products that we may develop will depend upon the degree of market acceptance of our products among physicians, patients, health care payors, private health insurers and the medical community.

Our ability to commercialize any products that we may develop will be highly dependent upon the extent to which these products gain market acceptance among physicians, patients, health care payors, such as Medicare and Medicaid, private health insurers, including managed care organizations and group purchasing organizations, and the medical community. If these products do not achieve an adequate level of acceptance, we may not generate adequate product revenues, and we may not become profitable. The degree of market acceptance of our product candidates, if approved for commercial sale, will depend upon a number of factors, including:

- the effectiveness, or perceived effectiveness, of our products in comparison to competing products;
- the existence of any significant side effects, as well as their severity in comparison to any competing products;
- potential advantages over alternative treatments;
- the ability to offer our products for sale at competitive prices;
- relative convenience and ease of administration;
- the strength of marketing and distribution support; and
- sufficient third-party coverage or reimbursement.

If we are unable to establish sales and marketing capabilities or enter into agreements with third parties to market and sell our product candidates, we may be unable to generate product revenues.

We have no experience as a company in the sales, marketing and distribution of pharmaceutical products and do not currently have a sales and marketing organization. Developing a sales and

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marketing force would be expensive and time-consuming, could delay any product launch, and we may never be able to develop this capacity. To the extent that we enter into arrangements with third parties to provide sales, marketing and distribution services, our product revenues are likely to be lower than if we market and sell any products that we develop ourselves. If we are unable to establish adequate sales, marketing and distribution capabilities, independently or with others, we may not be able to generate product revenues.

If we are unable to obtain adequate coverage and reimbursement from third-party payors for any products that we may develop, our revenues and prospects for profitability will suffer.

Our ability to commercialize any products that we may develop will be highly dependent on the extent to which coverage and reimbursement for our products will be available from third-party payors, including governmental payors, such as Medicare and Medicaid, and private health insurers, including managed care organizations and group purchasing organizations. Many patients will not be capable of paying themselves for some or all of the products that we may develop and will rely on third-party payors to pay for, or subsidize, their medical needs. If third-party payors do not provide coverage or reimbursement for any products that we may develop, our revenues and prospects for profitability will suffer. In addition, even if third-party payors provide some coverage or reimbursement for our products, the availability of such coverage or reimbursement for prescription drugs under private health insurance and managed care plans often varies based on the type of contract or plan purchased.

A primary trend in the United States health care industry is toward cost containment. In December 2003, the President signed into law legislation creating a prescription drug benefit program for Medicare recipients. The new prescription drug program may have the effect of reducing the prices that we are able to charge for products we develop and sell through plans under the program. The new prescription drug program may also cause third-party payors other than the federal government, including the States under the Medicaid program, to discontinue coverage for products we develop or to lower the price that they will pay.

Proponents of drug reimportation may attempt to pass legislation, which would allow direct reimportation under certain circumstances. If legislation or regulations were passed allowing the reimportation of drugs, it could decrease the price we receive for any products that we may develop, thereby negatively affecting our revenues and prospects for profitability.

In addition, in some foreign countries, particularly the countries in the European Union, the pricing of prescription pharmaceuticals is subject to governmental control. In these countries, price negotiations with governmental authorities can take six to twelve months or longer after the receipt of regulatory marketing approval for a product. To obtain reimbursement and/or pricing approval in some countries, we may be required to conduct a clinical trial that compares the cost effectiveness of our product candidates or products to other available therapies. The conduct of such a clinical trial could be expensive and result in delays in the commercialization of our product candidates. Third-party payors are challenging the prices charged for medical products and services, and many third-party payors limit reimbursement for newly approved health care products. In particular, third-party payors may limit the indications for which they will reimburse patients who use any products that we may develop. Cost-control initiatives could decrease the price we might establish for products that we may develop, which would result in lower product revenues to us.

Our competitors may develop products and technologies that make our products and technologies obsolete.

The biotechnology industry is highly fragmented and is characterized by rapid technological change. In particular, the area of kinase-targeted therapies is a rapidly evolving and competitive field. We face, and will continue to face, intense competition from

large biotechnology and pharmaceutical

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companies, as well as academic research institutions, clinical reference laboratories and government agencies that are pursuing research activities similar to ours. Some of our competitors have entered into collaborations with leading companies within our target markets, including some of our existing collaborators. In addition, significant delays in the development of our product candidates could allow our competitors to bring products to market before us, which would impair our ability to commercialize our product candidates. Our future success will depend upon our ability to maintain a competitive position with respect to technological advances. Any products that are developed through our technologies will compete in highly competitive markets. Further, our competitors may be more effective at using their technologies to develop commercial products. Many of the organizations competing with us have greater capital resources, larger research and development staff and facilities, more experience in obtaining regulatory approvals and more extensive product manufacturing and marketing capabilities. As a result, our competitors may be able to more easily develop technologies and products that would render our technologies and products, and those of our collaborators, obsolete and noncompetitive. In addition, there may be product candidates of which we are not aware at an earlier stage of development that may compete with our product candidates.

We may not be able to manufacture our product candidates in commercial quantities, which would prevent us from commercializing our product candidates.

To date, our product candidates have been manufactured in small quantities for preclinical and clinical trials. If any of these product candidates are approved by the FDA or other regulatory agencies for commercial sale, we will need to manufacture them in larger quantities. We may not be able to successfully increase the manufacturing capacity, whether in collaboration with third-party manufacturers or on our own, for any of our product candidates in a timely or economic manner, or at all. Significant scale-up of manufacturing may require additional validation studies, which the FDA must review and approve. If we are unable to successfully increase the manufacturing capacity for a product candidate, the regulatory approval or commercial launch of that product candidate may be delayed or there may be a shortage in supply. Our product candidates require precise, high-quality manufacturing. The failure to achieve and maintain these high manufacturing standards, including the incidence of manufacturing errors, could result in patient injury or death, product recalls or withdrawals, delays or failures in product testing or delivery, cost overruns or other problems that could seriously hurt our business.

Risks Related to Our Intellectual Property

If we are unable to adequately protect our intellectual property, third parties may be able to use our technology, which could adversely affect our ability to compete in the market.

Our success will depend in part upon our ability to obtain patents and maintain adequate protection of the intellectual property related to our technologies and products. The patent positions of biotechnology companies, including our patent position, are generally uncertain and involve complex legal and factual questions. We will be able to protect our intellectual property rights from unauthorized use by third parties only to the extent that our technologies are covered by valid and enforceable patents or are effectively maintained as trade secrets. We will continue to apply for patents covering our technologies and products as and when we deem appropriate. However, these applications may be challenged or may fail to result in issued patents. In addition, because patent applications can take many years to issue, there may be currently pending applications, unknown to us, which may later result in issued patents that cover the production, manufacture, commercialization or use of our product candidates. Our existing patents and any future patents we obtain may not be sufficiently broad to prevent others from practicing our technologies or from developing competing products. Furthermore, others may independently develop similar or alternative technologies or design around our patents. In addition, our patents may be challenged or invalidated or may fail to provide us with any competitive advantages, if, for example, others were the first to invent or to file patent applications for these inventions.

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The laws of some foreign countries do not protect intellectual property rights to the same extent as the laws of the United States, and many companies have encountered significant problems in protecting and defending such rights in foreign jurisdictions. Many countries, including certain countries in Europe, have compulsory licensing laws under which a patent owner may be compelled to grant licenses to third parties (for example, the patent owner has failed to work the invention in that country or the third party has patented improvements). In addition, many countries limit the enforceability of patents against government agencies or government contractors. In these countries, the patent owner may have limited remedies, which could materially diminish the value of the patent. Compulsory licensing of life-saving drugs is also becoming increasingly popular in developing countries either through direct legislation or international initiatives. Such compulsory licenses could be extended to include some of our product candidates, which could limit our potential revenue opportunities. Moreover, the legal systems of certain countries, particularly certain developing countries, do not favor the aggressive enforcement of patent and other intellectual property protection, which makes it difficult to stop infringement. We rely on trade secret protection for our confidential and proprietary information. We have taken security measures to protect our proprietary information and trade secrets, but these measures may not provide adequate protection. While we seek to protect our proprietary information by entering into confidentiality agreements with employees, collaborators and consultants, we cannot assure you that our proprietary information will not be disclosed, or that we can meaningfully protect our trade secrets. In addition, our competitors may independently develop substantially equivalent proprietary information or may otherwise gain access to our trade secrets.

Litigation or third-party claims of intellectual property infringement could require us to spend substantial time and money and adversely affect our ability to develop and commercialize products.

Our commercial success depends in part upon our ability to avoid infringing patents and proprietary rights of third parties and not to breach any licenses that we have entered into with regard to our technologies. Other parties have filed, and in the future are likely to file, patent applications covering genes and gene fragments, techniques and methodologies relating to model systems and products and technologies that we have developed or intend to develop. If patents covering technologies required by our operations are issued to others, we may have to obtain licenses from third parties, which may not be available on commercially reasonable terms, or at all, and may require us to pay substantial royalties, grant a cross-license to some of our patents to another patent holder or redesign the formulation of a product candidate so that we do not infringe third-party patents, which may be impossible to obtain or could require substantial time and expense.

Third parties may accuse us of employing their proprietary technology without authorization. In addition, third parties may obtain patents that relate to our technologies and claim that use of such technologies infringes on their patents. Regardless of their merit, such claims could require us to incur substantial costs, including the diversion of management and technical personnel, in defending ourselves against any such claims or enforcing our patents. In the event that a successful claim of infringement is brought against us, we may be required to pay damages and obtain one or more licenses from third parties. We may not be able to obtain these licenses at a reasonable cost, or at all. Defense of any lawsuit or failure to obtain any of these licenses could adversely affect our ability to develop and commercialize products.

We may be subject to damages resulting from claims that we, our employees or independent contractors have wrongfully used or disclosed alleged trade secrets of their former employers.

Many of our employees and independent contractors were previously employed at universities, other biotechnology or pharmaceutical companies, including our competitors or potential competitors. We may be subject to claims that these employees, independent contractors or we have inadvertently or

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otherwise used or disclosed trade secrets or other proprietary information of their former employers. Litigation may be necessary to defend against these claims. Even if we are successful in defending against these claims, litigation could result in substantial costs and be a distraction to management. If we fail in defending such claims, in addition to paying money claims, we may lose valuable intellectual property rights or personnel. A loss of key research personnel and/or their work product could hamper or prevent our ability to commercialize certain product candidates, which could severely harm our business.

Risks Related to Employees, Growth and Location

The loss of key personnel or the inability to attract and retain additional personnel could impair our ability to expand our operations.

We are highly dependent upon the principal members of our management and scientific staff, the loss of whose services might adversely impact the achievement of our objectives and the continuation of existing collaborations. Also, we do not currently have sufficient technical personnel to fully execute our business plan. Recruiting and retaining qualified scientific and clinical personnel will be critical to support activities related to advancing our clinical and preclinical development programs, and supporting our collaborative arrangements and our internal proprietary research and development efforts. Competition is intense for experienced technical personnel, and we may be unable to retain or recruit scientists with the expertise or experience necessary to allow us to pursue collaborations, develop our products and core technologies or expand our operations to the extent otherwise possible. Further, all of our employees are employed at will and, therefore, may leave our employment at any time.

Our collaborations with outside scientists may be subject to restriction and change.

We work with scientific and clinical advisors and collaborators at academic and other institutions that assist us in our research and development efforts. These advisors and collaborators are not our employees and may have other commitments that limit their availability to us. Although they generally agree not to do competing work, if a conflict of interest between their work for us and their work for another entity arises, we may lose their services. In addition, although our advisors and collaborators sign agreements not to disclose our confidential information, it is possible that valuable proprietary knowledge may become publicly known through them.

Difficulties we may encounter managing our growth may divert resources and limit our ability to successfully expand our operations.

We have experienced a period of rapid and substantial growth that has placed, and our anticipated growth in the future will continue to place, a strain on our research, administrative and operational infrastructure. As our operations expand, we will need to continue to manage multiple locations and additional relationships with various collaborative partners, suppliers and other third parties. Our ability to manage our operations and growth effectively requires us to continue to improve our reporting systems and procedures as well as our operational, financial and management controls. In addition, SEC rules and regulations have increased the internal control and regulatory requirements under which we operate. We may not be able to successfully implement improvements to our management information and control systems in an efficient or timely manner to meet future requirements.

Our headquarters are located near known earthquake fault zones, and the occurrence of an earthquake or other disaster could damage our facilities and equipment, which could harm our operations.

Given our headquarters location in South San Francisco, California, our facilities are vulnerable to damage from earthquakes. We currently do not carry earthquake insurance. We are also vulnerable to

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damage from other types of disasters, including fire, floods, power loss, communications failures, terrorism and similar events since any insurance we may maintain may not be adequate to cover our losses. If any disaster were to occur, our ability to operate our business at our facilities could be seriously, or potentially completely, impaired. In addition, the unique nature of our research activities could cause significant delays in our programs and make it difficult for us to recover from a disaster. Accordingly, an earthquake or other disaster could materially and adversely harm our ability to conduct business.

Security breaches may disrupt our operations and harm our operating results.

Our network security and data recovery measures may not be adequate to protect against computer viruses, break-ins, and similar disruptions from unauthorized tampering with our computer systems. The misappropriation, theft, sabotage or any other type of security breach with respect to any of our proprietary and confidential information that is electronically stored, including research or clinical data, could have a material adverse impact on our business, operating results and financial condition. Additionally, any break-in or trespass of our facilities that results in the misappropriation, theft, sabotage or any other type of security breach with respect to our proprietary and confidential information, including research or clinical data, or that results in damage to our research and development equipment and assets could have a material adverse impact on our business, operating results and financial condition.

Risks Related to Environmental and Product Liability

We use hazardous chemicals and radioactive and biological materials in our business. Any claims relating to improper handling, storage or disposal of these materials could be time consuming and costly.

Our research and development processes involve the controlled use of hazardous materials, including chemicals and radioactive and biological materials. Our operations produce hazardous waste products. We cannot eliminate the risk of accidental contamination or discharge and any resultant injury from these materials. Federal, state and local laws and regulations govern the use, manufacture, storage, handling and disposal of hazardous materials. We may be sued for any injury or contamination that results from our use or the use by third parties of these materials, and our liability may exceed our insurance coverage and our total assets. Compliance with environmental laws and regulations may be expensive, and current or future environmental regulations may impair our research, development and production efforts.

In addition, our collaborators may use hazardous materials in connection with our collaborative efforts. In the event of a lawsuit or investigation, we could be held responsible for any injury caused to persons or property by exposure to, or release of, these hazardous materials used by these parties. Further, we may be required to indemnify our collaborators against all damages and other liabilities arising out of our development activities or products produced in connection with these collaborations.

We face potential product liability exposure far in excess of our limited insurance coverage.

We may be held liable if any product we or our collaborators develop causes injury or is found otherwise unsuitable during product testing, manufacturing, marketing or sale. Regardless of merit or eventual outcome, product liability claims could result in decreased demand for our product candidates, injury to our reputation, withdrawal of patients from our clinical trials, substantial

monetary awards to trial participants and the inability to commercialize any products that we may develop. These claims might be made directly by consumers, health care providers, pharmaceutical companies or others selling or testing our products. We have obtained limited product liability insurance coverage for our clinical trials in the amount of $10.0 million per occurrence and $10.0 million in the aggregate. However, our insurance may not reimburse us or may not be sufficient to reimburse us for expenses or losses we may suffer.

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Moreover, if insurance coverage becomes more expensive, we may not be able to maintain insurance coverage at a reasonable cost or in sufficient amounts to protect us against losses due to liability. If we obtain marketing approval for any of our product candidates, we intend to expand our insurance coverage to include the sale of commercial products, but we may be unable to obtain commercially reasonable product liability insurance for any products approved for marketing. On occasion, juries have awarded large judgments in class action lawsuits for claims based on drugs that had unanticipated side effects. In addition, the pharmaceutical and biotechnology industries, in general, have been subject to significant medical malpractice litigation. A successful product liability claim or series of claims brought against us would decrease our cash reserves and could cause our stock price to fall.

Risks Related to Genetic Engineering of Agricultural Products

Social issues may limit the public acceptance of genetically engineered products, which could reduce demand for our products.

Although our technology is not dependent upon genetic engineering, genetic engineering plays a prominent role in our approach to product development. For example, research efforts focusing on plant traits may involve either selective breeding or modification of existing genes in the plant under study. Public attitudes may be influenced by claims that genetically engineered products are unsafe for consumption or pose a danger to the environment. The commercial success of our future products will depend, in part, upon public acceptance of the use of genetically engineered products, including drugs and plant and animal products.

The subject of genetically modified organisms has received negative publicity, which has aroused public debate. For example, certain countries in Europe require labeling of products that contain genetic modifications or are genetically modified . In addition, the European Union has implemented rules that regulate the placing on the market of food and feed products containing or consisting of genetically modified organisms. These rules also provide for the labeling of such products to the final consumer. Adverse publicity has resulted in greater regulation internationally and trade restrictions on imports of genetically altered products. If similar action is taken in the United States or other countries, genetic research and genetically engineered products could be subject to greater domestic regulation, including stricter labeling requirements. To date, our business has not been hampered by these activities. However, such publicity in the future may prevent any products resulting from our research from gaining market acceptance and reduce demand for our products, which are developed using genetic engineering.

Laws and regulations may reduce our ability to sell genetically engineered products that we or our collaborators develop in the future.

We or our collaborators may develop genetically engineered agricultural and animal products. The field-testing, production and marketing of genetically engineered products are subject to regulation by federal, state, local and foreign governments. Regulatory agencies administering existing or future regulations or legislation may prevent us from producing and marketing genetically engineered products in a timely manner or under technically or commercially feasible conditions. In addition, regulatory action or private litigation could result in expenses, delays or other impediments to our product development programs and the commercialization of products. The FDA has released a policy statement stating that it will apply the same regulatory standards to foods developed through genetic engineering as it applies to foods developed through traditional plant breeding. Genetically engineered food products will be subject to premarket review, however, if these products raise safety questions or are deemed to be food additives. Our product candidates may be subject to lengthy FDA reviews and unfavorable FDA determinations if they raise questions regarding safety or if our products are deemed to be food additives.

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To date, the FDA has not required genetically engineered agricultural products to be labeled as such, provided that these products are as safe and have the same nutritional characteristics as conventionally developed products. The FDA may reconsider or change its policies, and local or state authorities may enact labeling requirements, either of which could have a material adverse effect on our ability or the ability of our collaborators to develop and market products resulting from our efforts.

Risks Related to Our Common Stock

We expect that our quarterly results of operations will fluctuate, and this fluctuation could cause our stock price to decline, causing investor losses.

Our quarterly operating results have fluctuated in the past and are likely to fluctuate in the future. A number of factors, many of which we cannot control, could subject our operating results and stock price to volatility, including:

- recognition of upfront licensing or other fees;
- payments of non-refundable upfront or licensing fees to third parties;
- acceptance of our technologies and platforms;
- the success rate of our discovery efforts leading to milestone payments and royalties;
- the introduction of new technologies or products by our competitors;
- the timing and willingness of collaborators to commercialize our products;
- our ability to enter into new collaborative relationships;
- the termination or non-renewal of existing collaborations;
- the timing and amount of expenses incurred for clinical development and manufacturing of our product candidates;
- the impairment of acquired goodwill and other assets; and
- general and industry-specific economic conditions that may affect our collaborators research and development expenditures.

A large portion of our expenses, including expenses for facilities, equipment and personnel, are relatively fixed in the short term. In addition, we expect operating expenses to increase significantly as we move more compounds into clinical development. Accordingly, if our revenues decline or do not grow as anticipated due to the expiration or termination of existing contracts, our failure to obtain new contracts or our inability to meet milestones or because of other factors, we may not be able to correspondingly reduce our operating expenses. Failure to achieve anticipated levels of revenues could therefore significantly harm our operating results for a particular fiscal period.

Due to the possibility of fluctuations in our revenues and expenses, we believe that quarter-to-quarter comparisons of our operating results are not a good indication of our future performance. As a result, in some future quarters, our operating results may not meet the expectations of stock market analysts and investors, which could result in a decline in the price of our common stock.

Our stock price may be extremely volatile.

