

EXELIXIS INC
 Form 424B5
 September 11, 2007
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Filed pursuant to Rule 424(b)(5)
 File No. 333-145965

CALCULATION OF REGISTRATION FEE

Title of Each Class of Securities to be Registered	Amount to be Registered	Maximum Offering Price per Share(1)	Maximum Aggregate Offering Price(1)	Amount of Registration Fee(2)
Common Stock, par value \$.001 per share	8,050,000	\$11.145	\$89,717,250	\$2,755

- (1) Estimated pursuant to Rule 457(c) under the Securities Act of 1933, as amended, the offering price and registration fee are based on the average of the high and low prices for the Common Stock on September 4, 2007, as reported on the Nasdaq Global Select Market.
- (2) Calculated in accordance with Rule 457(r) under the Securities Act of 1933, as amended.

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Prospectus Supplement to Prospectus dated September 10, 2007.

7,000,000 Shares

Common Stock

Exelixis, Inc. is offering 7,000,000 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 10, 2007 was \$11.16 per share.

See Risk Factors beginning on page S-6 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.

Goldman, Sachs & Co. has agreed to purchase the common stock from Exelixis at a price of \$10.30 per share, which will result in \$72,100,000 of proceeds to Exelixis before deducting offering expenses.

Goldman, Sachs & Co. may offer the common stock in transactions on the Nasdaq Global Select Market, in the over-the-counter market or through negotiated transactions at market prices or at negotiated prices.

To the extent that Goldman, Sachs & Co. sells more than 7,000,000 shares of common stock, Goldman, Sachs & Co. has the option to purchase up to an additional 1,050,000 shares from Exelixis at a price of \$10.30 per share within 30 days of the date of this prospectus supplement.

Goldman, Sachs & Co. expects to deliver the shares against payment in New York, New York on September 13, 2007.

Goldman, Sachs & Co.

Prospectus Supplement dated September 10, 2007.

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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 September 10, 2007, 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, the company, us and our refer to Exelixis, Inc. and its subsidiaries and 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 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. Investors should carefully consider the information set forth under *Risk Factors* in this prospectus supplement.*

Exelixis, Inc.

We are committed to developing innovative therapies for cancer and other serious diseases. Through our drug discovery and development activities, we are building a portfolio of novel compounds that we believe have the potential to be high-quality, differentiated pharmaceutical products. Our most advanced pharmaceutical programs focus on drug discovery and development of small molecules in cancer.

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 quickly in research and development. This approach allows us to select highly qualified drug candidates that meet our extensive development criteria from a large pool of compounds.

To date, we have filed 14 investigational new drug applications, or INDs, with the United States Food and Drug Administration, or FDA. We believe that our deep pool of drug candidates will enable us to continue to file multiple 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.

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, a share of the profits and the opportunity to receive milestone payments and royalties (as applicable) from research results and subsequent product development activities. We also have collaborations in which we retain the right to co-promote products in the United States. We have ongoing commercial collaborations with several leading pharmaceutical and biotechnology companies, including GlaxoSmithKline, Bristol-Myers Squibb Company and Genentech, Inc. 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.

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Our current development portfolio includes the following compounds, for which we are leading development:

Compound	Principal Targets	Indication	Stage of Development
XL647*	EGFR, HER2, VEGFR2	Cancer	Phase 2
XL784*	ADAM10, MMP2	Diabetic nephropathy	Phase 2
XL880	MET, VEGFR2	Cancer	Phase 2
XL999*	VEGFR2, PDGFR, FGFR, FLT3	Cancer	Phase 1
XL820	KIT, VEGFR2, PDGFR	Cancer	Phase 1
XL184	MET, VEGFR2, RET	Cancer	Phase 1
XL844	CHK1, CHK2	Cancer	Phase 1
XL518**	MEK	Cancer	Phase 1
XL418	AKT, S6K	Cancer	Phase 1
XL281	RAF	Cancer	Phase 1
XL228	ABL, SRC, IGF1R	Cancer	Phase 1
XL147	PI3K	Cancer	Phase 1
XL765	PI3K, mTOR	Cancer	Phase 1
XL019	JAK2	Cancer	Phase 1

* Out-licensed to Symphony Evolution, Inc. and subject to a repurchase option.