The trading price of our common stock has been highly volatile, and we believe the trading price of our common stock will remain highly volatile and may fluctuate substantially due to factors such as the following:

adverse results or delays in clinical trials;

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announcement of FDA approval or non-approval, or delays in the FDA review process, of our or our collaborators product candidates or those of our competitors or actions taken by regulatory agencies with respect to our, our collaborators or our competitors clinical trials;

the announcement of new products by us or our competitors;

quarterly variations in our or our competitors results of operations;

litigation, including intellectual property infringement lawsuits, involving us;

failure to achieve operating results projected by securities analysts;

changes in earnings estimates or recommendations by securities analysts;

financing transactions;

developments in the biotechnology or pharmaceutical industry;

sales of large blocks of our common stock or sales of our common stock by our executive officers, directors and significant stockholders;

departures of key personnel or board members;

developments concerning current or future collaborations;

FDA or international regulatory actions;

third-party reimbursement policies;

acquisitions of other companies or technologies;

disposition of any of our subsidiaries, technologies or compounds; and

general market conditions and other factors, including factors unrelated to our operating performance or the operating performance of our competitors.

These factors, as well as general economic, political and market conditions, may materially adversely affect the market price of our common stock.

In the past, following periods of volatility in the market price of a company s securities, securities class action litigation has often been instituted. A securities class action suit against us could result in substantial costs and divert management s attention and resources, which could have a material and adverse effect on our business.

We are exposed to risks associated with acquisitions.

We have made, and may in the future make, acquisitions of, or significant investments in, businesses with complementary products, services and/or technologies. Acquisitions involve numerous risks, including, but not limited to:

- difficulties and increased costs in connection with integration of the personnel, operations, technologies and products of acquired companies;
- diversion of management s attention from other operational matters;
- the potential loss of key employees;
- the potential loss of key collaborators;
- lack of synergy, or the inability to realize expected synergies, resulting from the acquisition; and
- acquired intangible assets becoming impaired as a result of technological advancements or worse-than-expected performance of the acquired company.

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Mergers and acquisitions are inherently risky, and the inability to effectively manage these risks could materially and adversely affect our business, financial condition and results of operations.

Future sales of our common stock may depress our stock price.

If our stockholders sell substantial amounts of our common stock (including shares issued upon the exercise of options and warrants) in the public market, the market price of our common stock could fall. These sales also might make it more difficult for us to sell equity or equity-related securities in the future at a time and price that we deem appropriate. For example, following an acquisition, a significant number of shares of our common stock held by new stockholders may become freely tradable or holders of registration rights could cause us to register their shares for resale. Sales of these shares of common stock held by existing stockholders could cause the market price of our common stock to decline.

Some of our existing stockholders can exert control over us, and their interests could conflict with the best interests of our other stockholders.

Due to their combined stock holdings, our officers, directors and principal stockholders (stockholders holding more than 5% of our common stock), acting together, may be able to exert significant influence over all matters requiring stockholder approval, including the election of directors and approval of significant corporate transactions. In addition, this concentration of ownership may delay or prevent a change in control of our company, even when a change may be in the best interests of our stockholders. In addition, the interests of these stockholders may not always coincide with our interests as a company or the interests of other stockholders. Accordingly, these stockholders could cause us to enter into transactions or agreements that would not be widely viewed as beneficial.

Anti-takeover provisions in our charter documents and under Delaware law could make an acquisition of us, which may be beneficial to our stockholders, more difficult and may prevent or deter attempts by our stockholders to replace or remove our current management.

Provisions in our corporate charter and bylaws may discourage, delay or prevent an acquisition of our company, a change in control, or attempts by our stockholders to replace or remove members of our current Board of Directors. Because our Board of Directors is responsible for appointing the members of our management team, these provisions could in turn affect any attempt by our stockholders to replace current members of our management team. These provisions include:

- a classified Board of Directors;
- a prohibition on actions by our stockholders by written consent;
- the inability of our stockholders to call special meetings of stockholders;

the ability of our Board of Directors to issue preferred stock without stockholder approval, which could be used to institute a poison pill that would work to dilute the stock ownership of a potential hostile acquirer, effectively preventing acquisitions that have not been approved by our Board of Directors;

limitations on the removal of directors; and

advance notice requirements for director nominations and stockholder proposals.

Moreover, because we are incorporated in Delaware, we are governed by the provisions of Section 203 of the Delaware General Corporation Law, which prohibits a person who owns in excess of 15% of our outstanding voting stock from merging or combining with us for a period of three years after the date of the transaction in which the person acquired in excess of 15% of our outstanding voting stock, unless the merger or combination is approved in a prescribed manner.

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FORWARD-LOOKING STATEMENTS

Some of the statements in this prospectus supplement, the accompanying prospectus and the documents incorporated by reference are forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, as amended, and Section 21E of the Securities Exchange Act of 1934, as amended. These statements are based on our current expectations, assumptions, estimates and projections about our business and our industry, and involve known and unknown risks, uncertainties and other factors that may cause our or our industry s results, levels of activity, performance or achievement to be materially different from any future results, levels of activity, performance or achievements expressed or implied in or contemplated by the forward-looking statements. Words such as believe , anticipate , expect , intend , plan , will , may , should , estimate , pre and continue , or the negative of such terms or other similar expressions, may identify forward-looking statements, but the absence of these words does not necessarily mean that a statement is not forward-looking. In addition, any statements that refer to expectations, projections or other characterizations of future events or circumstances are forward-looking statements. Our actual results could differ materially from those anticipated in such forward-looking statements as a result of the factors more fully described under the caption Risk Factors beginning on page S-8 of this prospectus supplement and in the documents incorporated by reference. The forward-looking statements made in this prospectus supplement and the accompanying prospectus speak only as of the date on which the statements are made.

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USE OF PROCEEDS

We estimate that the net proceeds from the sale of the 9.0 million shares of common stock we are offering will be approximately $75.9 million, assuming a public offering price of $9.00 per share and after deducting the estimated underwriting discount and the estimated offering expenses payable by us. If the underwriters exercise in full their option to purchase additional shares, we estimate that the net proceeds to us will be approximately $87.3 million. Each $1.00 increase (decrease) in the assumed public offering price of $9.00 per share would increase (decrease) the net proceeds to us from this offering by approximately $8.5 million, assuming the number of shares offered by us, as set forth on the cover page of this prospectus supplement, remains the same. We may also increase or decrease the number of shares we are offering. An increase of 1.0 million shares in the number of shares offered by us, to a total of 10.0 million shares, together with a concomitant $1.00 increase in the assumed public offering price of $9.00 per share, would increase the net proceeds to us from this offering by approximately $17.9 million. Similarly, a decrease of 1.0 million shares in the number of shares offered by us, to a total of 8.0 million shares, together with a concomitant $1.00 decrease in the assumed public offering price of $9.00 per share, would decrease the net proceeds to us from this offering by approximately $16.0 million. We do not expect that a change in the offering price or the number of shares by these amounts would have a material effect on our uses of the proceeds from this offering, although it may impact the amount of time prior to which we will need to seek additional capital.

We anticipate using the net proceeds to us from the sale of the common stock in this offering to fund clinical development of product candidates and for working capital and general corporate purposes. We may also use a portion of the net proceeds to acquire or invest in businesses, products and technologies that are complementary to our own, although we are not currently planning or negotiating any such transactions.

Pending the use of the net proceeds, we may invest the net proceeds in investment grade, interest-bearing securities.

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PRICE RANGE OF OUR COMMON STOCK

Since April 11, 2000, our common stock has been quoted and traded on The Nasdaq Global Select Market (formerly The Nasdaq National Market) under the symbol EXEL . The following table sets forth, for the periods indicated, the reported high and low intraday sales prices per share of our common stock on The Nasdaq Global Select Market:

	High	Low
Year ended December 31, 2004		
First Quarter	$ 9.50	$ 6.81
Second Quarter	10.64	8.04
Third Quarter	10.10	6.11
Fourth Quarter	9.79	7.97
Year ended December 31, 2005		
First Quarter	$ 9.69	$ 6.02
Second Quarter	8.57	6.51
Third Quarter	9.37	7.10
Fourth Quarter	9.96	6.53
Year ending December 31, 2006		
First Quarter	$ 12.21	$ 9.22
Second Quarter	12.49	9.00
Third Quarter (through September 26, 2006)	10.24	7.53

The reported last sale price of our common stock on The Nasdaq Global Select Market on September 26, 2006 was $9.00 per share. As of September 25, 2006, there were approximately 698 stockholders of record of our common stock.

DIVIDEND POLICY

We have never declared or paid cash dividends on our capital stock. We currently intend to retain earnings, if any, to support the development of our business and do not anticipate paying cash dividends for the foreseeable future.

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DILUTION

Our net tangible book value (deficit) on June 30, 2006 was $(18.8) million, or approximately $(0.22) per share. Net tangible book value (deficit) per share is equal to the amount of our total tangible assets, less total liabilities, divided by the aggregate number of shares of common stock outstanding as of June 30, 2006. Dilution in net tangible book value (deficit) per share represents the difference between the amount per share paid by purchasers of shares of common stock in this offering and the net tangible book value (deficit) per share of our common stock immediately after this offering. After giving effect to the sale of 9.0 million shares of common stock in this offering at an assumed public offering price of $9.00 per share, and after deducting the estimated underwriting discount and estimated offering expenses payable by us, our net tangible book value on June 30, 2006 would have been approximately $57.1 million, or approximately $0.61 per share. This represents an immediate dilution of $8.39 per share to new investors purchasing shares of common stock in this offering. The following table illustrates this dilution:

Assumed public offering price per share		$ 9.00
Net tangible book value (deficit) per share as of June 30, 2006	$ (0.22)	
Increase per share attributable to new investors	0.83	
Net tangible book value per share as of June 30, 2006 after giving effect to this offering		0.61
Dilution per share to new investors		$ 8.39

Each $1.00 increase (decrease) in the assumed public offering price of $9.00 per share would increase (decrease) our as adjusted net tangible book value by $8.5 million, or $0.09 per share, and the dilution in as adjusted net tangible book value per share to investors in this offering by $0.91 per share, assuming that the number of shares offered by us, as set forth on the cover page of this prospectus supplement, remains the same and after deducting the estimated underwriting discount and estimated offering expenses payable by us. We may also increase or decrease the number of shares we are offering. An increase of 1.0 million shares in the number of shares offered by us, to a total of 10.0 million shares, together with a concomitant $1.00 increase in the assumed public offering price of $9.00 per share, would increase our as adjusted net tangible book value by $17.9 million, or $0.19 per share, and the dilution in as adjusted net tangible book value per share to investors in this offering by $0.81 per share. Similarly, a decrease of 1.0 million shares in the number of shares offered by us, to a total of 8.0 million shares, together with a concomitant $1.00 decrease in the assumed public offering price of $9.00 per share, would decrease our as adjusted net tangible book value by $16.0 million, or $0.16 per share, and the dilution in as adjusted net tangible book value per share to investors in this offering by $0.84 per share. The as adjusted information discussed above is illustrative only and will be adjusted based on the actual public offering price and other terms of this offering determined at pricing.

The foregoing discussion and table do not take into account further dilution to new investors that could occur upon the exercise of outstanding options and warrants having a per share exercise price less than the per share offering price to the public in this offering. As of June 30, 2006, there were:

- 17,695,763 shares of common stock underlying options and warrants outstanding at a weighted average exercise price of $10.28 per share;

- 6,134,376 shares available for future issuance under our 2000 Equity Incentive Plan, 1,428,798 shares available for future issuance under our 2000 Employee Stock Purchase Plan and 1,259,696 shares available for future issuance under our 2000 Non-Employee Directors Stock Option Plan; and

9,184,391 shares issuable upon conversion of our convertible debt (assuming that the debt had been converted as of June 30, 2006).

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BUSINESS

Overview

We are a biotechnology company focused on the discovery and development of novel small molecule therapeutics for cancer and other serious diseases. Through our discovery research and clinical development activities, we are building a portfolio of novel compounds that we believe have the potential to be high-quality, differentiated pharmaceutical products.

Utilizing our library of more than four million compounds, we integrate high-throughput processes, medicinal chemistry, bioinformatics, structural biology and early *in vivo* testing in parallel to characterize thousands of compounds, a process that is designed to enable us to move with speed in research and development. This approach enables us to identify and select from this large pool of compounds those highly qualified drug candidates that meet our stringent list of development criteria.

To date, we have filed nine investigational new drug applications (INDs), eight of which were developed using our internal drug discovery efforts. We believe that our deep pool of drug candidates will enable us to continue to file several new INDs each year for the foreseeable future. As our compounds advance into clinical development, we expect to generate a critical mass of data that will help us to understand the full clinical and commercial potential of our product candidates. In addition to guiding the potential commercialization of our innovative therapies, these data may contribute to the understanding of disease and help improve treatment outcomes.

Our current pipeline includes the following compounds:

Compound	Target(s)	Indication	Stage of Development
XL119*	Topoisomerase 2	Biliary Tract Cancer	Phase 3
XL999**	VEGFR2, PDGFR, FGFR, FLT3	Renal Cell Carcinoma, Colorectal, Ovarian, Non-Small Cell Lung Cancer, Acute Myelogenous Leukemia, Multiple Myeloma	Phase 2
XL784**	ADAM-10, MMP2	Diabetic Nephropathy	Phase 2
XL880	c-MET, VEGFR2	Papillary Renal Cell Carcinoma	Phase 2
XL647**	VEGFR2, EGFR, HER2	Non-Small Cell Lung Cancer	Phase 2
XL820	c-KIT, VEGFR2, PDGFR	Solid Tumors	Phase 1
XL844	CHK1, CHK2	Solid Tumors and Hematologic Malignancies	Phase 1
XL184	c-MET, VEGFR2	Solid Tumors	Phase 1
XL228	ABL, IGF1R, SRC	Solid Tumors and Hematologic Malignancies	IND Filed
XL281	RAF	Solid Tumors	Preclinical
XL418	AKT, S6K	Solid Tumors	Preclinical
XL518	MEK	Solid Tumors	Preclinical
XL147	PI-3K	Solid Tumors	Preclinical
XL765	PI-3K, mTOR	Solid Tumors	Preclinical
XL019	JAK2	Hematologic Malignancies	Preclinical
XL550*	MR	Hypertension	Preclinical
XL335*	FXR	Atherosclerosis	Preclinical
EXEL2255*	LXR	Atherosclerosis	Preclinical

* XL119, XL550, XL335 and EXEL2255 are out-licensed to Helsinn, Sankyo, Wyeth and Bristol-Myers Squibb, respectively.
** Out-licensed to Symphony Evolution, Inc. and subject to exclusive repurchase options as described in this report.

Pursuant to a product development and commercialization agreement between Exelixis and GlaxoSmithKline, GlaxoSmithKline has the option, after completion of clinical proof-of-concept by Exelixis, to elect to develop up to three compounds in Exelixis product pipeline, which may include XL784 and the cancer compounds identified in the table above (other than XL119, XL518, XL147, XL765 and XL019).

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We have established collaborations with major pharmaceutical and biotechnology companies based on the strength of our expertise in biology, drug discovery and development that allow us to retain economic participation in compounds and support additional development of our proprietary products. Through these collaborations, we obtain license fees, research funding, and the opportunity to receive milestone payments and royalties from research results and subsequent product development activities. We have ongoing commercial collaborations with several leading pharmaceutical and biotechnology companies, including GlaxoSmithKline, Bristol-Myers Squibb Company, Wyeth, Sankyo and Genentech. We expect to continue to use corporate partnering as a strategic tool to cultivate our assets, fund our operations and expand the therapeutic and commercial potential of our pipeline.

As our company has matured and our development efforts have intensified, we have restructured our organization as needed to reallocate resources and enhance the efficiency of our operations. We believe that these efforts have strengthened us by enabling us to achieve an appropriate functional balance within our organization.

Areas of Expertise

Integrated Drug Research, Discovery and Development Capabilities

We have built a multidisciplinary, integrated research and development platform that supports the complex, iterative nature of drug research, discovery and clinical development. Our platform has been designed to include all of the critical functions and expertise required to advance from high-throughput screening lead to drug in a consistent and streamlined fashion. Our integrated drug discovery platform has also allowed us to move compounds rapidly into the clinic and is responsible for our high success rate to date in advancing our compounds into Phase 2 clinical trials. In 2005, we filed three INDs, and we expect to file an additional three INDs in 2006.

We have industrialized the discovery process and utilize a variety of high-throughput technologies to discover and characterize compounds rapidly and extensively and to select compounds with the best potential for further evaluation and development. We have combined our ability to identify and understand the interaction and synergistic biological activity of various biological targets with a state-of-the-art drug discovery platform to work at the interface of chemical and biological sciences. In addition, we have built critical mass in all key operational areas. We believe that these human and technological resources enable us to: (i) identify and validate novel targets effectively and rapidly; (ii) identify and optimize proprietary lead compounds; (iii) discover compounds with a spectrum of activity that demonstrate potent activity in preclinical disease models and may confer unique clinical benefit; and (iv) perform the broad range of preclinical testing required to fuel our pipeline and advance promising compounds through all stages of development. We believe that our integrated drug discovery and development process is a key competitive advantage, which enables us to effectively collaborate internally and to streamline our decision-making processes and advance our discovery and development programs expeditiously.

Drug Discovery

Our integrated platform combines advanced capabilities in target identification and drug discovery. It is designed to operate in a fully integrated, high-throughput manner across the complete drug discovery and development continuum. This integrated approach enables us to: (i) identify disease-related targets; (ii) discover potent and biologically active compounds; (iii) optimize lead compounds to enhance drug properties such as safety and potency; (iv) fully characterize the interactions between compounds and

targets; (v) analyze *in vitro* and *in vivo* pharmacology; and (vi) perform the full range of pharmacodynamic, pharmacokinetic and safety analyses required to

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advance compounds into and through preclinical development and subsequently, into clinical development. This industrialized approach allows us to move from high-throughput screening to development candidate selection in as little as 12 months. Key capabilities include:

Target Identification and Validation

Model System Genetics and Comparative Genomics our unique skill-set and know-how in the area of model system genetics and comparative genomics enable us to understand the fundamental biology of complex genetic pathways. Our goal is to identify and validate genes that play a causative role in diseases and that are druggable , that is, can be targeted for inhibition through the intervention of small molecule or antibody-based therapeutics.

Target Validation we possess the capability to develop assays and produce adequate supplies of purified proteins and reagents to conduct high-throughput and high-content experiments to validate the therapeutic relevance of our targets. This process also provides high-quality reagents and information to our internal discovery group for use in high-throughput drug screening, pharmacology and structural biology.

Discovery

Biochemical assays validate the target and assess selectivity of the compound. This helps to select compounds that bind specifically to the desired target, with little to no interaction with other proteins, a key factor in limiting unwanted side effects.

Cellular assays provide insight into the mechanism by which compounds modulate the activity of the target and the effects of this modulation. These assays show what happens to gene expression and cellular activity profiles after exposure to the compound.

Drug metabolism and pharmacokinetic (DMPK) assays evaluate the absorption, distribution, metabolism and excretion (ADME) of a compound *in vitro* and assess pharmacokinetic properties *in vivo.* These assays are used to identify and optimize compounds for high-potency, long duration of action and favorable safety and tolerability profiles.

Pharmacodynamic assays provide additional insight into the mechanism of action and the effects of target modulation using *in vivo* models.

Efficacy models evaluate the safety, tolerability and therapeutic effect of a compound in relevant animal models of human disease.

Non-Good Laboratory Practice (GLP) toxicity assays a series of *in vitro* and *in vivo* tests that identify potential side-effects or toxicities.

Development

Our development group has the expertise to move our development candidate compounds from preclinical testing through all phases of clinical development. Our integrated development strategy supports advancement of candidate compounds from development candidate status to IND in as little as 12 months. In particular, the development group possesses expertise in the following areas:

Pharmaceutical Development (PD) provides drugs in adequate quantity with appropriate purity and in a suitable dosage form to allow the program to proceed without delay. While our PD group initially relied exclusively on external resources to accomplish its mission, the growth in our pipeline has allowed us to develop significant internal capabilities at our South San Francisco facilities. Our PD scientists can develop and refine methods for synthesizing compounds, as well as the testing methods required to establish their purity and stability. In addition, we have the internal capabilities to develop formulations for our compounds in clinical development. By building these internal capabilities, we have significantly enhanced our ability to meet tight timelines.

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Non-Clinical Development is responsible for the safety testing of our development compounds, as well as characterizing the absorption, distribution, metabolism and excretion of those compounds. With extensive experience and expertise in these disciplines, the group has the capabilities to provide all the non-clinical support required for our development programs from IND-enabling studies through all phases of clinical development and registration.

Clinical Development is a multidisciplinary team with depth and experience in all critical areas required for effective clinical development. In addition to core expertise in medicine and clinical science, the group includes drug development professionals with specialized skills including clinical trial design and direction, study implementation and oversight, biostatistics and data management, drug safety evaluation and adverse event reporting. With broad experience from IND preparation and submission to successful implementation of Phase 1, 2 and 3 clinical trials, the group has the capabilities to expeditiously advance our clinical pipeline from development to registration.

Regulatory Affairs is responsible for assuring that our development programs are conducted in compliance with all regulatory requirements. These professionals combine the ability to continuously monitor and assess the ever-changing regulatory requirements with the ability to translate those regulations into pragmatic advice for our development projects.

Agriculture

Our unique expertise in model systems biology also has applications in the agricultural arena. In the area of *crop protection,* we are leveraging our expertise in target identification, high-throughput screening and chemistry to work with corporate partners in the discovery of more specifically targeted chemical products. In the area of *plant trait discovery,* we are working with corporate partners to develop crops with superior yield and improved nutritional profiles in oil content and protein composition. In the area of *metabolic engineering*, we are developing cells that produce high levels of valuable biochemical compounds. We believe that we have been a leader in utilizing plants as factories to produce high-value compounds that are naturally produced in plant cells.

Artemis Pharmaceuticals

Artemis Pharmaceuticals, based in Cologne, Germany is a wholly owned subsidiary of Exelixis. Its activities are directed towards providing transgenic mouse generation services, tools and related licenses to the industrial and academic community. In addition, it has two internal research programs, one dedicated to the development of transgenic approaches to produce animal-wide RNAi knock down in mice *in vivo*, and the second dedicated to the provision of humanized mouse models for drug testing purposes. To date, we have derived all of our revenues from external customers through Artemis. For the year ended December 31, 2005, Artemis had total revenues of $5.8 million and a net loss of $0.6 million. Artemis had total assets of $2.7 million as of December 31, 2005.

Our Strategy

Our business strategy is to become a fully integrated biotechnology company by leveraging our drug discovery capabilities to generate a deep pipeline of diverse compounds with first-in-class or best-in-class potential that fulfill unmet medical needs in the treatment of cancer and other serious diseases. Because our continued success and growth as a company depend in part on our ability to advance current and future compounds successfully in clinical development, we intend to commit substantial resources to building a premier clinical development organization to accommodate our expanding pipeline of compounds. We continue to build

critical mass of key internal expertise and capabilities to facilitate conducting multiple clinical trial programs with speed and rigor. To execute our strategy we intend to continue to establish

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strategic alliances with world-class pharmaceutical and biotechnology companies that generate near-term revenues, reduce our risk of product failure and allow us to retain meaningful long-term value. Specifically, our business strategy includes the following key elements:

Selectively Develop Therapeutic Products with First-In-Class or Best-In-Class Potential

We have invested and plan to continue to invest significant funds in discovering and developing proprietary product candidates, particularly in the area of cancer. We have committed substantial resources to building a first-rate drug discovery effort that is integrated with our unique understanding of the biological basis of a disease. Part of our strategy is to generate a large pipeline of diverse product candidates that provides us with the flexibility to select only those compounds that have both clinical and commercial potential. In developing compounds, our strategy is to pursue a variety of clinically validated, novel and proprietary targets. These decisions are data-driven, based on stringent criteria that incorporate intrinsic potency, selectivity, preclinical efficacy and tolerability and commercial viability. Our strategy is to commit resources only to those compounds that are commercially viable and have the potential to be first-in-class or best-in-class therapeutics.

Target Multiple Pathways

We have extensive expertise and experience in modifying gene function *in vitro* and *in vivo* as a result of our work on model organisms for the discovery of novel targets and pathways relevant to the development, progression and treatment of cancer and other diseases. We believe that the most effective therapies for cancer will target multiple pathways, simultaneously turn off growth signals, increase rates of programmed cell death and reduce the growth of blood vessels necessary to support tumor growth.

We have two distinct approaches in our drug discovery efforts:

Spectrum Selective Kinase Inhibitors (SSKIs)

Our clinical pipeline includes a number of Spectrum Selective Kinase Inhibitors (XL999, XL647, XL880, XL820 and XL184). These compounds have been optimized for balanced potency, specificity, tolerability and pharamacologic parameters and are designed to target multiple members of a family of proteins known as receptor tyrosine kinases (RTKs) in a concerted manner. RTKs are validated targets for drug development, as evidenced by several recent approved cancer therapies. We believe SSKIs may provide more effective treatment than compounds that target only one RTK, or multiple unrelated RTKs, because interactions among multiple RTKs contribute to the progression of a variety of diseases. In addition, we believe SSKIs may provide enhanced safety profiles compared to the use of multiple single-target drugs that have not been optimized for use together. About half of the RTKs are validated targets for drug development, as evidenced by several approved cancer therapies.

Intracellular Signaling Pathway Inhibitors

Our second generation of compounds, which include XL281, XL418 and XL228, focus on intracellular pathways, which are known to regulate growth, proliferation and survival of cancer cells. Signals from RTKs converge on several critical intracellular signaling

pathways and mutational activation of these pathways is common in tumors. This activation leads to tumor progression and also represents an important mechanism of resistance to both targeted drugs and chemotherapy. We are developing multiple inhibitors of these important intracellular signaling cascades, including the PI-3 kinase and mTOR (key controllers of cell growth and proliferation), Erk (a mediator of cell growth and differentiation), and Jak2 pathways (important in the intracellular transduction of cytokine signals).

Leverage Strategic Collaborations

We are committed to retaining significant equity in the value of our pipeline and product candidates. Our strategy is to leverage the strength of our extensive data and the broad potential of our

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development compounds to establish strategic alliances with world-class pharmaceutical and biotechnology companies that generate near-term revenues, reduce our risk of product failure and allow us to retain meaningful long-term value. Our collaborations to date have provided us with substantial committed funding for our research and development efforts, the potential to earn significant milestones as well as opportunities to receive significant future payments, if our collaborators successfully develop and market products that result from our collaborative work. In addition, many of our strategic relationships permit us to obtain co-development, co-promotion or other rights to any products identified or developed in such collaborative relationships as a result of our efforts.

Management of Our Financial Resources

Fiscal discipline and pragmatic allocation of our resources are key components of our corporate strategy. We believe that making significant investments in preclinical development enhances our ability to generate multiple new, high-quality INDs and to rapidly advance these new drug candidates through clinical development. We believe the return on this investment will come in the form of higher clinical success rates, funding and partnership terms that allow us to retain increasing equity in the long-term value of our pipeline. We believe that this approach will enhance the quality and growth of our pipeline while maintaining our ability to fulfill obligations to corporate partners. We seek to finance our activities through a blend of funding opportunities, including (i) executing under our existing partnerships, which potentially triggers substantial milestones; (ii) exploring opportunities for new partnerships for our unpartnered assets, which has the potential to bring in near-term cash and defray late-stage development costs; (iii) evaluating the suitability of third-party financing vehicles with the aim to off-load a significant portion of our near-term clinical development expense and clinical risks; and (iv) opportunistically accessing the capital markets.

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Clinical and Preclinical Pipeline

Clinical Pipeline

We have an extensive pipeline of compounds in various stages of development that will potentially treat cancer, renal disease and various metabolic and cardiovascular disorders. The following table summarizes the status of our clinical and preclinical development pipeline.

We currently have 18 compounds in clinical and preclinical development. XL119, which has been exclusively licensed to Helsinn Healthcare S.A., is in a multi-national Phase 3 clinical trial for the treatment of bile duct tumors that continues to recruit patients as anticipated. XL999 is being evaluated in Phase 2 clinical trials in patients with renal cell, colorectal, ovarian and non-small cell lung cancer, as well as acute myelogenous leukemia (AML) and multiple myeloma. We commenced a Phase 2 clinical trial of XL784 in March 2006 to test its efficacy in patients with renal failure. In June 2006, we initiated a Phase 2 clinical trial for XL880 in papillary renal cell carcinoma and we expect to initiate three additional Phase 2 clinical trials for XL880 in the first quarter of 2007 (one in head and neck cancer and two in gastric cancer). In August 2006, we initiated a Phase 2 clinical trial for XL647 in patients with non-small cell lung cancer and we expect to initiate three additional Phase 2 clinical trials for XL647 in the first quarter of 2007 (two in non-small cell lung cancer and one in metastatic breast

cancer). In addition, we have Phase 1 clinical trials ongoing for XL820, XL844 and XL184 and expect to initiate Phase I trials for XL228 in the fourth quarter of 2006. These compounds are being tested in patients with various solid tumors for which there is no other treatment option with the exception of XL844, which is being tested in patients with chronic lymphocytic leukemia (CLL).

All of our compounds, with the exception of XL119 (which was in-licensed from Bristol-Myers Squibb), were generated through our internal drug discovery efforts. The oncology program currently is comprised of 15 compounds nine in clinical development and six in preclinical development. We plan to continue the preclinical work on XL281 and XL418 with the goal of filing two INDs in 2006. We further plan to continue preclinical work on XL518, XL147, XL765 and XL019, all of which are potential IND candidates in 2007.

XL999 is a potent inhibitor of key RTKs implicated in the development and maintenance of tumor vasculature and in the proliferation of some tumor cells. It inhibits the fibroblast growth factor receptor (FGFR), vascular endothelial growth factor receptor2 (VEGFR2) and platelet-derived growth factor receptor (PDGFR) RTKs and is also a potent inhibitor of FMS-like tyrosine kinase type 3 (FLT3), an important driver of leukemia cell proliferation in some patients with AML. XL999 exhibited excellent activity in target-specific cellular functional assays.

In a Phase 1 trial, XL999 demonstrated that it had an acceptable safety profile and was well tolerated at 2.4 mg/kg dosed once weekly. Data from the Phase 1 trial of XL999 in patients with advanced solid tumors were presented by investigators in November 2005 at the AACR-NCI-EORTC International Conference on Molecular Targets and Cancer Therapeutics. At that time, of 22 patients who had been administered XL999 once every two weeks and followed for eight weeks, there were two partial responses (liver and thyroid), one minor response (28% reduction; renal cell), and four patients with durable stable disease for 3-7 months (thyroid [n=2], renal cell [n=2]). Of 37 patients dosed at various levels and schedules for whom Phase 1 data were presented by investigators at the annual meeting of the American Society for Clinical Oncology (ASCO) held from June 2-6, 2006, there were three partial responses in patients and eight patients with prolonged stable disease (3 to 11 months).

A multi-trial Phase 2 clinical development program for XL999 was initiated in December 2005. The Phase 2 program is composed of six trials that will evaluate XL999 in a variety of cancer indications: renal cell, colorectal, ovarian and non-small cell lung cancer, as well as AML and multiple myeloma. Patients will be dosed at 2.4 mg/kg weekly. The Phase 2 trials will evaluate the compound as a single agent, looking for responses in patients who have failed prior therapies. Some of the studies are also designed to evaluate single-agent activity of XL999 in previously untreated patients for whom conventional therapy is not appropriate. The trials will be conducted at multiple centers throughout the United States. Additionally, we are considering combination trials of XL999 either in combination with other anti-angiogenic compounds or with cytotoxic chemotherapy.

XL784 is the first small molecule compound developed from our proprietary drug discovery engine and is being developed for diabetic nephropathy, an area with significant unmet patient needs. The compound is a potent inhibitor of the metalloproteases (MMP) ADAM-10 (a disintegrin and metalloprotease domain 10) and MMP2. XL784 was specifically designed not to inhibit MMP1, thus potentially significantly enhancing its safety profile and allowing higher dosing compared with other previously studied MMP inhibitors. Results of a single dose Phase 1 clinical trial of XL784 administered orally to 70 healthy volunteers demonstrated that XL784 has attractive safety and pharmacokinetic profiles. A repeat-dose Phase 1 clinical trial of a capsule formulation of XL784 was completed in October 2005 in healthy volunteers in preparation for a Phase 2 program to investigate the utility of the compound in patients with diabetic nephropathy. A Phase 2 clinical trial was initiated in March 2006 employing a double-blind, placebo-controlled design in which approximately 130 patients will be randomized to one

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of two study groups. One group will receive angiotensin receptor blockers and/or angiotensin-converting enzyme therapy while the second group will receive XL784 as well as angiotensin receptor blockers and/or angiotensin-converting enzyme therapy. The endpoint of the Phase 2 clinical trial is a reduction in proteinuria.

XL647 is a potent inhibitor of RTKs that are implicated in driving tumor proliferation and vascularization (blood vessel formation). XL647 inhibits the epidermal growth factor receptor (EGFR), human epidermal growth factor receptor 2 (HER2) and VEGF RTKs simultaneously in preclinical studies. The compound has been optimized for high potency and oral bioavailability, demonstrates excellent activity in target-specific cellular functional assays, and has shown sustained inhibition of target RTKs preclinically *in vivo* following a single oral dose.

Interim results from the Phase 1 clinical trial were presented by investigators in November 2005 at the AACR-NCI-EORTC International Conference on Molecular Targets and Cancer Therapeutics in Philadelphia. Data on 40 patients treated in the Phase 1 clinical trial were subsequently presented by investigators at the 2006 ASCO meeting. XL647 was shown to be well tolerated and achieved its maximum tolerated dose. The investigators reported that one patient with non-small-cell lung cancer (NSCLC) treated at the lowest dose had a partial response and 12 others (NSCLC [n=3], chordoma [n=2], adenoid cystic carcinoma [n=2], adrenocortical carcinoma, colorectal, ovarian, mesothelioma and head and neck cancer) had prolonged stable disease (>3.5 months). In August 2006, we initiated a Phase 2 clinical trial for XL647 in patients with non-small cell lung cancer and we expect to initiate three additional Phase 2 clinical trials for XL647 in the first quarter of 2007 (two in with non-small lung cancer and one in metastatic breast cancer).

XL880 is a potent inhibitor of the hepatocyte growth factor receptor (Met) and VEGFR2 (KDR), which play synergistic roles in promoting tumor growth and angiogenesis. Activation or overexpression of Met has been documented as a negative prognostic indicator in patients with various carcinomas, and in patients with multiple myeloma, glioma, and other solid tumors. Interim data from an ongoing Phase 1 study of XL880 were presented by investigators in November 2005 at the AACR-NCI-EORTC International Conference on Molecular Targets and Cancer Therapeutics. Additional data from the Phase 1 clinical trial were presented by investigators at the 2006 ASCO meeting. Investigators reported that of 25 patients in the Phase 1 clinical trial, the two patients with papillary renal cell (PRC) carcinoma experienced a partial response. There were also seven patients with various tumors achieving stable disease. In June 2006, we initiated a Phase 2 clinical trial for XL880 in papillary renal cell carcinoma and we expect to initiate three additional Phase 2 clinical trials for XL880 in the first quarter of 2007 (one in head and neck cancer and two in gastric cancer).

XL820 demonstrated potent preclinical inhibitory activity against wild-type and mutant variance of the stem cell factor receptor (c-KIT) as well as VEGFR2 and PDGFR, 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. XL820 demonstrated excellent activity in target-specific cellular functional assays. In biochemical and cellular assays, XL820 also potently inhibits the mutationally activated forms of c-KIT that are found in human disease. XL820 has good oral bioavailability and has shown sustained inhibition of target RTKs *in vivo* following a single oral dose. A Phase 1 clinical trial of XL820, which is ongoing, was initiated in July 2005 in patients with solid tumors for whom there are no other available therapies known to prolong survival. We expect to start a Phase 2 clinical trial for XL820 in 2006.

XL844 potently inhibits the Csk homologous kinases (CHK) CHK1 and CHK2, kinases that induce cell cycle arrest in response to a variety of DNA damaging agents. We believe that XL844 is the first selective small molecule CHK inhibitor to advance into the clinic. In preclinical studies, XL844 has been shown to enhance the efficacy of chemotherapeutic agents in tumor

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models without increasing systemic toxicity and has demonstrated significant potency in biochemical and cellular assays, oral bioavailability and an attractive pharmacokinetic profile. A Phase 1 clinical trial of XL844 in patients with Chronic Lymphocytic Leukemia was initiated in September 2005 and is ongoing.

XL184 inhibits VEGFR2 and Met, key drivers for tumor formation and growth. The compelling preclinical efficacy of XL880, our first VEGFR2/Met inhibitor, increased our interest in inhibitors of these RTKs and resulted in the discovery and development of XL184. XL184 has a distinct profile of inhibition of these RTKs, which may result in potentially differentiated clinical utility. This compound has also demonstrated dose-dependent growth inhibition and tumor regression in a variety of preclinical tumor models including breast, colorectal and small cell lung cancer and glioblastoma. A Phase 1 clinical trial in patients with solid tumors was initiated in September 2005 and is ongoing.

XL119 (becatecarin) is an anticancer compound for which we have initiated a Phase 3 clinical trial as a potential treatment for bile duct tumors. XL119 has been exclusively licensed to Helsinn. The Phase 3 trial began in June 2004 and includes several centers in North America and Europe. The trial was designed under a Special Protocol Assessment (SPA) with the U.S. Food and Drug Administration (FDA) under which it was mutually agreed that the trial would include up to 600 patients with a primary endpoint of an increase in survival of at least two months. The trial is designed to have two interim analyses at a specified number of patient events (deaths) at which the data from the trial will be independently reviewed. At these interim analyses a decision to halt or continue the trial will be made. In March 2004, the drug was granted orphan drug status in bile duct cancer. In January 2006, the IND and management of the Phase 3 clinical trial was transferred to Helsinn, which going forward is responsible for the management of the trial. On June 2, 2006, we received a $4.0 million milestone payment from Helsinn for the successful delivery of drug supply. Under our license agreement with Helsinn, we may receive further milestones of up to $17.0 million.

XL228 targets the insulin-like growth factor 1 receptor (IGF1R), which is an RTK that promotes cell growth and survival in response to the binding of its ligand, insulin-like growth factor. IGF1R is highly expressed and activated in a broad range of human tumors and is thought to promote tumor growth, survival and resistance to chemotherapeutic agents. We have identified potent inhibitors of IGF1R that show potential efficacy in a variety of tumor xenograft models. In addition, XL228 also potently inhibits the T315I mutant form of the Abelson tyrosine kinase (ABL), a kinase that is resistant to other breakpoint cluster region (BCR)/ABL inhibitors when expressed in CML. We filed an IND for XL228 in August 2006 and expect to commence
Phase I trials in the fourth quarter of 2006.

We have licensed to Symphony Evolution, Inc. (SEI) our intellectual property rights, including commercialization rights, to XL647, XL999 and XL784 in exchange for SEI s investment of $80.0 million to advance the clinical development of these compounds. We have retained exclusive options to reacquire the compounds at specified prices. We continue to be primarily responsible for the development of these product candidates in accordance with a specified development plan and related development budget.

Preclinical Development Pipeline

Currently, we have nine compounds in preclinical development that target cancer and metabolic and cardiovascular diseases. We hope to move these compounds into clinical development within the next year and expect to file two additional INDs by the end of 2006. Our programs in metabolic and cardiovascular diseases originated from our acquisition of X-Ceptor Therapeutics, Inc. in October 2004.

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Cancer Compounds

XL281 specifically targets mitogen activated protein kinases (MAPK or RAF), which are cytoplasmic serine/threonine kinases that lie immediately downstream of RAS, and are key components of the RAS/RAF/MAPK kinase (MEK)/extracellular signal-related kinase (ERK) pathway that is frequently activated in human tumors. Inappropriate activation of this pathway promotes cell growth in the absence of exogenous growth factors. Activating mutations in B-RAF occur in approximately 60% of melanoma patients indicating a potentially pivotal role for deregulation of this kinase in the progression of melanoma. We have identified potent and highly selective inhibitors of RAF kinases that are orally bioavailable and show efficacy in tumor xenograft models. We are currently characterizing a set of advanced lead compounds and have advanced XL281 to development candidate status. We anticipate filing an IND for XL281 in 2006.

XL418 targets protein kinase B (PKB or AKT) and S6 kinase (S6K), which are kinases downstream of the lipid phosphatase phosphoinosotide-3 (PI-3) kinase. Their activation is a frequent event in human tumors and promotes cell growth, survival and resistance to chemotherapy and radiotherapy. Regulation of the pathway is complex, and inhibition at a single point (e.g., mammalian target of rapamycin [mTOR]) can result in upregulation in the activity of other pathway components. AKT inhibitors that effectively inactivate the pathway are expected to induce apoptosis (programmed cell death) in tumor cells and sensitize them to a wide range of chemotherapy. We have identified potent inhibitors that simultaneously target the kinases AKT and S6K with good oral bioavailability and efficacy in tumor xenograft models. XL418 was advanced to development candidate status in 2005 and we anticipate filing an IND in early 2007.