** In co-development collaboration with Genentech, Inc.

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 except XL518, XL147, XL765 and XL019. On July 26, 2007, we announced that GlaxoSmithKline decided not to exercise this option with respect to XL647.

In addition to the compounds identified in the above table, we have compounds in various stages of development that are being developed by our partners, such as Bristol-Myers Squibb, Daiichi Sankyo Company Limited and Wyeth Pharmaceuticals. We also have compounds in preclinical development that we are developing internally.

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 prospectus supplement. Our website address is included in this prospectus supplement as an inactive textual reference only.

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The Offering

Common stock offered by Exelixis	7,000,000 shares
Common stock to be outstanding after the offering	104,273,574 shares
Use of proceeds	To fund clinical development and for working capital and general corporate purposes.
Risk factors	See Risk Factors beginning on page S-6 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, 2007. As of that date, we had 97,273,574 shares of common stock outstanding, excluding:

20,659,561 shares of common stock underlying options and warrants outstanding as of June 30, 2007 at a weighted average exercise price of \$10.22 per share;

7,404,960 shares available for future grant under our 2000 Equity Incentive Plan, 1,282,844 shares available for future issuance under our 2000 Employee Stock Purchase Plan and 1,174,696 shares available for future grant under our 2000 Non-Employee Directors Stock Option Plan, all as of June 30, 2007; and

8,652,615 shares issuable upon conversion of our convertible debt (assuming that the debt had been converted as of June 30, 2007).

Unless we specifically state otherwise, the information in this prospectus supplement assumes that the underwriter does not exercise its option to purchase up to 1,050,000 additional shares of our common stock within 30 days after the date of this prospectus supplement.

Table of Contents**Summary Consolidated Financial Data**

We derived the following information from our audited consolidated financial statements for each of the three years ended December 31, 2004, 2005 and 2006, our unaudited condensed consolidated balance sheet as of June 30, 2007 and our unaudited condensed consolidated statements of operations for the six months ended June 30, 2006 and 2007. In the opinion of our management, our unaudited 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, 2007 are not necessarily indicative of the results that may be expected for the year ending December 31, 2007. 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".

In 2006, Exelixis adopted a 52- or 53-week fiscal year that ends on the last Friday in December, and the fiscal quarters end on the last Friday of the quarter. Fiscal year 2006, a 52-week year, ended on December 29, 2006 and fiscal year 2007, a 52-week year, will end on December 28, 2007. For convenience, references in this prospectus supplement as of and for the fiscal year ended December 29, 2006 are indicated on a calendar year basis, ending December 31, 2006, and as of and for the three- and six-month periods ended June 29, 2007 are indicated as ending June 30, 2007.

	Year Ended December 31,			Six Months Ended	
	2004	2005	2006	2006	2007
				June 30, (unaudited)	
(in thousands, except per share data)					
Consolidated Statement of Operations Data					
Total revenues	\$ 52,857	\$ 75,961	\$ 98,670	\$ 45,359	\$ 57,395
Total operating expenses	\$ 188,059	\$ 169,952	\$ 225,424	\$ 106,799	\$ 129,054
Net loss	\$ (137,245)	\$ (84,404)	\$ (101,492)	\$ (51,113)	\$ (52,763)
Net loss per share, basic and diluted	\$ (1.89)	\$ (1.07)	\$ (1.17)	\$ (0.61)	\$ (0.55)
Shares used in computing basic and diluted net loss per share	72,504	78,810	86,602	83,867	96,694

	As of June 30, 2007	
	Actual	Adjusted(1)
	(unaudited)	
(in thousands)		
Consolidated Balance Sheet Data		
Cash and cash equivalents and short-term and long-term marketable securities (including restricted cash and investments of \$8.9 million and investments held by Symphony Evolution, Inc. of \$44.7 million)	\$ 253,006	\$ 324,806
Working capital	\$ 125,064	\$ 196,864
Total assets	\$ 371,788	\$ 443,588
Long-term obligations, less current portion	\$ 125,968	\$ 125,968
Accumulated deficit	\$ (758,032)	\$ (758,032)
Total stockholders' equity	\$ 19,784	\$ 91,584

- (1) As adjusted to give effect to the purchase from us of 7,000,000 shares of common stock offered pursuant to this prospectus supplement at a price of \$10.30 per share, after deducting the estimated offering expenses payable by us.