XL518 is a potent and specific inhibitor of MEK kinase, a key component of the RAS/RAF/MEK/ERK signaling cascade. Inappropriate activation of this pathway promotes cell growth in the absence of exogenous growth factors. In particular, activating mutations in B-RAF occur in approximately 60% of melanoma patients, and cells with such mutations are sensitive to inhibition of MEK. In preclinical testing, XL518 demonstrated low metabolic liabilities, and long duration of action and did not appreciably inhibit MEK in the brain. XL518 has pharmacodynamic and anti-tumor activity in multiple xenograft models, with complete tumor regression and delayed tumor regrowth in some models. XL518 is currently in late preclinical development, and we anticipate filing an IND for XL518 in 2006.

XL147 is a potent inhibitor of class I PI-3 kinases. PI-3 kinase signaling plays a central role in the growth, proliferation and survival of tumor cells, and is perhaps the most frequently deregulated pathway in tumor cells. In particular, activating mutations in PI-3 kinases and loss of the tumor suppressor PTEN are prevalent in many different types of malignancies. XL147 inhibits PI-3 kinases *in vitro* and in cell-based assays. Pharmacokinetic studies in multiple species indicate that XL147 is highly orally bioavailable and achieves high plasma exposure with good tolerability. XL147 has pharmacodynamic and anti-tumor activity (including regression) in multiple xenograft models, using tumor cells with a variety of PI-3 kinase pathway lesions. XL147 is currently in preclinical development and we anticipate filing an IND by the second quarter of 2007.

XL765 is a dual inhibitor of PI-3 kinase and mTOR. PI-3 kinase signaling plays a central role in the growth, proliferation and survival of tumor cells, and is perhaps the most frequently deregulated pathway in tumor cells. mTOR is an important regulator of cellular growth that integrates PI-3 kinase signaling with cellular nutritional status, energy level and oxygenation. Several mTOR inhibitors are in clinical trials and there are some early signs of clinical efficacy. We believe that the combination of mTOR and PI-3 kinase inhibition offers the possibility of enhanced effects on tumor growth, proliferation and survival. XL765 inhibits both PI-3 kinase and mTOR *in vitro* and has a potent antiproliferative effect in cells. XL765 is orally available in

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multiple species and has potent pharmacodynamic and anti-tumor activity (including regression) in multiple xenograft models at well-tolerated doses. XL765 is currently in preclinical development, and we anticipate filing an IND in first quarter of 2007.

XL019 targets JAK2, a key component of the downstream signaling cascades associated with numerous growth factors. Activation of JAK2 is associated with a number of myeloid and lymphoid malignancies, and more than 50% of patients with myeloproliferative disorders have activating mutations in JAK2. Inhibition of key kinase targets in this pathway may provide superior efficacy, safety and tolerability and may enable a new approach to cancer therapy. XL019 was moved to development candidate status in the second quarter of 2006.

Under the terms of our research and development collaboration with SmithKline Beecham Corporation (which does business as GlaxoSmithKline), which was established in October 2002 and amended in January 2005, GlaxoSmithKline has the right to select, after completion of clinical proof-of-concept two of the compounds (or possibly three if the collaboration is extended) in our pipeline (other than XL119, XL518, XL147 and XL765) for further development. Compounds subject to selection include XL784, XL647, XL999, XL880, XL844, XL184, XL820, XL281, XL418, XL228 and two earlier stage oncology programs. Selection of any of these compounds would trigger significant milestone payments and royalties from GlaxoSmithKline and would provide us with co-promotion rights should a compound be successfully commercialized.

Metabolic Disorders and Cardiovascular Compounds

XL550 targets the Mineralocortiocoid Receptor (MR), which is an antagonist used in the treatment of hypertension and congestive heart failure. We have developed proprietary, potent and selective non-steroidal MR antagonists that are highly effective in animal models of hypertension and congestive heart failure. They also provide protection for the vasculature. Our lead compounds, including XL550, have shown excellent oral bioavailability and drug metabolism and pharmacokinetics properties. The compounds have exhibited a significantly better pharmacokinetic and pharmacodynamic profile than existing steroid drugs. We believe that these novel proprietary non-steroidal MR antagonists have the potential to offer highly effective and safe therapeutic approaches for the treatment of hypertension. In addition, we believe that these drug candidates should be effective in the treatment of congestive heart failure and for protecting the vasculature during chronic inflammatory insult. In March 2006, we entered into a collaboration agreement with Sankyo Company, a wholly-owned subsidiary of Daiichi Sankyo Company Limited (Sankyo), pursuant to which we granted Sankyo an exclusive, worldwide license with respect to certain intellectual property primarily relating to compounds that modulate MR. After completion of the research term, Sankyo will be responsible for all further preclinical and clinical development, regulatory, manufacturing and commercialization activities for the compounds.

XL335 targets the Farnesoid X Receptor (FXR), a nuclear hormone receptor that has been shown to function as a bile acid receptor regulating genes involved in lipid, cholesterol and bile acid homeostasis. We have identified proprietary, potent and selective FXR ligands (a compound that binds to a receptor) that have good oral bioavailability and drug metabolism and pharmacokinetic properties. In rodent models of dyslipidemia, these compounds lowered triglycerides by decreasing triglyceride synthesis and secretion. In addition, they improved the high-density lipoprotein (HDL)/low-density lipoprotein (LDL) ratio and are anti-atherogenic (preventing the formation of lipid deposits in the arteries) in animal models of atherosclerosis. XL335 is also effective in models of cholestasis (a condition in which bile excretion from the liver is blocked), cholesterol gallstones and liver fibrosis. These data suggest that small molecule ligands targeting FXR should function as novel therapeutic agents for treating symptoms and disease states associated with metabolic syndrome as well as certain liver disorders. In December 2005, we licensed the FXR program to Wyeth Pharmaceuticals, a

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division of Wyeth. Wyeth will be responsible for all further preclinical and clinical development, regulatory, manufacturing and commercialization activities for the compounds.

EXEL2255 targets the Liver X Receptor (LXR), a nuclear hormone receptor that regulates cellular cholesterol outflow from the macrophage (an immune cell) to the blood and ultimately to the liver where cholesterol is removed from the body. This process is known as reverse cholesterol transport. Using our drug discovery platform, we have identified potent, proprietary and highly selective LXR ligands that have shown excellent drug metabolism and pharmacokinetic properties including good oral bioavailability. The lead compounds that are part of this program, including EXEL2255, have been highly efficacious in rodent models of atherosclerosis (a condition that involves the thickening and hardening of artery walls which leads to interference with blood flow). These data suggest that LXR is a novel molecular target that provides the opportunity for discovering first-in-class small molecule therapeutics that prevent and induce regression of atherosclerosis. In December 2005, we entered into a collaboration with Bristol-Myers Squibb to discover, develop and commercialize compounds targeting LXR. Exelixis and Bristol-Myers Squibb will jointly identify drug candidates that are ready for IND-enabling studies. Bristol-Myers Squibb will undertake further preclinical development and will be responsible for clinical development, regulatory, manufacturing and sales/marketing activities for such compounds.

Corporate Collaborations

We have established collaborations with major pharmaceutical and biotechnology companies based on the strength of our technologies and biological expertise to support additional development of our proprietary products. Through these collaborations, we obtain license fees, research funding, and the opportunity to receive milestone payments and royalties from research results and subsequent product development activities. Many of our collaborations have been structured strategically to provide us with access to technology that may help to advance our internal programs while at the same time enabling us to retain rights to use these technologies in different industries. We have also established collaborations with leading companies in the agrochemical industries that allow us to continue expanding our internal development capabilities while providing our partners with novel targets and assays. We expect to continue to execute collaboration agreements that provide funding along with development and commercial infrastructure.

Pharmaceutical Collaborations

GlaxoSmithKline

In October 2002, we entered into a broad development and commercialization collaboration with SmithKlineBeecham Corporation, which does business as GlaxoSmithKline, to discover and develop small molecule drugs in the areas of cancer, vascular biology and inflammatory disease. The collaboration involved three agreements: (i) a Product Development and Commercialization Agreement (PDA); (ii) a Stock Purchase and Stock Issuance Agreement (SPA); and (iii) a Loan and Security Agreement (LSA). Under the original PDA, GlaxoSmithKline paid us $30.0 million in an upfront fee and agreed to pay $90.0 million in research and development funding over the first six years of the collaboration.

In January 2005, we amended the terms of our collaboration with GlaxoSmithKline. Under the amended PDA, GlaxoSmithKline selected a modified program election which shifted the focus of the collaboration to 12 internal programs at various stages of development (XL784, XL647, XL999, XL880, XL184, XL820, XL844, XL281, XL418, XL228 and two earlier stage oncology programs). Each program centers on compounds that are directed against one or more targets identified in the collaboration. GlaxoSmithKline has the right to select from these programs up to two compounds at clinical proof-of-concept or three compounds if GlaxoSmithKline extends the collaboration. If

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GlaxoSmithKline selects three compounds, we could receive substantial acceptance milestones. The actual amount of acceptance milestones that we receive from GlaxoSmithKline will depend on the number of compounds selected and the timing of the selection of the compounds. Delays in obtaining clinical proof-of-concept for compounds subject to GlaxoSmithKline s election rights may decrease the size of any GlaxoSmithKline milestones and negatively impact our financial position. Prior to the end of a specified development term, GlaxoSmithKline retains exclusivity rights to the 32 specified targets that are encompassed by the 12 programs.

In May 2005, we filed the third of three INDs required by the amended PDA to achieve a $30.0 million milestone, which we received from GlaxoSmithKline in May 2005. In May 2005, we also submitted two new development candidates to GlaxoSmithKline, thereby triggering an additional $5.0 million milestone payment, which we received in May 2005. Under the original PDA, GlaxoSmithKline would have paid the first milestone upon its selection of a compound that had completed proof-of-concept for further development. We may also receive additional development related milestones and royalties on product sales and have certain co-promotion rights to products in North America. In addition, under the amended PDA, GlaxoSmithKline agreed to provide research funding of $47.5 million over the remaining three-year term of the collaboration, of which we received $12.5 million in 2005. To date, we have received $65.0 million in upfront and milestone payments, $50.0 million in research and development funding, and loans in the principal amount of $85.0 million. We may receive additional development-related milestones and GlaxoSmithKline has agreed to provide additional research funding over the remaining term of the collaboration as well as double digit royalties on product sales and co-promotion rights to products in North America.

Pursuant to the terms of the original SPA and as a result of its modified program election, GlaxoSmithKline purchased an additional 1.0 million shares of our common stock in January 2005 at an aggregate purchase price of $11.1 million, of which $2.2 million was a premium to the then fair value of the shares. We have no further option to sell, and GlaxoSmithKline has no further obligation to purchase, additional shares of our common stock.

Bristol-Myers Squibb

In July 2001, we entered into a collaboration with Bristol-Myers Squibb involving three agreements: (a) a Stock Purchase Agreement; (b) a Cancer Collaboration Agreement; and (c) a License Agreement. Under the terms of the collaboration, Bristol-Myers Squibb: (i) purchased 600,600 shares of Exelixis common stock in a private placement at a purchase price of $33.30 per share, for cash proceeds to Exelixis of $20.0 million; (ii) agreed to pay Exelixis a $5.0 million upfront license fee and provide Exelixis with $3.0 million per year in research funding for a minimum of three years; and (iii) granted to Exelixis a worldwide, fully-paid, exclusive license to becatecarin (XL119) developed by Bristol-Myers Squibb, which is currently in a Phase 3 clinical trial as a potential treatment for bile duct tumors. In January 2005, we granted Helsinn Healthcare an exclusive worldwide royalty-bearing license to XL119.

In December 2003, the cancer collaboration was extended until January 2007, with the right for Bristol-Myers Squibb to continue the collaboration until July 2009. The goal of the extension is to increase the total number and degree of validation of cancer targets that we will deliver to Bristol-Myers Squibb. Each company maintains the option to obtain exclusive worldwide rights to equal numbers of validated targets arising from the collaboration. Under the terms of the extended collaboration, Bristol-Myers Squibb provided us with an upfront payment and will provide increased annual research funding and milestones on certain cancer targets arising from the collaboration that progress through specified stages of validation. We will also be entitled to receive milestones on compounds in the event of successful clinical and regulatory events and royalties on commercialized products.

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In December 2005, we entered into a collaboration agreement with Bristol-Myers Squibb for the discovery, development and commercialization of novel therapies targeted against LXR. This agreement became effective in January 2006, at which time we granted Bristol-Myers Squibb an exclusive, worldwide license with respect to certain intellectual property primarily relating to compounds that modulate LXR. During the research term, we and Bristol-Myers Squibb expect to jointly identify drug candidates that are ready for IND-enabling studies. After the selection of a drug candidate for further clinical development by Bristol-Myers Squibb, Bristol-Myers Squibb has agreed to be solely responsible for further preclinical development as well as clinical development, regulatory, manufacturing and sales/marketing activities for the selected drug candidate.

Under the LXR collaboration agreement, Bristol-Myers Squibb paid us a nonrefundable upfront payment in the amount of $17.5 million and is obligated to provide research and development funding of $10.0 million per year for an initial research period of two years. Bristol-Myers Squibb has the option to extend the research period for an additional one-year term. Under the agreement, Bristol-Myers Squibb is required to pay us development and regulatory milestones of up to $140.0 million per product for up to two products from the collaboration. In addition, we are also entitled to receive sales milestones and royalties on sales of any products commercialized under the collaboration. Subject to certain terms and conditions, Bristol-Myers Squibb has the option to terminate the collaboration agreement starting in January 2008.

Genentech

In May 2005, Exelixis and Genentech established a collaboration to discover and develop therapeutics for the treatment of cancer, inflammatory diseases, and tissue growth and repair. Under the terms of the agreement, we granted to Genentech a license to certain intellectual property. Genentech paid us a nonrefundable upfront license payment and is obligated to provide research and development funding over the three-year research term, totaling $16.0 million.

Under the agreement, Genentech will have primary responsibility in the field of cancer for research and development activities as well as rights for commercialization of any products. In the fields of inflammatory disease and tissue growth and repair, we will initially have primary responsibility for research activities and after the expiration of the research term, we will have the option to elect to share a portion of the costs and profits associated with the development, manufacturing and commercialization of products. The research term under the agreement is three years and may be extended upon mutual consent for one-year terms. For all products under the agreement that are not elected as cost/profit share products, we may receive milestone and royalty payments.

Wyeth Pharmaceuticals

In December 2005, Exelixis and Wyeth entered into a license agreement related to compounds targeting FXR. Under the terms of the agreement, we granted to Wyeth an exclusive, worldwide license with respect to certain intellectual property primarily relating to compounds that modulate FXR. Wyeth paid us a nonrefundable upfront payment of $10.0 million and is obligated to pay additional development and commercialization milestones of up to $147.5 million, as well as royalties on sales of any products commercialized by Wyeth under the agreement. Wyeth will be responsible for all further preclinical and clinical development, regulatory, manufacturing and commercialization activities for the compounds. Subject to certain terms and conditions, Wyeth has the option to terminate the license agreement starting in December 2006.

Sankyo Company

In March 2006, Exelixis and Sankyo entered into a collaboration agreement for the discovery, development and commercialization of novel therapies targeted against the mineralocorticoid receptor (MR), a nuclear hormone receptor implicated in a variety of cardiovascular and metabolic diseases.

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Under the terms of the agreement, we granted to Sankyo an exclusive, worldwide license to certain intellectual property primarily relating to compounds that modulate MR. After completion of the research term, Sankyo will be responsible for all further preclinical and clinical development, regulatory, manufacturing and commercialization activities for the compounds.

Sankyo paid us an upfront payment of $20.0 million and is obligated to provide research and development funding of $3.8 million over a 15-month research term. For each product from the collaboration, we are also entitled to receive payments upon attainment of pre-specified development, regulatory and commercialization milestones. In addition, we are entitled to receive double-digit royalties on any sales of certain products commercialized under the collaboration. Sankyo may terminate the agreement upon 90 days written notice in which case Sankyo s payment obligations will cease, its license relating to compounds that modulate MR will terminate and revert to us and we will receive, subject to certain terms and conditions, licenses from Sankyo to research, develop and commercialize compounds that were discovered under the agreement.

Helsinn Healthcare

In June 2005, Exelixis and Helsinn entered into a license agreement for the development and commercialization of XL119 (becatecarin). Under the terms of the agreement, we granted to Helsinn an exclusive worldwide, royalty bearing license to XL119. We have retained an option to reacquire the commercial rights to XL119 for North America. If we decide to exercise the option, we have the right to negotiate with Helsinn to reach an agreement on commercially reasonable terms and conditions to reacquire the commercial rights to XL119 for North America for use in the indications of gall bladder cancer and bile duct tumors. Helsinn paid us a nonrefundable upfront payment in the amount of $4.0 million and was obligated to pay additional development and commercialization milestones of up to $21.0 million, as well as royalties on worldwide sales. Helsinn also assumed all future costs incurred for the ongoing multi-national Phase 3 clinical trial for XL119. In January 2006, the IND and management of the Phase 3 clinical trial was transferred to Helsinn, which going forward is responsible for the costs and management of the trial. On June 2, 2006, we received a $4.0 million milestone payment from Helsinn for the successful delivery of certain clinical trial materials. Under our license agreement with Helsinn, we may receive further development and commercialization milestones of up to $17.0 million.

Beginning in June 2006, if Helsinn determines, based on reasonable business judgment from scientific or economic evidence, that it is unable to carry out further development or marketing of XL119, it may terminate the license agreement upon six months prior written notice.

Symphony Evolution

On June 9, 2005 we closed a transaction involving a series of related agreements providing for the financing of the clinical development of XL999, XL784 and XL647. Pursuant to the agreements, SEI and its investors have invested $80.0 million to fund the clinical development of our product candidates XL999, XL784 and XL647 and we have licensed to SEI our intellectual property rights related to these product candidates. SEI is a wholly-owned subsidiary of Symphony Evolution Holdings LLC (Holdings), which provided $40.0 million in funding to SEI on June 9, 2005 and which provided an additional $40.0 million in funding to SEI on June 9, 2006. We continue to be primarily responsible for the development of XL999, XL784 and XL647 in accordance with a specified development plan and related development budget. We have determined that SEI is a variable interest entity of which we are the primary beneficiary and, accordingly, we include the financial condition and results of operations of SEI in our consolidated financial statements.

Pursuant to the agreements, we have received an exclusive purchase option that gives us the right to acquire all of the equity of SEI, thereby allowing us to reacquire all of the product candidates. This purchase option is exercisable at any time until June 9, 2009 (subject to an earlier exercise right

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in limited circumstances) at a price equal to the sum of: (i) the total amount of capital invested in SEI by Holdings and (ii) an amount equal to 25% per year on such funded capital (with respect to the initial funded capital, compounded from the closing date and, with respect to the second draw amount, compounded from the second draw date) subject to adjustment based on the cash and liabilities of SEI as of the closing of the purchase option. The purchase price will be subject to a premium if we exercise the purchase option before December 11, 2006. The purchase option exercise price may be paid for in cash or in a combination of cash and our common stock, in our sole discretion, provided that the common stock portion may not exceed 33% of the purchase option exercise price. If we pay a portion of the purchase option exercise price in shares, then we will be required to register such shares for resale under a resale registration statement pursuant to the terms of a registration rights agreement.

We have also received an exclusive program option from SEI that allows us under certain conditions to separately reacquire from SEI one of the three programs during a period ending on December 9, 2006. The program option is exercisable in our sole discretion at a premium exercise price, which is payable in cash only and will be fully creditable against the exercise price for any subsequent exercise of the purchase option.

Pursuant to the agreements, on June 9, 2005, we issued to Holdings a five-year warrant to purchase 750,000 shares of our common stock at $8.90 per share. On June 9, 2006, in connection with a second capital draw of $40.0 million by SEI, we issued to Holdings an additional five-year warrant to purchase 750,000 shares of our common stock at $8.90 per share. In addition, if the purchase option expires unexercised at June 9, 2009 or the 90th day after SEI provides us with financial statements showing cash and cash equivalents of less than $5.0 million, we are obligated to issue to Holdings an additional five-year warrant to purchase 500,000 shares of our common stock at a price per share equal to 125% of the market price of our common stock at the time of expiration of the purchase option.

The product candidates licensed to SEI are subject to our collaboration with GlaxoSmithKline, and GlaxoSmithKline may continue to select at proof-of-concept for further development one or more of program candidates in which case we would need to repurchase the selected candidate or candidates through the exercise of our purchase option or program option. Under the terms of the amended PDA, GlaxoSmithKline has agreed to increase the acceptance milestones for the program candidates that are funded through SEI to compensate us for the cost of capital associated with these funding arrangements.

Manufacturing and Raw Materials

We currently do not have manufacturing capabilities necessary to enable us to produce materials for our clinical trials. Raw materials and supplies required for the production of our product candidates are generally available from multiple suppliers. However, in some instances materials are available only from one supplier. In those cases where raw materials are only available through one supplier, we manage supplies, to the extent feasible, by ordering raw materials well in advance of scheduled needs. However, clinical trial schedules may be delayed due to interruptions of raw material supplies.

Government Regulation

The following section contains some general background information regarding the regulatory environment and processes affecting our industry and is designed to illustrate in general terms the nature of our business and the potential impact of government regulations on our business. It is not intended to be comprehensive or complete. Depending on specific circumstances, the information below may or may not apply to us or any of our product candidates. In addition, the information is not necessarily a

description of activities that we have undertaken in the past or will undertake in the future. The regulatory context in which we operate is complex and constantly changing.

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The FDA and comparable regulatory agencies in state and local jurisdictions and in foreign countries impose substantial requirements upon the clinical development, manufacture and marketing of pharmaceutical products. These agencies and other federal, state and local entities regulate research and development activities and the testing, manufacture, quality control, safety, effectiveness, labeling, storage, record keeping, approval, advertising and promotion of our products.

The process required by the FDA before product candidates may be marketed in the United States generally involves the following:

- preclinical laboratory and animal tests;
- submission of an IND, which must become effective before clinical trials may begin;
- adequate and well-controlled human clinical trials to establish the safety and efficacy of the proposed drug candidate for its intended use;
- pre-approval inspection of manufacturing facilities and selected clinical investigators; and
- FDA approval of a New Drug Application (NDA), or NDA supplement, for an approval of a new indication if the product is already approved for another indication.

The testing and approval process requires substantial time, effort and financial resources.

Prior to commencing the first clinical trial with a product candidate, we must submit an IND to the FDA. The IND automatically becomes effective 30 days after receipt by the FDA, unless the FDA, within the 30-day time period, raises concerns or questions about the conduct of the clinical trial. In such a case, the IND sponsor and the FDA must resolve any outstanding concerns before the clinical trial can begin. Our submission of an IND may not result in FDA authorization to commence a clinical trial. A separate submission to the existing IND must be made for each successive clinical trial conducted during product development, and the FDA must grant permission for each clinical trial to start and continue. Further, an independent institutional review board for each medical center proposing to conduct the clinical trial must review and approve the plan for any clinical trial before it commences at that center. Regulatory authorities or an institutional review board or the sponsor may suspend a clinical trial at any time on various grounds, including a finding that the subjects or patients are being exposed to an unacceptable health risk.

For purposes of NDA approval, human clinical trials are typically conducted in three sequential phases that may overlap.

- Phase 1 Studies are initially conducted in a limited patient population to test the product candidate for safety, dosage tolerance, absorption, metabolism, distribution and excretion in healthy humans or patients.
- Phase 2 Studies are conducted with groups of patients afflicted with a specified disease in order to provide enough data to evaluate the preliminary efficacy, optimal dosages and expanded evidence of safety. Multiple Phase 2 clinical trials may be conducted by the sponsor to obtain information prior to beginning larger and more expensive Phase 3 clinical trials. In

some cases, a sponsor may decide to run what is referred to as a Phase 2b evaluation, which is a second, confirmatory Phase 2 trial that could, if positive, serve as a pivotal trial in the approval of a product candidate.

Phase 3 When Phase 2 evaluations demonstrate that a dosage range of the product is effective and has an acceptable safety profile, Phase 3 trials are undertaken in large patient populations to further evaluate dosage, to provide statistically significant evidence of clinical efficacy and to further test for safety in an expanded patient population at multiple clinical trial sites.

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The FDA may require, or companies may pursue, additional clinical trials after a product is approved. These so-called Phase 4 studies may be made a condition to be satisfied after a drug receives approval. The results of Phase 4 studies can confirm the effectiveness of a product candidate and can provide important safety information to augment the FDA s voluntary adverse drug reaction reporting system.

The results of product development, preclinical studies and clinical trials are submitted to the FDA as part of an NDA, or as part of an NDA supplement. The FDA may deny approval of an NDA or NDA supplement if the applicable regulatory criteria are not satisfied, or it may require additional clinical data and/or an additional pivotal Phase 3 clinical trial. Even if such data are submitted, the FDA may ultimately decide that the NDA or NDA supplement does not satisfy the criteria for approval. Once issued, the FDA may withdraw product approval if ongoing regulatory standards are not met or if safety problems occur after the product reaches the market. In addition, the FDA may require testing and surveillance programs to monitor the effect of approved products which have been commercialized, and the FDA has the power to prevent or limit further marketing of a product based on the results of these post-marketing programs.

Satisfaction of FDA requirements or similar requirements of state, local and foreign regulatory agencies typically takes several years and the actual time required may vary substantially based upon the type, complexity and novelty of the product or disease. Government regulation may delay or prevent marketing of product candidates or new diseases for a considerable period of time and impose costly procedures upon our activities. The FDA or any other regulatory agency may not grant approvals for new indications for our product candidates on a timely basis, if at all. Success in early stage clinical trials does not ensure success in later stage clinical trials. Data obtained from clinical activities is not always conclusive and may be susceptible to varying interpretations, which could delay, limit or prevent regulatory approval. Even if a product candidate receives regulatory approval, the approval may be significantly limited to specific disease states, patient populations and dosages. Further, even after regulatory approval is obtained, later discovery of previously unknown problems with a product may result in restrictions on the product or even complete withdrawal of the product from the market.

Any products manufactured or distributed by us pursuant to FDA approvals are subject to continuing regulation by the FDA, including record-keeping requirements and reporting of adverse experiences with the drug. Drug manufacturers and their subcontractors are required to register their establishments with the FDA and certain state agencies, and are subject to periodic unannounced inspections by the FDA and certain state agencies for compliance with good manufacturing practices, which impose certain procedural and documentation requirements upon us and our third-party manufacturers. We cannot be certain that we or our present or future suppliers will be able to comply with the good manufacturing practices regulations and other FDA regulatory requirements. If our present or future suppliers are not able to comply with these requirements, the FDA may halt our clinical trials, require us to recall a drug from distribution, or withdraw approval of the NDA for that drug.

The FDA closely regulates the marketing and promotion of drugs. A company can make only those claims relating to safety and efficacy that are approved by the FDA. Failure to comply with these requirements can result in adverse publicity, warning letters, corrective advertising and potential civil and criminal penalties. Physicians may prescribe legally available drugs for uses that are not described in the product s labeling and that differ from those tested by us and approved by the FDA. Such off-label uses are common across medical specialties. Physicians may believe that such off-label uses are the best treatment for many patients in varied circumstances. The FDA does not regulate the behavior of physicians in their choice of treatments. The FDA does, however, restrict manufacturer s communications on the subject of off-label use.

The FDA s policies may change and additional government regulations may be enacted which could prevent or delay regulatory approval of our product candidates or approval of new diseases for

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our product candidates. We cannot predict the likelihood, nature or extent of adverse governmental regulation that might arise from future legislative or administrative action, either in the United States or abroad.

Competition

There are many companies focused on the development of small molecules and antibodies for diseases including cancer and metabolic and cardiovascular disorders. Our potential competitors include major pharmaceutical and biotechnology companies as well as agricultural companies. Many of our potential competitors have significantly more financial, technical and other resources than we do, which may allow them to have a competitive advantage. Any products that we may develop or discover are likely to be in highly competitive markets. Many of our competitors may succeed in developing products that may render our products and those of our collaborators obsolete or noncompetitive.

We believe that our ability to successfully compete will depend on, among other things:

- efficacy, safety and reliability of our product candidates;
- timing and scope of regulatory approval;
- the speed at which we develop product candidates;
- our ability to complete preclinical testing and clinical development and obtaining regulatory approvals for product candidates;
- our ability to manufacture and sell commercial quantities of a product to the market;
- obtaining reimbursement for product use in approved indications;
- product acceptance by physicians and other health care providers;
- quality and breadth of our technology;
- skills of our employees and our ability to recruit and retain skilled employees;
- protection of our intellectual property; and
- availability of substantial capital resources to fund development and commercialization activities.

Research and Development Expenses

Research and development expenses consist primarily of personnel expenses, laboratory supplies, consulting and facilities costs. Research and development expenses were $87.3 million for the six months ended June 30, 2006 compared to $69.9 million for the six months ended June 30, 2005 and were $141.1 million for the year ended December 31, 2005, compared to $137.7 million for 2004 and $127.6 million for 2003.

Revenues from Significant Collaborators

In 2005, we derived 37% and 32% of our revenues from GlaxoSmithKline and Genoptera, respectively. While we expect to continue to derive the largest portion of our revenues from GlaxoSmithKline in future periods, we will not receive any further revenues from Genoptera after 2005 due to the termination of this collaboration in 2005.

Proprietary Rights

We have obtained licenses from various parties that give us rights to technologies that we deem to be necessary or desirable for our research and development. These licenses (both exclusive and non-exclusive) may require us to pay royalties as well as upfront and milestone payments.

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Patents extend for varying periods according to the date of patent filing or grant and the legal term of patents in the various countries where patent protection is obtained. The actual protection afforded by a patent, which can vary from country to country, depends on the type of patent, the scope of its coverage and the availability of legal remedies in the country.

While trade secret protection is an essential element of our business and we have taken security measures to protect our proprietary information and trade secrets, we cannot give assurance that our unpatented proprietary technology will afford us significant commercial protection. We seek to protect our trade secrets by entering into confidentiality agreements with third parties, employees and consultants. Our employees and consultants are also required to sign agreements obligating them to assign to us their interests in intellectual property arising from their work for us. All employees sign an agreement not to engage in any conflicting employment or activity during their employment with us and not to disclose or misuse our confidential information. However, it is possible that these agreements may be breached or invalidated, and if so, there may not be an adequate corrective remedy available. Accordingly, we cannot ensure that employees, consultants or third parties will not breach the confidentiality provisions in our contracts, infringe or misappropriate our trade secrets and other proprietary rights or that measures we are taking to protect our proprietary rights will be adequate.

In the future, third parties may file claims asserting that our technologies or products infringe on their intellectual property. We cannot predict whether third parties will assert such claims against us or against the licensors of technology licensed to us, or whether those claims will harm our business. If we are forced to defend ourselves against such claims, whether they are with or without merit and whether they are resolved in favor of, or against, our licensors or us, we may face costly litigation and the diversion of management s attention and resources. As a result of such disputes, we may have to develop costly non-infringing technology or enter into licensing agreements. These agreements, if necessary, may be unavailable on terms acceptable to us, or at all.

Employees

As of June 30, 2006 we had 599 full-time employees worldwide, 191 of whom hold Ph.D. and/or M.D. degrees, most of whom were engaged in full-time research and development activities. We plan to hire additional staff and to expand our internal development efforts. Our success will depend upon our ability to attract and retain qualified employees. We face competition in this regard from other companies in the biotechnology, pharmaceutical and high technology industries, as well as research and academic institutions. None of our employees are represented by a labor union, and we consider our employee relations to be good.

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UNDERWRITING

The company and the underwriters named below have entered into an underwriting agreement with respect to the shares being offered. Subject to certain conditions, each underwriter has severally agreed to purchase the number of shares indicated in the following table. Goldman, Sachs & Co., Cowen and Company, LLC, Banc of America Securities LLC and Piper Jaffray & Co. are the representatives of the underwriters.

Underwriters	Number of Shares
Goldman, Sachs & Co.	
Cowen and Company, LLC	
Banc of America Securities LLC	
Piper Jaffray & Co.	
Total	9,000,000

The underwriters are committed to take and pay for all of the shares being offered, if any are taken, other than the shares covered by the option described below unless and until this option is exercised.

If the underwriters sell more shares than the total number set forth in the table above, the underwriters have an option to buy up to an additional 1,350,000 shares from the company to cover such sales. They may exercise that option for a period of 30 days after the date of the underwriting agreement. If any shares are purchased pursuant to this option, the underwriters will severally purchase shares in approximately the same proportion as set forth in the table above.

The following table shows the per share and total underwriting discount to be paid to the underwriters by the company. Such amounts are shown assuming both no exercise and full exercise of the underwriters option to purchase 1,350,000 additional shares.

Paid by Exelixis	No Exercise	Full Exercise
Per share	$	$
Total	$	$

Shares sold by the underwriters to the public will initially be offered at the initial public offering price set forth on the cover of this prospectus supplement. Any shares sold by the underwriters to securities dealers may be sold at a discount of up to $ per share from the initial public offering price. If all the shares are not sold at the initial public offering price, the representatives may change the offering price and the other selling terms.

Exelixis and certain of its directors and executive officers have agreed not to dispose of or hedge any shares of the common stock or any securities convertible into or exchangeable for shares of the common stock during the period ending 90 days after the date of this prospectus supplement, subject to certain permitted exceptions, except with the prior written consent of Goldman, Sachs & Co. However, these agreements do not prohibit any sales pursuant to a Rule 10b5-1 sales plan of Exelixis chief executive officer (provided that no more than 2,500 shares may be sold each week under such plan during the 90-day lock-up period), any sales pursuant to a Rule 10b5-1 sales plan of one of Exelixis directors, Charles Cohen (provided that no more than 10,000 shares may be sold each month under such plan during the 90-day lock-up period), the issuance of shares of common stock or any securities convertible into or exchangeable for shares of common stock by Exelixis pursuant to its existing equity incentive plans or 401(k) plan, or the issuance by Exelixis following the date 45 days after the date of this prospectus supplement of shares of common stock or any securities convertible into or exchangeable for shares of common stock in an amount up to an aggregate of 10% of Exelixis outstanding shares of common

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stock after giving effect to this offering if such shares are issued for cash in connection with a strategic transaction that includes a commercial relationship involving Exelixis; provided that in the case of any issuances in connection with a strategic transaction, the recipients of these shares agree to be bound by the 90 day lock-up agreement described above. Goldman, Sachs & Co., in its sole discretion, may release any of the securities subject to these lock-up agreements at any time without notice.

In connection with the offering, the underwriters may purchase and sell shares of common stock in the open market. These transactions may include short sales, stabilizing transactions and purchases to cover positions created by short sales. Short sales involve the sale by the underwriters of a greater number of shares than they are required to purchase in the offering. Covered short sales are sales made in an amount not greater than the underwriters option to purchase additional shares from the company in the offering. The underwriters may close out any covered short position by either exercising their option to purchase additional shares or purchasing shares in the open market. In determining the source of shares to close out the covered short position, the underwriters will consider, among other things, the price of shares available for purchase in the open market as compared to the price at which they may purchase additional shares pursuant to the option granted to them. Naked short sales are any sales in excess of such option. The underwriters must close out any naked short position by purchasing shares in the open market. A naked short position is more likely to be created if the underwriters are concerned that there may be downward pressure on the price of the common stock in the open market after pricing that could adversely affect investors who purchase in the offering. Stabilizing transactions consist of various bids for or purchases of common stock made by the underwriters in the open market prior to the completion of the offering.

The underwriters may also impose a penalty bid. This occurs when a particular underwriter repays to the underwriters a portion of the underwriting discount received by it because the representatives have repurchased shares sold by or for the account of such underwriter in stabilizing or short-covering transactions.

Purchases to cover a short position and stabilizing transactions, as well as other purchases by the underwriters for their own accounts, may have the effect of preventing or retarding a decline in the market price of the company s stock, and together with the imposition of the penalty bid, may stabilize, maintain or otherwise affect the market price of the common stock. As a result, the price of the common stock may be higher than the price that otherwise might exist in the open market. If these activities are commenced, they may be discontinued at any time. These transactions may be effected on NASDAQ, in the over-the-counter market or otherwise.

Each of the underwriters has represented and agreed that:

(a) it has not made or will not make an offer of shares to the public in the United Kingdom within the meaning of section 102B of the Financial Services and Markets Act 2000 (as amended) (FSMA) except to legal entities which are authorized or regulated to operate in the financial markets or, if not so authorized or regulated, whose corporate purpose is solely to invest in securities or otherwise in circumstances which do not require the publication by the company of a prospectus pursuant to the Prospectus Rules of the Financial Services Authority (FSA);

(b) it has only communicated or caused to be communicated and will only communicate or cause to be communicated an invitation or inducement to engage in investment activity (within the meaning of section 21 of FSMA) to persons who have professional experience in matters relating to investments falling within Article 19(5) of the Financial Services and Markets Act 2000 (Financial Promotion) Order 2005 or in circumstances in which section 21 of FSMA does not apply to the company; and

(c) it has complied with, and will comply with all applicable provisions of FSMA with respect to anything done by it in relation to the shares in, from or otherwise involving the United Kingdom.

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In relation to each Member State of the European Economic Area which has implemented the Prospectus Directive (each, a Relevant Member State), each underwriter has represented and agreed that with effect from and including the date on which the Prospectus Directive is implemented in that Relevant Member State (the Relevant Implementation Date) it has not made and will not make an offer of shares to the public in that Relevant Member State prior to the publication of a prospectus in relation to the shares which has been approved by the competent authority in that Relevant Member State or, where appropriate, approved in another Relevant Member State and notified to the competent authority in that Relevant Member State, all in accordance with the Prospectus Directive, except that it may, with effect from and including the Relevant Implementation Date, make an offer of shares to the public in that Relevant Member State at any time:

(a) to legal entities which are authorized or regulated to operate in the financial markets or, if not so authorized or regulated, whose corporate purpose is solely to invest in securities;

(b) to any legal entity which has two or more of (1) an average of at least 250 employees during the last financial year; (2) a total balance sheet of more than €43,000,000 and (3) an annual net turnover of more than €50,000,000, as shown in its last annual or consolidated accounts; or

(c) in any other circumstances which do not require the publication by the company of a prospectus pursuant to Article 3 of the Prospectus Directive.

For the purposes of this provision, the expression an offer of shares to the public in relation to any shares in any Relevant Member State means the communication in any form and by any means of sufficient information on the terms of the offer and the shares to be offered so as to enable an investor to decide to purchase or subscribe the shares, as the same may be varied in that Relevant Member State by any measure implementing the Prospectus Directive in that Relevant Member State and the expression Prospectus Directive means Directive 2003/71/EC and includes any relevant implementing measure in each Relevant Member State.

The shares may not be offered or sold by means of any document other than (i) in circumstances which do not constitute an offer to the public within the meaning of the Companies Ordinance (Cap. 32, Laws of Hong Kong), (ii) to professional investors within the meaning of the Securities and Futures Ordinance (Cap. 571, Laws of Hong Kong) and any rules made thereunder, or (iii) in other circumstances which do not result in the documents being a prospectus within the meaning of the Companies Ordinance (Cap. 32, Laws of Hong Kong), and no advertisement, invitation or document relating to the shares may be issued or may be in the possession of any person for the purpose of issue (in each case whether in Hong Kong or elsewhere), which is directed at, or the contents of which are likely to be accessed or read by, the public in Hong Kong (except if permitted to do so under the Laws of Hong Kong) other than with respect to shares which are intended to be disposed of only to persons outside Hong Kong or only to professional investors within the meaning of the Securities and Futures Ordinance (Cap. 571, Laws of Hong Kong) and any rules made thereunder.

This prospectus supplement has not been registered as a prospectus with the Monetary Authority of Singapore. Accordingly, this prospectus supplement and any other document or material in connection with the offer or sale, or invitation for subscription or purchase, of the shares may not be circulated or distributed, nor may the shares be offered or sold, or be made the subject of an invitation for subscription or purchase, whether directly or indirectly, to persons in Singapore other than (i) to an institutional investor under Section 274 of the Securities and Futures Act, Chapter 289 of Singapore (the SFA), (ii) to a relevant person, or any person pursuant to Section 275(1A), and in accordance with the conditions, specified in Section 275 of the SFA or (iii) otherwise pursuant to, and in accordance with the conditions of, any other applicable provision of the SFA.

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Where the shares are subscribed or purchased under Section 275 by a relevant person which is: (a) a corporation (which is not an accredited investor) the sole business of which is to hold investments and the entire share capital of which is owned by one or more individuals, each of whom is an accredited investor; or (b) a trust (where the trustee is not an accredited investor) whose sole purpose is to hold investments and each beneficiary is an accredited investor, shares, debentures and units of shares and debentures of that corporation or the beneficiaries rights and interest in that trust shall not be transferable for 6 months after that corporation or that trust has acquired the shares under Section 275 except: (1) to an institutional investor under Section 274 of the SFA or to a relevant person, or any person pursuant to Section 275(1A), and in accordance with the conditions, specified in Section 275 of the SFA; (2) where no consideration is given for the transfer; or (3) by operation of law.