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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, 2007, we had \$253.0 million in cash and cash equivalents and short-term and long-term marketable securities, which included investments held by Symphony Evolution, Inc., or SEI, of \$44.7 million and restricted cash and investments of \$8.9 million. We anticipate that the anticipated net proceeds of this offering and our current cash and cash equivalents, short-term and long-term 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 a period of at least 12 months following the date of this prospectus supplement. 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 currently anticipate. These factors include:

the timing and progress of the clinical development of our product candidates XL647, XL999 and XL784, which are out-licensed to SEI. If any of the Phase 2 clinical trials for XL647, XL999 or XL784 show positive results that support further clinical development of any such product candidate, in order for us or, with respect to XL999 and XL784, GlaxoSmithKline, to pursue further development of such product candidate(s), we would be required to reacquire all three product candidates (XL647, XL999 and XL784) from SEI's investors through the exercise of our exclusive purchase option, which is described in our Quarterly Report on Form 10-Q for the quarterly period ended June 29, 2007, which is incorporated by reference into this prospectus supplement. Under our amended purchase option agreement with SEI, we cannot repurchase a single product candidate without also repurchasing the other two product candidates. The purchase price, which may be paid in cash and/or shares of our common stock, at our sole discretion, would be equal to the sum of (i) the total amount of capital invested in SEI by its investors (\$80.0 million) and (ii) an amount equal to 25% per year on such funded capital;

whether and when GlaxoSmithKline selects at clinical proof-of-concept for further development XL999 or XL784, which would require us to repurchase all three product candidates from SEI through the exercise of our purchase option. GlaxoSmithKline has the right to select for further

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clinical development at clinical proof-of-concept XL999 and XL784, two of the product candidates licensed to SEI. If GlaxoSmithKline selects any of these product candidates, it would be necessary for us to repurchase all three product candidates licensed to SEI through the exercise of our purchase option in order to satisfy our contractual obligations to GlaxoSmithKline. GlaxoSmithKline has decided not to exercise this right at clinical proof-of-concept for XL647;

the amount of any selection milestones received from GlaxoSmithKline as a result of a product candidate selection by GlaxoSmithKline compared to the amount we are required to pay to reacquire XL647, XL999 and XL784 from SEI's investors through the exercise of our purchase option. Under our product development and commercialization agreement with GlaxoSmithKline, a product candidate selection by GlaxoSmithKline would trigger milestone payments. The size of these milestone payments depends largely on how quickly we can advance product candidates to clinical proof-of-concept. As described in this prospectus supplement, on July 26, 2007, we announced that GlaxoSmithKline decided not to exercise its option under our product development and commercialization agreement to elect to develop and commercialize XL647 at clinical proof-of-concept. Since GlaxoSmithKline did not select XL647, if it later selects XL999 or XL784, and there are delays in obtaining clinical proof-of-concept for XL999 or XL784, the amount of any GlaxoSmithKline milestone payments would be significantly decreased due to the delays and would therefore cover only a small portion of the purchase price with respect to SEI. In addition, the selection milestone payment for the first compound selected by GlaxoSmithKline will be reduced by \$36.0 million to account for a milestone payment that GlaxoSmithKline advanced to us in 2005 as part of an amendment to the product development and commercialization agreement;

whether any future milestone payments from GlaxoSmithKline relate to product candidates licensed to SEI. Under our product development and commercialization agreement with GlaxoSmithKline, any milestone payments relating to product candidates not licensed to SEI must be used to pay down our loan with GlaxoSmithKline as long as the loan is outstanding. As of June 30, 2007, the aggregate principal and interest outstanding under our GlaxoSmithKline loan was \$96.9 million;

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 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;

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;

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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.

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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 anticipate. 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, 2007, our working capital was \$125.1 million and our cash and investments were \$244.1 million. 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 \$96.9 million at June 30, 2007.

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 since inception, including a net loss of \$28.6 million for the three month period ended June 30, 2007 and \$52.8 million for the six month period ended June 30, 2007. As of that date, we had an accumulated deficit of \$758.0 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 Pharmaceuticals, our only revenues to date are license revenues and revenues under contracts with our partners. The amount 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 additional IND applications for additional product candidates within the next 12 months. 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

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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 option to acquire these product candidates in the future. We may not have the financial resources to exercise this option or sufficient clinical data in order to determine whether we should exercise this option.

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, and granted to SEI five-year warrants to purchase shares of our common stock. In exchange, 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. The option exercise price may be paid in cash and/or shares of our common stock, at our sole discretion.

If we elect to exercise the purchase option, 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 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 option prior to its expiration, our rights to purchase all of the equity in SEI and to reacquire XL647, XL999 and XL784 will terminate. We may not have the financial resources to exercise the option, 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 option.

In addition, under our collaboration with GlaxoSmithKline, GlaxoSmithKline may continue to select at clinical proof-of-concept for further development one or more of the product candidates licensed to SEI, in which case we would be required under our amended purchase option agreement with SEI to repurchase all product candidates licensed to SEI through the exercise of our purchase option. If, after receiving any selection milestones from GlaxoSmithKline, we are unable to pay the purchase option exercise price in cash and/or delivery of our shares of our common stock, we could be in breach of our product development and commercialization 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 have a significant adverse effect on our business, operating results and financial condition.

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

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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.

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.

Any serious adverse cardiovascular events observed in our phase 1 clinical trial evaluating XL999 in patients with non-small cell lung cancer, or NSCLC, may result in significant delays or termination of clinical testing, which could harm our business, operating results and financial condition.

In April 2007, we were notified by the FDA that it had completed its review of a clinical trial protocol for a phase 1 dose-escalation trial of XL999 in patients with NSCLC and agreed that the trial may be initiated. XL999 was previously evaluated in phase 1 and 2 clinical trials in which cardiovascular adverse events were observed. These observations caused us to suspend new patient

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enrollment in the ongoing XL999 clinical trials in November 2006. The FDA subsequently placed the clinical program on partial clinical hold in December 2006. The previous phase 1 and 2 clinical trials will not be re-initiated at this time. Given acceptance by the FDA of the new clinical trial protocol for XL999 in patients with NSCLC, the XL999 development program will now focus on this indication.

We may experience a number of events that could continue to delay or prevent development of XL999, including:

analysis of data from the new XL999 clinical trial may show that XL999 cannot be administered safely at a therapeutic dose;

failure to enroll patients in the new XL999 clinical trial in a timely manner or at all;

regulators or institutional review boards may not authorize or may delay, suspend or terminate the clinical trial program for XL999 due to the observed adverse cardiovascular or other effects; and

any disagreements between SEI and the company regarding the further clinical development of XL999.

In addition, because the size of acceptance milestones is reduced over time under our agreement with GlaxoSmithKline, delays in the clinical development of XL999 may result in reduced acceptance milestone payments if GlaxoSmithKline selects XL999 for further clinical development. The occurrence of any of the foregoing events could delay or prevent commercialization of XL999 and harm our business, operating results and financial condition.

Risks Related to Our Relationships with Third Parties

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 are 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 us 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

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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. 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 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.

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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 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 have a significant adverse affect on 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,

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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 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

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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, if at all, 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 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, President Bush 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.

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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 biotechnology and pharmaceutical 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

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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.

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

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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 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 clinical development personnel to fully execute our business plan. Recruiting and retaining qualified clinical and scientific 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 clinical personnel, and we may be unable to retain or recruit clinical personnel 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

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employees and may have other commitments that limit their availability to us. Although these advisors and collaborators 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 such a circumstance, we may lose work performed by them, and our development efforts with respect to the matters on which they were working maybe significantly delayed or otherwise adversely affected. 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, development, 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, rules and regulations implemented by the Securities and Exchange Commission 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 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.

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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 face liability for any injury or contamination that results from our use or the use by third parties of these materials, and such 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. 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 could harm our reputation and business and would decrease our cash reserves.

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;

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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;

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;

conflicts or litigation with our collaborators;

litigation, including intellectual property infringement and product liability lawsuits, involving us;

failure to achieve operating results projected by securities analysts;

changes in earnings estimates or recommendations by securities analysts;

financing transactions;

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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.

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

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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, project, 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-6 of this prospectus supplement, in the documents incorporated by reference or as a result of other circumstances beyond our control. 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.

USE OF PROCEEDS

We estimate that the net proceeds from the sale of the 7,000,000 shares of common stock we are offering will be approximately \$71.8 million, after deducting the estimated offering expenses payable by us. If the underwriter exercises in full its option to purchase additional shares, we estimate that the net proceeds to us will be approximately \$82.6 million.