The securities have not been and will not be registered under the Securities and Exchange Law of Japan (the Securities and Exchange Law) and each underwriter has agreed that it will not offer or sell any securities, directly or indirectly, in Japan or to, or for the benefit of, any resident of Japan (which term as used herein means any person resident in Japan, including any corporation or other entity organized under the laws of Japan), or to others for re-offering or resale, directly or indirectly, in Japan or to a resident of Japan, except pursuant to an exemption from the registration requirements of, and otherwise in compliance with, the Securities and Exchange Law and any other applicable laws, regulations and ministerial guidelines of Japan.

The company estimates that its share of the total expenses of the offering, excluding the underwriting discount, will be approximately $260,000.

The company has agreed to indemnify the several underwriters and their controlling persons against certain liabilities, including liabilities under the Securities Act of 1933.

Certain of the underwriters and their respective affiliates have, from time to time, performed, and may in the future perform, various financial advisory and investment banking services for the company, for which they received or will receive customary fees and expenses.

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VALIDITY OF COMMON STOCK

The validity of the common stock offered hereby will be passed upon for us by Cooley Godward LLP, Palo Alto, California, and for the underwriters by Sullivan & Cromwell LLP, Palo Alto, California.

EXPERTS

Ernst & Young LLP, an independent registered public accounting firm, has audited our consolidated financial statements included in our Annual Report on Form 10-K for the year ended December 31, 2005, and management s assessment of the effectiveness of our internal control over financial reporting as of December 31, 2005, as set forth in their reports, which are incorporated by reference in this prospectus supplement and accompanying prospectus and elsewhere in the registration statement of which the accompanying prospectus is a part. Our consolidated financial statements and management s assessment are incorporated by reference in reliance on Ernst & Young LLP s reports, given on their authority as experts in accounting and auditing.

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PROSPECTUS

EXELIXIS, INC.

$200,000,000

Common Stock

Preferred Stock

Debt Securities

Warrants

Units

From time to time, we may sell common stock, preferred stock, debt securities and/or warrants, either individually or in units. We may also offer common stock or preferred stock upon conversion of debt securities, common stock upon conversion of preferred stock or common stock, preferred stock or debt securities upon the exercise of warrants.

We will provide the specific terms of these securities in one or more supplements to this prospectus. You should read this prospectus and any prospectus supplement, as well as any documents incorporated by reference in this prospectus and any prospectus supplement, carefully before you invest.

Our common stock is traded on The Nasdaq National Market under the trading symbol EXEL. The applicable prospectus supplement will contain information, where applicable, as to any other listing (if any) on The Nasdaq National Market or any securities exchange of the securities covered by the prospectus supplement. On October 25, 2004, the last reported sale price of our common stock on The Nasdaq National Market was $8.56 per share.

THIS PROSPECTUS MAY NOT BE USED TO OFFER OR SELL ANY SECURITIES UNLESS ACCOMPANIED BY A PROSPECTUS SUPPLEMENT.

If any underwriters are involved in the sale of any securities with respect to which this prospectus is being delivered, the names of such underwriters and any applicable commissions or discounts will be set forth in a prospectus supplement. The net proceeds we expect to receive from such sale will also be set forth in a prospectus supplement.

NEITHER THE SECURITIES AND EXCHANGE COMMISSION NOR ANY STATE SECURITIES COMMISSION HAS APPROVED OR DISAPPROVED OF THESE SECURITIES OR DETERMINED IF THIS PROSPECTUS IS TRUTHFUL OR COMPLETE. ANY REPRESENTATION TO THE CONTRARY IS A CRIMINAL OFFENSE.

INVESTING IN OUR SECURITIES INVOLVES A HIGH DEGREE OF RISK. SEE THE SECTION ENTITLED RISK FACTORS ON PAGE 2 OF THIS PROSPECTUS.

The date of this prospectus is January 12, 2005

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EXELIXIS, INC.

Our primary mission is to develop proprietary human therapeutics by leveraging our integrated discovery platform to increase the speed, efficiency and quality of pharmaceutical product discovery and development. We have generated a substantial development pipeline of small molecule compounds that we believe are therapeutically differentiated and commercially valuable. The pipeline is led by XL119, our Phase 3 cancer compound, and includes XL784, XL647, XL999, XL880, XL820, XL844, XL184 and multiple compounds in preclinical development for diseases including cancer, lipid disorders, hyperlipidemia and congestive heart failure.

We have collaborations with several leading pharmaceutical, biotechnology and agrochemical companies based on the strength of our technologies and biological expertise in order to support the development of our proprietary product candidates. Through these collaborations, we obtain license fees and research funding, together with the opportunity to receive milestone payments and royalties from research results and subsequent product development. In addition, many of our collaborations have been structured strategically to provide us access to technology to more rapidly advance our internal programs.

We were incorporated in Delaware in November 1994 as Exelixis Pharmaceuticals, Inc. and we changed our name to Exelixis, Inc. in February 2000. Our principal executive offices are located at 170 Harbor Way, P.O. Box 511, South San Francisco, California 94083. Our telephone number is (650) 837-7000 and our website is http://www.exelixis.com. We have not incorporated by reference into this prospectus the information on our website, and you should not consider it to be a part of this document. Our website address is included in this document as an inactive textual reference only.

Exelixis, Inc., the Exelixis, Inc. logo, Artemis Pharmaceuticals, ACTTAG, Conditional and all other Exelixis product and service names are trademarks of Exelixis, Inc. in the United States and in other selected countries. All other brand names or trademarks appearing in this prospectus are the property of their respective holders.

ABOUT THIS PROSPECTUS

This prospectus is part of a registration statement that we filed with the Securities and Exchange Commission using a shelf registration process. Under this shelf registration process, we may sell common stock, preferred stock, debt securities and/or warrants, either individually or in units, in one or more offerings, up to a total dollar amount of $200 million. This prospectus provides you with a general description of the securities we may offer. Each time we sell common stock, preferred stock, debt securities and/or warrants, we will provide a prospectus supplement that will contain more specific information, as set forth below under The Securities We May Offer. We may also add, update or change in the prospectus supplement any of the information contained in this prospectus. However, no prospectus supplement shall fundamentally change the terms that are set forth in this prospectus or offer a security that is not registered and described in this prospectus at the time of its effectiveness. This prospectus, together with applicable prospectus supplements, includes all material information relating to this offering. Please carefully read both this prospectus and any prospectus supplement together with the additional information described below under Where You Can Find More Information.

You should rely only on the information we have provided or incorporated by reference in this prospectus or any prospectus supplement. We have not authorized anyone to provide you with information different from that contained in this prospectus. No dealer, salesperson or other person is authorized to give any information or to represent anything not contained in this prospectus. You must not rely on any unauthorized information or representation. This prospectus is an offer to sell only the securities offered hereby, but only under circumstances and in jurisdictions where it is lawful to do so. You should assume that the information in this prospectus or any prospectus supplement is accurate only

as of the date on the front of the document and that any information we have incorporated by reference is accurate only as of the date of the document incorporated by reference, regardless of the time of delivery of this prospectus or any sale of a security.

Unless otherwise mentioned or unless the context requires otherwise, all references in this prospectus to Exelixis, we, our or similar references mean Exelixis, Inc. together with its subsidiaries.

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RISK FACTORS

Investment in our securities involves a high degree of risk. You should consider carefully the risk factors in any prospectus supplements and in our most recent annual and quarterly filings with the Securities and Exchange Commission, as well as other information in this prospectus and any prospectus supplements and the documents incorporated by reference herein or therein, before purchasing any of our securities. Each of the risk factors could adversely affect our business, operating results and financial condition, as well as adversely affect the value of an investment in our securities.

THE SECURITIES WE MAY OFFER

We may offer shares of our common stock and preferred stock, various series of debt securities and/or warrants to purchase any of such securities, individually or in units, with a total value of up to $200 million, from time to time under this prospectus at prices and on terms to be determined by market conditions at the time of offering. This prospectus provides you with a general description of the securities we may offer. Each time we offer a type or series of securities, we will provide a prospectus supplement that will describe the specific amounts, prices and other important terms of the securities, including, to the extent applicable:

- designation or classification;
- aggregate principal amount or aggregate offering price;
- maturity, if applicable;
- rates and times of payment of interest or dividends, if any;
- redemption, conversion or sinking fund terms, if any;
- voting or other rights, if any;
- conversion prices, if any; and
- important federal income tax considerations.

The prospectus supplement also may add, update or change information contained in this prospectus or in documents we have incorporated by reference. However, no prospectus supplement shall fundamentally change the terms that are set forth in this prospectus or offer a security that is not registered and described in this prospectus at the time of its effectiveness.

This Prospectus May Not Be Used to Consummate a Sale of Securities Unless It Is Accompanied by a Prospectus Supplement.

We may sell the securities directly to or through agents, underwriters or dealers. We, and our agents or underwriters, reserve the right to accept or reject all or part of any proposed purchase of securities. If we offer securities through agents or underwriters, we will include in the applicable prospectus supplement:

the names of those agents or underwriters;

applicable fees, discounts and commissions to be paid to them; and

the net proceeds to us.

Common Stock. We may issue shares of our common stock from time to time. Holders of common stock are entitled to one vote per share on all matters submitted to a vote of stockholders. Subject to any preferences of outstanding shares of preferred stock, holders of common stock are entitled to dividends when and if declared by our board of directors.

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Preferred Stock. We may issue shares of our preferred stock from time to time, in one or more series. Our board of directors may determine the rights, preferences, privileges and restrictions of the preferred stock, including dividend rights, conversion rights, voting rights, terms of redemption, liquidation preferences, sinking fund terms and the number of shares constituting any series or the designation of any series. Convertible preferred stock will be convertible into our common stock. Conversion may be mandatory or at your option and would be at prescribed conversion rates.

Debt Securities. We may offer debt securities from time to time, in one or more series, as either senior or subordinated debt or as senior or subordinated convertible debt. The senior debt securities will rank equally with any other unsecured and unsubordinated debt. The subordinated debt securities will be subordinate and junior in right of payment, to the extent and in the manner described in the instrument governing the debt, to all of our senior indebtedness. Convertible debt securities will be convertible into or exchangeable for our common stock or other securities of ours. Conversion may be mandatory or at your option and would be at prescribed conversion rates.

The debt securities will be issued under one or more documents called indentures, which are contracts between us and a national banking association, as trustee. In this prospectus, we have summarized certain general features of the debt securities. We urge you, however, to read the prospectus supplements related to the series of debt securities being offered, as well as the complete indentures that contain the terms of the debt securities. Forms of indentures have been filed as exhibits to the registration statement of which this prospectus is a part, and supplemental indentures and forms of debt securities containing the terms of debt securities being offered will be filed as exhibits to the registration statement of which this prospectus is a part or will be incorporated by reference from reports we file with the Securities and Exchange Commission.

Warrants. We may issue warrants for the purchase of common stock, preferred stock and/or debt securities, in one or more series. We may issue warrants independently or together with common stock, preferred stock and/or debt securities, and the warrants may be attached to or separate from these securities. In this prospectus, we have summarized certain general features of the warrants. We urge you, however, to read the prospectus supplements related to the series of warrants being offered, as well as the warrant agreements that contain the terms of the warrants. Forms of the warrant agreements and forms of warrants containing the terms of the warrants being offered have been filed as exhibits to the registration statement of which this prospectus is a part, and supplemental agreements and forms of warrants will be filed as exhibits to the registration statement of which this prospectus is a part or will be incorporated by reference from reports we file with the Securities and Exchange Commission.

We will evidence each series of warrants by warrant certificates that we will issue under a separate agreement. We will enter into the warrant agreements with a warrant agent. Each warrant agent will be a bank that we select. We will indicate the name and address of the warrant agent in the applicable prospectus supplement relating to a particular series of warrants.

Units. We may issue units consisting of common stock, preferred stock, debt securities and/or warrants for the purchase of common stock, preferred stock and/or debt securities in one or more series. In this prospectus, we have summarized certain general features of the units. We urge you, however, to read the prospectus supplements related to the series of units being offered, as well as the unit agreements that contain the terms of the units. Forms of the unit agreements containing the terms of the units being offered have been filed as exhibits to the registration statement of which this prospectus is a part, and supplemental agreements will be filed as exhibits to the registration statement of which this prospectus is a part or will be incorporated by reference from reports we file with the Securities and Exchange Commission.

We will evidence each series of units by unit certificates that we will issue under a separate agreement. We will enter into the unit agreements with a unit agent. Each unit agent will be a bank that we select. We will indicate the name and address of the unit agent in the applicable prospectus supplement relating to a particular series of units.

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FORWARD-LOOKING INFORMATION

This prospectus, including the documents that we incorporate by reference, contains statements indicating expectations about future performance and other forward-looking statements that involve risks and uncertainties. We usually use words such as may, will, should, expect, plan, anticipate, believe, estimate, predict, future, intend, potential or continue or the negative of these terms or similar expressions to ide forward-looking statements. These statements appear throughout this prospectus and are statements regarding our current intent, belief or expectation, primarily with respect to our operations and related industry developments. Examples of these statements include, but are not limited to, statements regarding the following: our business and scientific strategies; the progress of our product development programs, including clinical testing; our corporate collaborations, including revenues received from these collaborations; our drug discovery technologies; our research and development expenses; protection of our intellectual property; sufficiency of our cash resources; and our operations and legal risks. You should not place undue reliance on these forward-looking statements, which apply only as of the date of this prospectus. Our actual results could differ materially from those anticipated in these forward-looking statements for many reasons. Factors that could cause or contribute to such differences include, but are not limited to, those discussed in the section entitled RISK FACTORS contained in our filings made with the Securities and Exchange Commission from time to time, including quarterly reports on Form 10-Q, annual reports on Form 10-K and any supplements to this prospectus. Any forward-looking statement speaks only as of the date on which it is made, and we undertake no obligation to update any forward-looking statement to reflect events or circumstances after the date on which the statement is made or to reflect the occurrence of unanticipated events. New factors emerge from time to time, and it is not possible for us to predict which factors will arise. In addition, we cannot assess the impact of each factor on our business or the extent to which any factor, or combination of factors, may cause actual results to differ materially from those contained in any forward-looking statements.

RATIO OF EARNINGS TO FIXED CHARGES

Our earnings were insufficient to cover fixed charges in each of the years in the five-year period ended December 31, 2003 and in the six-month period ended June 30, 2004. Earnings consist of income (loss) from continuing operations before income taxes, extraordinary items, cumulative effect of accounting changes, equity in net losses of affiliates and fixed charges. Fixed charges consist of interest expense and the portion of operating lease expense that represents interest. The following table sets forth the computation of our ratio of earnings to fixed charges for the periods indicated:

	Six months ended June 30, 2004	Fiscal years ended December 31, 2003	2002	2001	2000	1999
Ratio of earnings to fixed charges(1)						

(1) For the six months ended June 30, 2004, and the fiscal years ended December 31, 2003, 2002, 2001, 2000 and 1999, our earnings were insufficient to cover fixed charges by $58.1 million, $95.1 million, $84.5 million, $71.2 million, $75.3 million and $18.7 million, respectively.

USE OF PROCEEDS

Except as described in any prospectus supplement, we intend to use the net proceeds from the sale of our securities for research and development and general corporate purposes. We may also use a portion of the net proceeds to acquire or invest in businesses, products and technologies that

are complementary to our own, although we currently are not planning or negotiating any such transactions. Pending these uses, the net proceeds will be invested in investment-grade, interest-bearing securities.

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DESCRIPTION OF CAPITAL STOCK

Our authorized capital stock consists of 200 million shares of common stock, $0.001 par value, and 10 million shares of preferred stock, $0.001 par value. As of October 20, 2004, there were 74,808,792 shares of our common stock outstanding and no shares of preferred stock outstanding. In addition, certain stockholders held warrants to purchase 257,053 shares of our common stock.

Common Stock

The holders of common stock are entitled to one vote for each share held of record on all matters submitted to a vote of the stockholders and do not have cumulative voting rights. Accordingly, holders of a majority of the shares of common stock entitled to vote in any election of directors may elect all of the directors standing for election. Subject to preferences that may be applicable to any outstanding shares of preferred stock, the holders of common stock are entitled to receive ratably such dividends as may be declared by the board of directors out of funds legally available therefor. Upon the liquidation, dissolution or winding up of Exelixis, holders of our common stock are entitled to share ratably in all assets remaining after payment of liabilities and the liquidation preferences of any outstanding shares of preferred stock. Holders of common stock have no preemptive rights and no right to convert their common stock into any other securities. There are no redemption or sinking fund provisions applicable to our common stock. All outstanding shares of our common stock are, and all shares of common stock that may be issued under this prospectus will be, fully paid and non-assessable.

The foregoing summary description of our common stock is based on the provisions of our restated certificate of incorporation, as amended, and bylaws and the applicable provisions of the Delaware General Corporation Law. This information may not be complete in all respects and is qualified entirely by reference to the provisions of our restated certificate of incorporation, as amended, bylaws and the Delaware General Corporation Law. For information on how to obtain copies of our restated certificate of incorporation, as amended, and bylaws, see Where You Can Find More Information.

Preferred Stock

Pursuant to our amended and restated certificate of incorporation, our board of directors has the authority, without further action by the stockholders, to issue up to 10 million shares of preferred stock, in one or more series. Our board of directors is authorized to fix or alter from time to time the designation, powers, preferences and rights of the shares of each series, including dividend rights, conversion rights, voting rights, terms of redemption, liquidation preferences and sinking fund terms, as well as the qualifications, limitations or restrictions of any unissued series of preferred stock. Our board of directors may also establish from time to time the number of shares constituting any series of preferred stock, and to increase or decrease the number of shares of any series subsequent to the issuance of shares of that series, but not below the number of shares of any series then outstanding.

We will fix the rights, preferences, privileges and restrictions of the preferred stock of each series in the certificate of designation relating to that series. We will incorporate by reference as an exhibit to the registration statement that includes this prospectus or as an exhibit to a current report on Form 8-K, the form of any certificate of designation that describes the terms of the series of preferred stock we are offering before the issuance of the related series of preferred stock. This description will include:

- the title and stated value;

the number of shares we are offering;

the liquidation preference per share;

the purchase price;

the dividend rate, period and payment date and method of calculation for dividends;

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whether dividends will be cumulative or non-cumulative and, if cumulative, the date from which dividends will accumulate;

the procedures for any auction and remarketing, if any;

the provisions for a sinking fund, if any;

the provisions for redemption or repurchase, if applicable, and any restrictions on our ability to exercise those redemption and repurchase rights;

any listing of the preferred stock on any securities exchange or market;

whether the preferred stock will be convertible into our common stock, and, if applicable, the conversion price, or how it will be calculated, and the conversion period;

whether the preferred stock will be exchangeable into debt securities, and, if applicable, the exchange price, or how it will be calculated, and the exchange period;

voting rights, if any, of the preferred stock;

preemption rights, if any;

restrictions on transfer, sale or other assignment, if any;

whether interests in the preferred stock will be represented by depositary shares;

a discussion of any material or special United States federal income tax considerations applicable to the preferred stock;

the relative ranking and preferences of the preferred stock as to dividend rights and rights if we liquidate, dissolve or wind up our affairs;

any limitations on issuance of any class or series of preferred stock ranking senior to or on a parity with the series of preferred stock as to dividend rights and rights if we liquidate, dissolve or wind up our affairs; and

any other specific terms, preferences, rights or limitations of, or restrictions on, the preferred stock.

If we issue shares of preferred stock under this prospectus, the shares will be fully paid and non-assessable and will not have, or be subject to, any preemptive or similar rights.

The General Corporation Law of the State of Delaware, the state of our incorporation, provides that the holders of preferred stock will have the right to vote separately as a class on any proposal involving fundamental changes in the rights of holders of that preferred stock. This right is in addition to any voting rights that may be provided for in the applicable certificate of designation.

The issuance of preferred stock could adversely affect the voting power, conversion or other rights of holders of common stock. Preferred stock could be issued quickly with terms designed to delay or prevent a change in control of our company or make removal of management more difficult. Additionally, the issuance of preferred stock may have the effect of decreasing the market price of our common stock.

Registration Rights

As of the date of this prospectus, certain holders of our common stock and a holder of a warrant to purchase our common stock are entitled to rights with respect to the registration of those shares of common stock under the Securities Act. These rights are provided under a fourth amended and restated registration rights agreement, dated February 26, 1999, a stock purchase and stock issuance agreement with GlaxoSmithKline, dated October 28, 2002, and a warrant originally issued on January 24, 1996. These registration rights require, among other things, that if we propose to register any of our securities under the Securities Act, either for our own account or for the account of others, the holders of these shares are entitled to notice of the registration and are entitled to

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include, at our expense, their shares of common stock in the registration and any related underwriting, provided, among other conditions, that the underwriters may limit the number of shares to be included in the registration and in some cases exclude these shares entirely. In addition, the holders of these shares may require us, at our expense and subject to certain limitations, to file a registration statement under the Securities Act with respect to their shares of our common stock. These holders have waived these registration rights in connection with the offerings that might be made under this registration statement.