We anticipate using the net proceeds to us from the sale of the common stock in this offering to fund clinical development 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.

Table of Contents**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, 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 ended December 31, 2006		
First Quarter	\$ 12.21	\$ 9.22
Second Quarter	12.49	9.00
Third Quarter	10.24	7.53
Fourth Quarter	10.65	7.81
Year ending December 31, 2007		
First Quarter	\$ 11.74	\$ 8.67
Second Quarter	12.77	9.92
Third Quarter (through September 10, 2007)	12.37	9.40

The reported last sale price of our common stock on the Nasdaq Global Select Market on September 10, 2007 was \$11.16 per share. As of September 7, 2007, there were approximately 662 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.

Table of Contents**DILUTION**

Our net tangible book value (deficit) on June 30, 2007 was approximately \$(26.0) million, or approximately \$(0.27) 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, 2007. 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 purchase from us of 7,000,000 shares of common stock in this offering at a price of \$10.30 per share, and after deducting the estimated offering expenses payable by us, our net tangible book value on June 30, 2007 would have been approximately \$45.8 million, or approximately \$0.44 per share. Based on an assumed public offering price of \$11.16 per share (which was the last reported sale price of our common stock on the date of this prospectus supplement), this represents an immediate dilution of \$10.72 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	\$ 11.16
Net tangible book value (deficit) per share as of June 30, 2007	\$ (0.27)
Increase per share attributable to new investors	0.71
Net tangible book value per share as of June 30, 2007 after giving effect to this offering	0.44
Dilution per share to new investors	\$ 10.72

The foregoing discussion and table do not take into account further dilution to new investors that could occur upon the exercise of the underwriter's option to purchase up to an additional 1,050,000 shares within 30 days of the date of this prospectus supplement or the exercise of other outstanding options and warrants having a per share exercise price less than the assumed per share offering price to the public in this offering. As of June 30, 2007, there were:

20,659,561 shares of common stock underlying options and warrants outstanding at a weighted average exercise price of \$10.22 per share;

7,404,960 shares available for future grant under our 2000 Equity Incentive Plan, 1,282,844 shares available for future issuance under our 2000 Employee Stock Purchase Plan and 1,174,696 shares available for future grant under our 2000 Non-Employee Directors' Stock Option Plan; and

8,652,615 shares issuable upon conversion of our convertible debt (assuming that the debt had been converted as of June 30, 2007).

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UNDERWRITING

The company and Goldman, Sachs & Co. have entered into an underwriting agreement with respect to the shares being offered. Subject to certain conditions, Goldman, Sachs & Co. has agreed to purchase all of the shares offered hereby.

Goldman, Sachs & Co. may receive from purchasers of the shares normal brokerage commissions in amounts agreed with such purchasers.

Goldman, Sachs & Co. proposes to offer the shares of common stock from time to time for sale in one or more transactions in the Nasdaq Global Select Market, in the over-the-counter market, through negotiated transactions or otherwise at market prices prevailing at the time of sale, at prices related to prevailing market prices or at negotiated prices, subject to receipt and acceptance by it and subject to its right to reject any order in whole or in part. In connection with the sale of the shares of common stock offered hereby, Goldman, Sachs & Co. may be deemed to have received compensation in the form of underwriting discounts. Goldman, Sachs & Co. may effect such transactions by selling shares of common stock to or through dealers, and such dealers may receive compensation in the form of discounts. Goldman, Sachs & Co. may effect such transactions by selling shares of common stock to or through dealers, and such dealers may receive compensation in the form of discounts, concessions or commissions from Goldman, Sachs & Co. and / or purchasers of shares of common stock for whom they may act as agents or to whom they may sell as principal.

Goldman, Sachs & Co. is 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 Goldman, Sachs & Co. sells more shares than the total number being offered, Goldman, Sachs & Co. has an option to buy up to an additional 1,050,000 shares from the company to cover such sales. Goldman, Sachs & Co. may exercise that option for 30 days after the date of this prospectus supplement.

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 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 8,125 shares may be sold each month under such plan during the 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 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 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, Goldman, Sachs & Co. 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 Goldman, Sachs &

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Co. of a greater number of shares than it is required to purchase in the offering. Covered short sales are sales made in an amount not greater than Goldman, Sachs & Co.'s option to purchase additional shares from the company in the offering. Goldman, Sachs & Co. may close out any covered short position by either exercising its 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, Goldman, Sachs & Co. will consider, among other things, the price of shares available for purchase in the open market as compared to the price at which it may purchase additional shares pursuant to the option granted to it. Naked short sales are any sales in excess of such option. Goldman, Sachs & Co. 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 Goldman, Sachs & Co. is 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 Goldman, Sachs & Co. in the open market prior to the completion of the offering.

Purchases to cover a short position and stabilizing transactions, as well as other purchases by Goldman, Sachs & Co. for its own account, may have the effect of preventing or retarding a decline in the market price of the company's stock, and 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.

Goldman, Sachs & Co. has represented and agreed that:

- (a) 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
- (b) 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.

In relation to each Member State of the European Economic Area which has implemented the Prospectus Directive (each, a Relevant Member State), Goldman, Sachs & Co. 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 authorised or regulated to operate in the financial markets or, if not so authorised 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;

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- (c) to fewer than 100 natural or legal persons (other than qualified investors as defined in the Prospectus Directive) subject to obtaining the prior consent of the representatives for any such offer; or

- (d) 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 to persons whose ordinary business is to buy or sell shares or debentures, whether as principal or agent, or in circumstances which do not constitute an offer to the public within the meaning of the Companies Ordinance (Cap. 32) of Hong Kong, and no advertisement, invitation or document relating to the shares may be issued, 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 securities laws of Hong Kong) other than with respect to shares which are or 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) 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.

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 Goldman, Sachs & Co. 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

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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 underwriting discounts, will be approximately \$300,000.

The company has agreed to indemnify Goldman, Sachs & Co. and its controlling persons against certain liabilities, including liabilities under the Securities Act of 1933.

Goldman, Sachs & Co. and its 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 it received or will receive customary fees and expenses.

VALIDITY OF COMMON STOCK

The validity of the common stock offered hereby will be passed upon for us by Cooley Godward Kronish LLP, Palo Alto, California, and for Goldman, Sachs & Co. 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 29, 2006, and management's assessment of the effectiveness of our internal control over financial reporting as of December 29, 2006, as set forth in their reports, which are incorporated by reference in this prospectus supplement and accompanying prospectus and elsewhere in the registration statement. Our 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.

Common Stock

From time to time, we may offer and sell shares of common stock in amounts, at prices and on terms described in one or more supplements to this prospectus.

This prospectus describes some of the general terms that may apply to an offering of our common stock. The specific terms and any other information relating to a specific offering will be set forth in a post-effective amendment to the registration statement of which this prospectus is a part or in a supplement to this prospectus or may be set forth in one or more documents incorporated by reference in 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.

We may offer and sell shares of common stock to or through one or more underwriters, dealers and agents, or directly to purchasers, on a continuous or delayed basis. The supplements to this prospectus will provide the specific terms of the plan of distribution.

Our common stock is traded on The Nasdaq Global Select Market under the trading symbol EXEL. On September 7, 2007, the last reported sale price of our common stock was \$11.35 per share.

Investing in our securities involves a high degree of risk. You should review carefully the risks and uncertainties described under the heading Risk Factors contained in any applicable prospectus supplement and under similar headings in the other documents that are incorporated by reference into this prospectus.

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.

The date of this Prospectus is September 10, 2007

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ABOUT THIS PROSPECTUS

This prospectus is part of a registration statement on Form S-3 that we filed with the Securities and Exchange Commission using the shelf registration process. By using a shelf registration statement, we may offer and sell from time to time in one or more offerings the common stock described in this prospectus. No limit exists on the aggregate number of shares of common stock we may sell pursuant to the registration statement.

You should rely only on the information contained in or incorporated by reference into this prospectus or any applicable prospectus supplement. We have not authorized anyone to provide you with different information. This document may only be used where it is legal to sell these securities. You should not assume that the information contained in this prospectus, or in any prospectus supplement, is accurate as of any date other than its date regardless of the time of delivery of the prospectus or prospectus supplement or any sale of the common stock. If there is any inconsistency between the information in this prospectus and a prospectus supplement, you should rely on the information in the prospectus supplement.