Anti-Takeover Effects of Provisions of Delaware Law and Our Charter Documents.

Delaware Takeover Statute. We are subject to the provisions of Section 203 of the Delaware General Corporation Law. In general, the statute prohibits a publicly-held Delaware corporation such as Exelixis from engaging in a business combination with an interested stockholder for a period of three years after the date of the transaction in which the person became an interested stockholder, unless the business combination is approved in a prescribed manner. For purposes of Section 203, a business combination includes a merger, asset sale or other transaction resulting in a financial benefit to the interested stockholder, and an interested stockholder is a person who, together with affiliates and associates, owns (or within three years prior, did own) 15% or more of our voting stock.

Charter Documents. Our amended and restated certificate of incorporation requires that any action required or permitted to be taken by our stockholders must be effected at a duly called annual or special meeting of stockholders and may not be effected by a consent in writing. Additionally, our amended and restated certificate of incorporation:

- substantially limits the use of cumulative voting in the election of directors;
- provides for a board of directors, classified into three classes of directors;
- provides that the authorized number of directors may be changed only by resolution of our board of directors; and
- provides for the authority of our board of directors to issue up to 10 million shares of blank check preferred stock and to determine the price, powers, preferences and rights of these shares, without stockholder approval.

Our amended and restated bylaws provide that candidates for director may be nominated only by our board of directors or by a stockholder who gives written notice to us no later than 60 days prior nor earlier than 90 days prior to the first anniversary of the last annual meeting of stockholders. The authorized number of directors is fixed in accordance with our amended and restated certificate of incorporation. Our board of directors currently consists of ten members, divided into three classes. As a result, a portion of the board of directors will be elected each year. The board of directors may appoint new directors to fill vacancies or newly created directorships. Our amended and restated bylaws also limit who may call a special meeting of stockholders.

Delaware law and these charter provisions may have the effect of deterring hostile takeovers or delaying changes in control of our management, which could depress the market price of our common stock.

Transfer Agent and Registrar

The transfer agent and registrar for our common stock is Mellon Investor Services LLC. Its address is 85 Challenger Road, Ridgefield Park, NJ 07660 and its telephone number is (800) 777-3674. The transfer agent for any series of preferred stock will be named and described in the prospectus supplement for that series.

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DESCRIPTION OF DEBT SECURITIES

The following description, together with the additional information we include in any applicable prospectus supplements, summarizes the material terms and provisions of the debt securities that we may offer under this prospectus. While the terms we have summarized below will apply generally to any future debt securities we may offer under this prospectus, we will describe the particular terms of any debt securities that we may offer in more detail in the applicable prospectus supplement. The terms of any debt securities we offer under a prospectus supplement may differ from the terms we describe below. However, no prospectus supplement shall fundamentally change the terms that are set forth in this prospectus or offer a security that is not registered and described in this prospectus at the time of its effectiveness.

We will issue the senior debt securities under the senior indenture that we will enter into with the trustee named in the senior indenture. We will issue the subordinated debt securities under the subordinated indenture that we will enter into with the trustee named in the subordinated indenture. We have filed forms of these documents as exhibits to the registration statement which includes this prospectus. We use the term indentures in this prospectus to refer to both the senior indenture and the subordinated indenture.

The indentures will be qualified under the Trust Indenture Act of 1939. We use the term debenture trustee to refer to either the senior trustee or the subordinated trustee, as applicable.

The following summaries of material provisions of the senior debt securities, the subordinated debt securities and the indentures are subject to, and qualified in their entirety by reference to, all the provisions of the indenture applicable to a particular series of debt securities. Except as we may otherwise indicate, the terms of the senior indenture and the subordinated indenture are identical.

General

We will describe in each prospectus supplement the following terms relating to a series of debt securities:

- the title;
- the principal amount being offered, and if a series, the total amount authorized and the total amount outstanding;
- any limit on the amount that may be issued;
- whether or not we will issue the series of debt securities in global form, the terms and who the depositary will be;
- the maturity date;

whether and under what circumstances, if any, we will pay additional amounts on any debt securities held by a person who is not a United States person for tax purposes, and whether we can redeem the debt securities if we have to pay such additional amounts;

the annual interest rate, which may be fixed or variable, or the method for determining the rate and the date interest will begin to accrue, the dates interest will be payable and the regular record dates for interest payment dates or the method for determining such dates;

whether or not the debt securities will be secured or unsecured, and the terms of any secured debt;

the terms of the subordination of any series of subordinated debt;

the place where payments will be payable;

restrictions on transfer, sale or other assignment, if any;

our right, if any, to defer payment of interest and the maximum length of any such deferral period;

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the date, if any, after which, and the price at which, we may, at our option, redeem the series of debt securities pursuant to any optional or provisional redemption provisions and the terms of those redemptions provisions;

the date, if any, on which, and the price at which we are obligated, pursuant to any mandatory sinking fund or analogous fund provisions or otherwise, to redeem, or at the holder s option to purchase, the series of debt securities and the currency or currency unit in which the debt securities are payable;

whether the indenture will restrict our ability and/or the ability of our subsidiaries to:

- incur additional indebtedness;
- issue additional securities;
- create liens;
- pay dividends and make distributions in respect of our capital stock and the capital stock of our subsidiaries;
- redeem capital stock;
- place restrictions on our subsidiaries ability to pay dividends, make distributions or transfer assets;
- make investments or other restricted payments;
- sell or otherwise dispose of assets;
- enter into sale-leaseback transactions;
- engage in transactions with stockholders and affiliates;
- issue or sell stock of our subsidiaries; or
- effect a consolidation or merger;

whether the indenture will require us to maintain any interest coverage, fixed charge, cash flow-based, asset based or other financial ratios;

a discussion of any material or special United States federal income tax considerations applicable to the debt securities;

information describing any book-entry features;

provisions for a sinking fund purchase or other analogous fund, if any;

the applicability of the provisions in the indenture on discharge;

whether the debt securities are to be offered at a price such that they will be deemed to be offered at an original issue discount as defined in paragraph (a) of Section 1273 of the Internal Revenue Code;

the denominations in which we will issue the series of debt securities, if other than denominations of $1,000 and any integral multiple thereof;

the currency of payment of debt securities if other than U.S. dollars and the manner of determining the equivalent amount in U.S. dollars; and

any other specific terms, preferences, rights or limitations of, or restrictions on, the debt securities, including any additional events of default or covenants provided with respect to the debt securities, and any terms that may be required by us or advisable under applicable laws or regulations.

Conversion or Exchange Rights

We will set forth in the prospectus supplement the terms on which a series of debt securities may be convertible into or exchangeable for common stock or other securities of ours or a third party. We will include

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provisions as to whether conversion or exchange is mandatory, at the option of the holder or at our option. We may include provisions pursuant to which the number of shares of common stock or other securities of ours or a third party that the holders of the series of debt securities receive would be subject to adjustment.

Consolidation, Merger or Sale

The indentures do not contain any covenant that restricts our ability to merge or consolidate, or sell, convey, transfer or otherwise dispose of all or substantially all of our assets. However, any successor to or acquirer of such assets must assume all of our obligations under the indentures or the debt securities, as appropriate. If the debt securities are convertible for our other securities or securities of other entities, the person with whom we consolidate or merge or to whom we sell all of our property must make provisions for the conversion of the debt securities into securities that the holders of the debt securities would have received if they had converted the debt securities before the consolidation, merger or sale.

Events of Default under the Indenture

The following are events of default under the indentures with respect to any series of debt securities that we may issue:

- if we fail to pay interest when due and payable and our failure continues for 90 days and the time for payment has not been extended or deferred;
- if we fail to pay the principal, premium or sinking fund payment, if any, when due and payable and the time for payment has not been extended or delayed;
- if we fail to observe or perform any other covenant contained in the debt securities or the indentures, other than a covenant specifically relating to another series of debt securities, and our failure continues for 90 days after we receive notice from the debenture trustee or holders of at least 25% in aggregate principal amount of the outstanding debt securities of the applicable series; and
- if specified events of bankruptcy, insolvency or reorganization occur.

If an event of default with respect to debt securities of any series occurs and is continuing, other than an event of default specified in the last bullet point above, the debenture trustee or the holders of at least 25% in aggregate principal amount of the outstanding debt securities of that series, by notice to us in writing, and to the debenture trustee if notice is given by such holders, may declare the unpaid principal of, premium, if any, and accrued interest, if any, due and payable immediately. If an event of default specified in the last bullet point above occurs with respect to us, the principal amount of and accrued interest, if any, of each issue of debt securities then outstanding shall be due and payable without any notice or other action on the part of the debenture trustee or any holder.

The holders of a majority in principal amount of the outstanding debt securities of an affected series may waive any default or event of default with respect to the series and its consequences, except defaults or events of default regarding payment of principal, premium, if any, or interest, unless we have cured the default or event of default in accordance with the indenture. Any waiver shall cure the default or event of default.

Subject to the terms of the indentures, if an event of default under an indenture shall occur and be continuing, the debenture trustee will be under no obligation to exercise any of its rights or powers under such indenture at the request or direction of any of the holders of the applicable series of debt securities, unless such holders have offered the debenture trustee reasonable indemnity. The holders of a majority in principal amount of the outstanding debt securities of any series will have the right to direct the time, method and place of conducting any proceeding for any remedy available to the debenture trustee, or exercising any trust or power conferred on the debenture trustee, with respect to the debt securities of that series, provided that:

the direction so given by the holder is not in conflict with any law or the applicable indenture; and

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subject to its duties under the Trust Indenture Act of 1939, the debenture trustee need not take any action that might involve it in personal liability or might be unduly prejudicial to the holders not involved in the proceeding.

A holder of the debt securities of any series will only have the right to institute a proceeding under the indentures or to appoint a receiver or trustee, or to seek other remedies if:

the holder has given written notice to the debenture trustee of a continuing event of default with respect to that series;

the holders of at least 25% in aggregate principal amount of the outstanding debt securities of that series have made written request, and such holders have offered reasonable indemnity to the debenture trustee to institute the proceeding as trustee; and

the debenture trustee does not institute the proceeding, and does not receive from the holders of a majority in aggregate principal amount of the outstanding debt securities of that series other conflicting directions within 90 days after the notice, request and offer.

These limitations do not apply to a suit instituted by a holder of debt securities if we default in the payment of the principal, premium, if any, or interest on, the debt securities.

We will periodically file statements with the debenture trustee regarding our compliance with specified covenants in the indentures.

Modification of Indenture; Waiver

We and the debenture trustee may change an indenture without the consent of any holders with respect to specific matters:

to fix any ambiguity, defect or inconsistency in the indenture;

to comply with the provisions described above under Consolidation, Merger or Sale;

to provide for uncertificated debt securities in addition to or in place of certificated debt securities;

to add to our covenants such new covenants, restrictions, conditions or provisions for the protection of the holders, and to make the occurrence, or the occurrence and the continuance, of a default in any such additional covenants, restrictions, conditions or provisions an event of default;

to add to, delete from or revise the conditions, limitations, and restrictions on the authorized amount, terms, or purposes of issue, authentication and delivery of debt securities, as set forth in the indenture;

to change anything that does not materially adversely affect the interests of any holder of debt securities of any series;

to provide for the issuance of and establish the form and terms and conditions of the debt securities of any series as provided under General to establish the form of any certifications required to be furnished pursuant to the terms of the indenture or any series of debt securities, or to add to the rights of the holders of any series of debt securities;

to evidence and provide for the acceptance of appointment hereunder by a successor trustee; or

to comply with any requirements of the Securities and Exchange Commission in connection with the qualification of any indenture under the Trust Indenture Act of 1939.

In addition, under the indentures, the rights of holders of a series of debt securities may be changed by us and the debenture trustee with the written consent of the holders of at least a majority in aggregate principal amount of the outstanding debt securities of each series that is affected. However, we and the debenture trustee may only make the following changes with the consent of each holder of any outstanding debt securities affected:

extending the fixed maturity of the series of debt securities;

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reducing the principal amount, reducing the rate of or extending the time of payment of interest, or reducing any premium payable upon the redemption of any debt securities; or

reducing the percentage of debt securities, the holders of which are required to consent to any amendment, supplement, modification or waiver.

Discharge

Each indenture provides that we can elect to be discharged from our obligations with respect to one or more series of debt securities, except for specified obligations, including obligations to:

register the transfer or exchange of debt securities of the series;

replace stolen, lost or mutilated debt securities of the series;

maintain paying agencies;

hold monies for payment in trust;

compensate and indemnify the debenture trustee;

appoint any successor trustee; and

recover excess money held by the debenture trustee.

In order to exercise our rights to be discharged, we must deposit with the debenture trustee money or government obligations sufficient to pay all the principal of, any premium, if any, and interest on, the debt securities of the series on the dates payments are due.

Form, Exchange and Transfer

We will issue the debt securities of each series only in fully registered form without coupons and, unless we otherwise specify in the applicable prospectus supplement, in denominations of $1,000 and any integral multiple thereof. The indentures provide that we may issue debt securities of a series in temporary or permanent global form and as book-entry securities that will be deposited with, or on behalf of, The Depository Trust Company or another depositary named by us and identified in a prospectus supplement with respect to that series. See Legal Ownership of Securities for a further description of the terms relating to any book-entry securities.

At the option of the holder, subject to the terms of the indentures and the limitations applicable to global securities described in the applicable prospectus supplement, the holder of the debt securities of any series can exchange the debt securities for other debt securities of the same series, in any authorized denomination and of like tenor and aggregate principal amount.

Subject to the terms of the indentures and the limitations applicable to global securities set forth in the applicable prospectus supplement, holders of the debt securities may present the debt securities for exchange or for registration of transfer, duly endorsed or with the form of transfer endorsed thereon duly executed if so required by us or the security registrar, at the office of the security registrar or at the office of any transfer agent designated by us for this purpose. Unless otherwise provided in the debt securities that the holder presents for transfer or exchange, we will make no service charge for any registration of transfer or exchange, but we may require payment of any taxes or other governmental charges.

We will name in the applicable prospectus supplement the security registrar, and any transfer agent in addition to the security registrar, that we initially designate for any debt securities. We may at any time designate additional transfer agents or rescind the designation of any transfer agent or approve a change in the office through which any transfer agent acts, except that we will be required to maintain a transfer agent in each place of payment for the debt securities of each series.

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If we elect to redeem the debt securities of any series, we will not be required to:

- issue, register the transfer of, or exchange any debt securities of that series during a period beginning at the opening of business 15 days before the day of mailing of a notice of redemption of any debt securities that may be selected for redemption and ending at the close of business on the day of the mailing; or

- register the transfer of or exchange any debt securities so selected for redemption, in whole or in part, except the unredeemed portion of any debt securities we are redeeming in part.

Information Concerning the Debenture Trustee

The debenture trustee, other than during the occurrence and continuance of an event of default under an indenture, undertakes to perform only those duties as are specifically set forth in the applicable indenture. Upon an event of default under an indenture, the debenture trustee must use the same degree of care as a prudent person would exercise or use in the conduct of his or her own affairs. Subject to this provision, the debenture trustee is under no obligation to exercise any of the powers given it by the indentures at the request of any holder of debt securities unless it is offered reasonable security and indemnity against the costs, expenses and liabilities that it might incur.

Payment and Paying Agents

Unless we otherwise indicate in the applicable prospectus supplement, we will make payment of the interest on any debt securities on any interest payment date to the person in whose name the debt securities, or one or more predecessor securities, are registered at the close of business on the regular record date for the interest.

We will pay principal of and any premium and interest on the debt securities of a particular series at the office of the paying agents designated by us, except that unless we otherwise indicate in the applicable prospectus supplement, we will make interest payments by check that we will mail to the holder or by wire transfer to certain holders. Unless we otherwise indicate in a prospectus supplement, we will designate the corporate trust office of the debenture trustee in the City of New York as our sole paying agent for payments with respect to debt securities of each series. We will name in the applicable prospectus supplement any other paying agents that we initially designate for the debt securities of a particular series. We will maintain a paying agent in each place of payment for the debt securities of a particular series.

All money we pay to a paying agent or the debenture trustee for the payment of the principal of or any premium or interest on any debt securities that remains unclaimed at the end of two years after such principal, premium or interest has become due and payable will be repaid to us, and the holder of the debt security thereafter may look only to us for payment thereof.

Governing Law

The indentures and the debt securities will be governed by and construed in accordance with the laws of the State of New York, except to the extent that the Trust Indenture Act of 1939 is applicable.

Subordination of Subordinated Debt Securities

The subordinated debt securities will be unsecured and will be subordinate and junior in priority of payment to certain of our other indebtedness to the extent described in a prospectus supplement. The subordinated indenture does not limit the amount of subordinated debt securities that we may issue. It also does not limit us from issuing any other secured or unsecured debt.

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DESCRIPTION OF WARRANTS

The following description, together with the additional information we may include in any applicable prospectus supplements, summarizes the material terms and provisions of the warrants that we may offer under this prospectus and the related warrant agreements and warrant certificates. While the terms summarized below will apply generally to any warrants that we may offer, we will describe the particular terms of any series of warrants in more detail in the applicable prospectus supplement. If we indicate in the prospectus supplement, the terms of any warrants offered under that prospectus supplement may differ from the terms described below. However, no prospectus supplement shall fundamentally change the terms that are set forth in this prospectus or offer a security that is not registered and described in this prospectus at the time of its effectiveness. Specific warrant agreements will contain additional important terms and provisions and will be incorporated by reference as an exhibit to the registration statement that includes this prospectus or as an exhibit to a current report on Form 8-K.

General

We will describe in the applicable prospectus supplement the terms of the series of warrants, including:

- the offering price and aggregate number of warrants offered;
- the currency for which the warrants may be purchased;
- if applicable, the designation and terms of the securities with which the warrants are issued and the number of warrants issued with each such security or each principal amount of such security;
- if applicable, the date on and after which the warrants and the related securities will be separately transferable;
- in the case of warrants to purchase debt securities, the principal amount of debt securities purchasable upon exercise of one warrant and the price at, and currency in which, this principal amount of debt securities may be purchased upon such exercise;
- in the case of warrants to purchase common stock or preferred stock, the number of shares of common stock or preferred stock, as the case may be, purchasable upon the exercise of one warrant and the price at which these shares may be purchased upon such exercise;
- the effect of any merger, consolidation, sale or other disposition of our business on the warrant agreements and the warrants;
- the terms of any rights to redeem or call the warrants;
- any provisions for changes to or adjustments in the exercise price or number of securities issuable upon exercise of the warrants;
- the dates on which the right to exercise the warrants will commence and expire;

the manner in which the warrant agreements and warrants may be modified;

federal income tax consequences of holding or exercising the warrants;

the terms of the securities issuable upon exercise of the warrants; and

any other specific terms, preferences, rights or limitations of or restrictions on the warrants.

Before exercising their warrants, holders of warrants will not have any of the rights of holders of the securities purchasable upon such exercise, including:

in the case of warrants to purchase debt securities, the right to receive payments of principal of, or premium, if any, or interest on, the debt securities purchasable upon exercise or to enforce covenants in the applicable indenture; or

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in the case of warrants to purchase common stock or preferred stock, the right to receive dividends, if any, or, payments upon our liquidation, dissolution or winding up or to exercise voting rights, if any.

Exercise of Warrants

Each warrant will entitle the holder to purchase the securities that we specify in the applicable prospectus supplement at the exercise price that we describe in the applicable prospectus supplement. Unless we otherwise specify in the applicable prospectus supplement, holders of the warrants may exercise the warrants at any time up to the specified time on the expiration date that we set forth in the applicable prospectus supplement. After the close of business on the expiration date, unexercised warrants will become void.

Holders of the warrants may exercise the warrants by delivering the warrant certificate representing the warrants to be exercised together with specified information, and paying the required amount to the warrant agent in immediately available funds, as provided in the applicable prospectus supplement. We will set forth on the reverse side of the warrant certificate and in the applicable prospectus supplement the information that the holder of the warrant will be required to deliver to the warrant agent.

Upon receipt of the required payment and the warrant certificate properly completed and duly executed at the corporate trust office of the warrant agent or any other office indicated in the applicable prospectus supplement, we will issue and deliver the securities purchasable upon such exercise. If fewer than all of the warrants represented by the warrant certificate are exercised, then we will issue a new warrant certificate for the remaining amount of warrants. If we so indicate in the applicable prospectus supplement, holders of the warrants may surrender securities as all or part of the exercise price for warrants.

Governing Law

The warrants and warrant agreements will be governed by and construed in accordance with the laws of the State of New York.

Enforceability of Rights by Holders of Warrants

Each warrant agent will act solely as our agent under the applicable warrant agreement and will not assume any obligation or relationship of agency or trust with any holder of any warrant. A single bank or trust company may act as warrant agent for more than one issue of warrants. A warrant agent will have no duty or responsibility in case of any default by us under the applicable warrant agreement or warrant, including any duty or responsibility to initiate any proceedings at law or otherwise, or to make any demand upon us. Any holder of a warrant may, without the consent of the related warrant agent or the holder of any other warrant, enforce by appropriate legal action its right to exercise, and receive the securities purchasable upon exercise of, its warrants.

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DESCRIPTION OF UNITS

The following description, together with the additional information we may include in any applicable prospectus supplements, summarizes the material terms and provisions of the units that we may offer under this prospectus and the related unit agreements. While the terms summarized below will apply generally to any units that we may offer, we will describe the particular terms of any series of units in more detail in the applicable prospectus supplement. If we indicate in the prospectus supplement, the terms of any units offered under that prospectus supplement may differ from the terms described below. However, no prospectus supplement shall fundamentally change the terms that are set forth in this prospectus or offer a security that is not registered and described in this prospectus at the time of its effectiveness. Specific unit agreements will contain additional important terms and provisions and will be incorporated by reference as an exhibit to the registration statement that includes this prospectus or as an exhibit to a current report on Form 8-K.

General

We may issue units comprised of one or more debt securities, shares of common stock, shares of preferred stock and warrants in any combination. Each unit will be issued so that the holder of the unit is also the holder of each security included in the unit. Thus, the holder of a unit will have the rights and obligations of a holder of each included security. The unit agreement under which a unit is issued may provide that the securities included in the unit may not be held or transferred separately, at any time or at any time before a specified date.

We will describe in the applicable prospectus supplement the terms of the series of units, including:

- the designation and terms of the units and of the securities comprising the units, including whether and under what circumstances those securities may be held or transferred separately;
- any provisions of the governing unit agreement that differ from those described below; and
- any provisions for the issuance, payment, settlement, transfer or exchange of the units or of the securities comprising the units.

The provisions described in this section, as well as those described under Description of Capital Stock, Description of Debt Securities and Description of Warrants will apply to each unit and to any common stock, preferred stock, debt security or warrant included in each unit, respectively.

Issuance in Series

We may issue units in such amounts and in numerous distinct series as we determine.

Enforceability of Rights by Holders of Units

Each unit agent will act solely as our agent under the applicable unit agreement and will not assume any obligation or relationship of agency or trust with any holder of any unit. A single bank or trust company may act as unit agent for more than one series of units. A unit agent will have no duty or responsibility in case of any default by us under the applicable unit agreement or unit, including any duty or responsibility to initiate any proceedings at law or otherwise, or to make any demand upon us. Any holder of a unit may, without the consent of the related unit agent or the holder of any other unit, enforce by appropriate legal action its rights as holder under any security included in the unit.

Title

Exelixis, the unit agents and any of their agents may treat the registered holder of any unit certificate as an absolute owner of the units evidenced by that certificate for any purpose and as the person entitled to exercise the rights attaching to the units so requested, despite any notice to the contrary. See Legal Ownership of Securities.

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LEGAL OWNERSHIP OF SECURITIES

We can issue securities in registered form or in the form of one or more global securities. We describe global securities in greater detail below. We refer to those persons who have securities registered in their own names on the books that we or any applicable trustee maintain for this purpose as the holders of those securities. These persons are the legal holders of the securities. We refer to those persons who, indirectly through others, own beneficial interests in securities that are not registered in their own names, as indirect holders of those securities. As we discuss below, indirect holders are not legal holders, and investors in securities issued in book-entry form or in street name will be indirect holders.

Book-Entry Holders

We may issue securities in book-entry form only, as we will specify in the applicable prospectus supplement. This means securities may be represented by one or more global securities registered in the name of a financial institution that holds them as depositary on behalf of other financial institutions that participate in the depositary s book-entry system. These participating institutions, which are referred to as participants, in turn, hold beneficial interests in the securities on behalf of themselves or their customers.

Only the person in whose name a security is registered is recognized as the holder of that security. Securities issued in global form will be registered in the name of the depositary or its nominee. Consequently, for securities issued in global form, we will recognize only the depositary as the holder of the securities, and we will make all payments on the securities to the depositary. The depositary passes along the payments it receives to its participants, which in turn pass the payments along to their customers who are the beneficial owners. The depositary and its participants do so under agreements they have made with one another or with their customers; they are not obligated to do so under the terms of the securities.

As a result, investors in a book-entry security will not own securities directly. Instead, they will own beneficial interests in a global security, through a bank, broker or other financial institution that participates in the depositary s book-entry system or holds an interest through a participant. As long as the securities are issued in global form, investors will be indirect holders, and not holders, of the securities.

Street Name Holders

We may terminate a global security or issue securities in non-global form. In these cases, investors may choose to hold their securities in their own names or in street name. Securities held by an investor in street name would be registered in the name of a bank, broker or other financial institution that the investor chooses, and the investor would hold only a beneficial interest in those securities through an account he or she maintains at that institution.

For securities held in street name, we will recognize only the intermediary banks, brokers and other financial institutions in whose names the securities are registered as the holders of those securities, and we will make all payments on those securities to them. These institutions pass along the payments they receive to their customers who are the beneficial owners, but only because they agree to do so in their customer agreements or because they are legally required to do so. Investors who hold securities in street name will be indirect holders, not holders, of those securities.

Legal Holders

Our obligations, as well as the obligations of any applicable trustee and of any third parties employed by us or a trustee, run only to the legal holders of the securities. We do not have obligations to investors who hold beneficial interests in global securities, in street name or by any other indirect means. This will be the case whether an investor chooses to be an indirect holder of a security or has no choice because we are issuing the securities only in global form.

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For example, once we make a payment or give a notice to the holder, we have no further responsibility for the payment or notice even if that holder is required, under agreements with depositary participants or customers or by law, to pass it along to the indirect holders but does not do so. Similarly, we may want to obtain the approval of the holders to amend an indenture, to relieve us of the consequences of a default or of our obligation to comply with a particular provision of the indenture or for other purposes. In such an event, we would seek approval only from the holders, and not the indirect holders, of the securities. Whether and how the holders contact the indirect holders is up to the holders.

Special Considerations for Indirect Holders

If you hold securities through a bank, broker or other financial institution, either in book-entry form or in street name, you should check with your own institution to find out:

- how it handles securities payments and notices;
- whether it imposes fees or charges;
- how it would handle a request for the holders consent, if ever required;
- whether and how you can instruct it to send you securities registered in your own name so you can be a holder, if that is permitted in the future;
- how it would exercise rights under the securities if there were a default or other event triggering the need for holders to act to protect their interests; and
- if the securities are in book-entry form, how the depositary s rules and procedures will affect these matters.

Global Securities

A global security is a security that represents one or any other number of individual securities held by a depositary. Generally, all securities represented by the same global securities will have the same terms.

Each security issued in book-entry form will be represented by a global security that we deposit with and register in the name of a financial institution or its nominee that we select. The financial institution that we select for this purpose is called the depositary. Unless we specify otherwise in the applicable prospectus supplement, The Depository Trust Company, New York, New York, known as DTC, will be the depositary for all securities issued in book-entry form.

A global security may not be transferred to or registered in the name of anyone other than the depositary, its nominee or a successor depositary, unless special termination situations arise. We describe those situations below under Special Situations When a Global Security Will Be

Terminated. As a result of these arrangements, the depositary, or its nominee, will be the sole registered owner and holder of all securities represented by a global security, and investors will be permitted to own only beneficial interests in a global security. Beneficial interests must be held by means of an account with a broker, bank or other financial institution that in turn has an account with the depositary or with another institution that does. Thus, an investor whose security is represented by a global security will not be a holder of the security, but only an indirect holder of a beneficial interest in the global security.

If the prospectus supplement for a particular security indicates that the security will be issued in global form only, then the security will be represented by a global security at all times unless and until the global security is terminated. If termination occurs, we may issue the securities through another book-entry clearing system or decide that the securities may no longer be held through any book-entry clearing system.

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Special Considerations for Global Securities

As an indirect holder, an investor s rights relating to a global security will be governed by the account rules of the investor s financial institution and of the depositary, as well as general laws relating to securities transfers. We do not recognize an indirect holder as a holder of securities and instead deal only with the depositary that holds the global security.

If securities are issued only in the form of a global security, an investor should be aware of the following:

- An investor cannot cause the securities to be registered in his or her name, and cannot obtain non-global certificates for his or her interest in the securities, except in the special situations we describe below;
- An investor will be an indirect holder and must look to his or her own bank or broker for payments on the securities and protection of his or her legal rights relating to the securities, as we describe above;
- An investor may not be able to sell interests in the securities to some insurance companies and to other institutions that are required by law to own their securities in non-book-entry form;
- An investor may not be able to pledge his or her interest in a global security in circumstances where certificates representing the securities must be delivered to the lender or other beneficiary of the pledge in order for the pledge to be effective;
- The depositary s policies, which may change from time to time, will govern payments, transfers, exchanges and other matters relating to an investor s interest in a global security. We and any applicable trustee have no responsibility for any aspect of the depositary s actions or for its records of ownership interests in a global security. We and the trustee also do not supervise the depositary in any way;
- The depositary may, and we understand that DTC will, require that those who purchase and sell interests in a global security within its book-entry system use immediately available funds, and your broker or bank may require you to do so as well; and
- Financial institutions that participate in the depositary s book-entry system, and through which an investor holds its interest in a global security, may also have their own policies affecting payments, notices and other matters relating to the securities. There may be more than one financial intermediary in the chain of ownership for an investor. We do not monitor and are not responsible for the actions of any of those intermediaries.

Special Situations When a Global Security Will Be Terminated

In a few special situations described below, the global security will terminate and interests in it will be exchanged for physical certificates representing those interests. After that exchange, the choice of whether to hold securities directly or in street name will be up to the investor. Investors must consult their own banks or brokers to find out how to have their interests in securities transferred to their own name, so that they will be direct holders. We have described the rights of holders and street name investors above.

The global security will terminate when the following special situations occur:

- if the depositary notifies us that it is unwilling, unable or no longer qualified to continue as depositary for that global security and we do not appoint another institution to act as depositary within 90 days;

- if we notify any applicable trustee that we wish to terminate that global security; or

- if an event of default has occurred with regard to securities represented by that global security and has not been cured or waived.

The prospectus supplement may also list additional situations for terminating a global security that would apply only to the particular series of securities covered by the prospectus supplement. When a global security terminates, the depositary, and not we or any applicable trustee, is responsible for deciding the names of the institutions that will be the initial direct holders.

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PLAN OF DISTRIBUTION

We may sell the securities through underwriters or dealers, through agents, or directly to one or more purchasers. One or more prospectus supplements will describe the terms of the offering of the securities, including:

- the name or names of any underwriters, if any;
- the purchase price of the securities and the proceeds we will receive from the sale;
- any over-allotment options under which underwriters may purchase additional securities from us;
- any agency fees or underwriting discounts and other items constituting agents or underwriters compensation;
- any initial public offering price;
- any discounts or concessions allowed or reallowed or paid to dealers; and
- any securities exchange or market on which the securities may be listed.

Only underwriters named in the prospectus supplement are underwriters of the securities offered by the prospectus supplement.

If underwriters are used in the sale, they will acquire the securities for their own account and may resell them from time to time in one or more transactions at a fixed public offering price. The obligations of the underwriters to purchase the securities will be subject to the conditions set forth in the applicable underwriting agreement. We may offer the securities to the public through underwriting syndicates represented by managing underwriters or by underwriters without a syndicate. Subject to certain conditions, the underwriters will be obligated to purchase all the securities of the series offered by the prospectus supplement. Any public offering price and any discounts or concessions allowed or reallowed or paid to dealers may change from time to time. We may use underwriters with whom we have a material relationship. We will describe in the prospectus supplement, naming the underwriter, the nature of any such relationship.

We may sell securities directly or through agents we designate from time to time. We will name any agent involved in the offering and sale of securities and we will describe any commissions we will pay the agent in the prospectus supplement.

Unless the prospectus supplement states otherwise, our agent will act on a best-efforts basis for the period of its appointment. However, no prospectus supplement shall fundamentally change the terms that are set forth in this prospectus or offer a security that is not registered and described in this prospectus at the time of its effectiveness.

We may authorize agents or underwriters to solicit offers by certain types of institutional investors to purchase securities from us at the public offering price set forth in the prospectus supplement pursuant to delayed delivery contracts providing for payment and delivery on a specified date in the future. We will describe the conditions to these contracts and the commissions we must pay for solicitation of these contracts in the prospectus supplement.

We may enter into derivative transactions with third parties, or sell securities not covered by this prospectus to third parties in privately negotiated transactions. If the related prospectus supplement so indicates, in connection with those derivatives, the third parties may sell securities covered by this prospectus and the related prospectus supplement, including in short sale transactions. If so, the third party may use securities pledged by us or borrowed from us or others to settle those sales or to close out any related open borrowings of stock and may use securities received from us in settlement of those derivatives to close out any related open borrowings of

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stock. The third party in such sale transactions will be an underwriter and, if not identified in this prospectus, will be identified in the related prospectus supplement (or a post-effective amendment). Such underwriters may include, among others, Goldman, Sachs & Co. and SG Cowen Securities Corporation.

We may provide agents and underwriters with indemnification against certain civil liabilities, including liabilities under the Securities Act, or contribution with respect to payments that the agents or underwriters may make with respect to such liabilities. Agents and underwriters may engage in transactions with, or perform services for, us in the ordinary course of business.

All securities we offer, other than common stock and other than securities issued upon a reopening of a previous series, will be new issues of securities with no established trading market. Any underwriters may make a market in these securities, but will not be obligated to do so and may discontinue any market making at any time without notice. We cannot guarantee the liquidity of the trading markets for any securities.

Any underwriter may engage in overallotment, stabilizing transactions, short covering transactions and penalty bids in accordance with Regulation M under the Securities Exchange Act of 1934, as amended. Overallotment involves sales in excess of the offering size, which create a short position. Stabilizing transactions permit bids to purchase the underlying security so long as the stabilizing bids do not exceed a specified maximum price. Short covering transactions involve purchases of the securities in the open market after the distribution is completed to cover short positions. Penalty bids permit the underwriters to reclaim a selling concession from a dealer when the securities originally sold by the dealer are purchased in a covering transaction to cover short positions. Those activities may cause the price of the securities to be higher than it would otherwise be. If commenced, the underwriters may discontinue any of the activities at any time.

Any underwriters who are qualified market makers on The Nasdaq National Market may engage in passive market making transactions in the securities on The Nasdaq National Market in accordance with Rule 103 of Regulation M under the Securities Exchange Act of 1934, as amended, during the business day prior to the pricing of the offering, before the commencement of offers or sales of the securities. Passive market makers must comply with applicable volume and price limitations and must be identified as passive market makers. In general, a passive market maker must display its bid at a price not in excess of the highest independent bid for such security; if all independent bids are lowered below the passive market maker s bid, however, the passive market maker s bid must then be lowered when certain purchase limits are exceeded.

In compliance with guidelines of the National Association of Securities Dealers, or NASD, the maximum consideration or discount to be received by any NASD member or independent broker dealer may not exceed 8% of the aggregate amount of the securities offered pursuant to this prospectus and any applicable prospectus supplement.

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LEGAL MATTERS

The validity of the securities being offered hereby will be passed upon by Cooley Godward LLP, Palo Alto, California.

EXPERTS

Ernst & Young LLP, independent auditors, have audited our consolidated financial statements included in our Annual Report on Form 10-K, as amended, for the year ended December 31, 2003, as set forth in their report, which is incorporated by reference in this prospectus and elsewhere in the registration statement. Our financial statements are incorporated by reference in reliance on Ernst & Young LLP s report, given on their authority as experts in accounting and auditing.

WHERE YOU CAN FIND MORE INFORMATION

We are a reporting company and file annual, quarterly and current reports, proxy statements and other information with the Securities and Exchange Commission. We have filed with the Securities and Exchange Commission a registration statement on Form S-3 under the Securities Act with respect to the securities we are offering under this prospectus. This prospectus does not contain all of the information set forth in the registration statement and the exhibits to the registration statement. For further information with respect to us and the securities we are offering under this prospectus, we refer you to the registration statement and the exhibits and schedules filed as a part of the registration statement. You may read and copy the registration statement, as well as our reports, proxy statements and other information, at the Securities and Exchange Commission s public reference room at Room 1024, 450 Fifth Street, N.W., Washington, D.C. 20549. You can request copies of these documents by writing to the Securities and Exchange Commission and paying a fee for the copying cost. Please call the Securities and Exchange Commission at 1-800-SEC-0330 for more information about the operation of the public reference room. Our Securities and Exchange Commission filings are also available at the Securities and Exchange Commission s web site at http://www.sec.gov. In addition, you can read and copy our Securities and Exchange Commission filings at the office of the National Association of Securities Dealers, Inc. at 1735 K Street, N.W., Washington, D.C. 20006.

The Securities and Exchange Commission allows us to incorporate by reference information that we file with it, which means that we can disclose important information to you by referring you to those documents. The information incorporated by reference is an important part of this prospectus. Information in this prospectus supersedes information incorporated by reference that we filed with the Securities and Exchange Commission prior to the date of this prospectus, while information that we file later with the Securities and Exchange Commission will automatically update and supersede this information. We incorporate by reference into this registration statement and prospectus the documents listed below and any future filings we will make with the Securities and Exchange Commission under Sections 13(a), 13(c), 14 or 15(d) of the Securities Exchange Act of 1934, as amended, after the date of the initial registration statement but prior to effectiveness of the registration statement and after the date of this prospectus but prior to the termination of the offering of the securities covered by this prospectus.

The following documents filed with the Securities and Exchange Commission are incorporated by reference in this prospectus:

1. Our annual report on Form 10-K, as amended, for the year ended December 31, 2003, filed with the Securities and Exchange Commission on February 20, 2004;

2. Our quarterly report on Form 10-Q for the quarter ended March 31, 2004, filed with the Securities and Exchange Commission on May 4, 2004;

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3. Our quarterly report on Form 10-Q for the quarter ended June 30, 2004, filed with the Securities and Exchange Commission on August 5, 2004;

4. Our current report on Form 8-K, filed with the Securities and Exchange Commission on February 17, 2004 (except for information contained in Item 12 or any related exhibit);

5. Our current report on Form 8-K, filed with the Securities and Exchange Commission on May 4, 2004 (except for information contained in Item 12 or any related exhibit);

6. Our current report on Form 8-K, filed with the Securities and Exchange Commission on June 30, 2004 (except for information contained in Item 9 or any related exhibit);

7. Our current report on Form 8-K, filed with the Securities and Exchange Commission on August 5, 2004 (except for information contained in Item 12 or any related exhibit);

8. Our current report on Form 8-K, filed with the Securities and Exchange Commission on September 16, 2004 (except for information contained in Item 9 or any related exhibit);

9. Our current report on Form 8-K, filed with the Securities and Exchange Commission on September 23, 2004;

10. Our current report on Form 8-K, filed with the Securities and Exchange Commission on September 28, 2004 (except for information contained in Item 7.01 or any related exhibit);

11. Our current report on Form 8-K, filed with the Securities and Exchange Commission on October 21, 2004 (except for information contained in Item 7.01 or any related exhibit); and

12. The description of our common stock set forth in our registration statement on Form 8-A, filed with the Securities and Exchange Commission on April 6, 2000, including any amendments or reports filed for the purposes of updating this description.

We will furnish without charge to you, upon written or oral request, a copy of any or all of the documents incorporated by reference, including exhibits to these documents. You should direct any requests for documents to Exelixis, Inc., Attention: Corporate Secretary, 170 Harbor Way, P.O. Box 511, South San Francisco, California 94083. Our phone number is (650) 837-7000.

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No dealer, salesperson or other person is authorized to give any information or to represent anything not contained in this prospectus supplement or the accompanying prospectus. You must not rely on any unauthorized information or representations. This prospectus supplement is an offer to sell only the shares offered hereby, but only under circumstances and in jurisdictions where it is lawful to do so. The information contained in this prospectus supplement and the accompanying prospectus is current only as of its date.

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Prospectus Supplement

9,000,000 Shares

Exelixis, Inc.

Common Stock

Goldman, Sachs & Co.

Cowen and Company

Banc of America Securities LLC

Piper Jaffray