This prospectus and the information incorporated herein by reference includes trademarks, service marks and trade names owned by us or others. All trademarks, service marks and trade names included or incorporated by reference into this prospectus or any applicable prospectus supplement are the property of their respective owners.

We urge you to read carefully both this prospectus and any applicable prospectus supplement, together with the information incorporated herein by reference as described under the heading "Where You Can Find More Information," before deciding whether to invest in any of the securities being offered.

References in this prospectus to Exelixis, we, us and our refer to Exelixis, Inc., a Delaware corporation and its subsidiaries. Our principal executive offices are located at 170 Harbor Way, P.O. Box 511, South San Francisco, CA 94083 and our telephone number is (650) 837-7000. Our web site address is <http://www.exelixis.com>. The information contained in, or that can be accessed through, our web site is not part of this prospectus.

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RISK FACTORS

Investment in our securities involves a high degree of risk. You should consider carefully the risk factors identified in any prospectus supplements and our most recent annual and quarterly filings with the Securities and Exchange Commission (the SEC), 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.

FORWARD-LOOKING STATEMENTS

This prospectus and the documents incorporated by reference contain forward-looking statements that are based on our management's beliefs and assumptions and on information currently available to our management. Discussions containing these forward-looking statements may be found, among other places, in Business, Risk Factors and Management's Discussion and Analysis of Financial Condition and Results of Operations incorporated by reference from our most recent annual report on Form 10-K and in our most recent quarterly report on Form 10-Q, as well as any amendments thereto reflected in subsequent filings with the SEC. Forward-looking statements include, but are not limited to, statements about:

our expectations with respect to potential commercialization of any of our product candidates;

our expectations with respect to regulatory submissions and approvals and our clinical trials;

our expectations with respect to our intellectual property position; and

our estimates regarding our capital requirements and our need for additional financing.

In some cases, you can identify forward-looking statements by terms such as may, will, should, could, would, expects, plan, anticipates, believes, estimates, projects, predicts, potential and similar expressions intended to identify forward-looking statements. These statements involve known and unknown risks, uncertainties and other factors which may cause our actual results, performance time frames or achievements to be materially different from any future results, performance, time frames or achievements expressed or implied by the forward-looking statements. We discuss many of these risks, uncertainties and other factors in greater detail under the heading Risk Factors contained in any applicable prospectus supplements and in our most recent annual report on Form 10-K and in our most recent quarterly report on Form 10-Q, as well as any amendments thereto reflected in subsequent filings with the SEC. Given these risks, uncertainties and other factors, you should not place undue reliance on these forward-looking statements. Also, these forward-looking statements represent our estimates and assumptions only as of the date such forward-looking statements are made. You should read carefully both this prospectus and any applicable prospectus supplements, together with the information incorporated herein by reference as described under the heading Where You Can Find More Information, completely and with the understanding that our actual future results may be materially different from what we expect. We hereby qualify all of our forward-looking statements by these cautionary statements.

Except as required by law, we assume no obligation to update these forward-looking statements publicly, or to update the reasons actual results could differ materially from those anticipated in these forward-looking statements, even if new information becomes available in the future.

USE OF PROCEEDS

Except as described in any prospectus supplement, we anticipate using the net proceeds to us from the sale of our common stock for research and development and other general corporate

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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 these uses, we intend to invest the net proceeds in investment-grade, interest-bearing securities.

DESCRIPTION OF CAPITAL STOCK

We may issue shares of our common stock from time to time in one or more offerings. We will set forth in the applicable prospectus supplement a description of the terms of the offering of common stock, including the offering price, the net proceeds to us and other offering material relating to such offering.

VALIDITY OF COMMON STOCK

The validity of the common stock being offered hereby will be passed upon for us by Cooley Godward Kronish LLP, Palo Alto, California, and for any underwriters, dealers or agents by counsel named in the applicable prospectus supplement. As of the date of this prospectus, certain partners and associates of Cooley Godward Kronish LLP own an aggregate of approximately 7,943 shares of our common stock, either individually or through investment partnerships.

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 29, 2006, and management's assessment of the effectiveness of our internal control over financial reporting as of December 29, 2006, as set forth in their reports, which are incorporated by reference in this prospectus and elsewhere in the registration statement. 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.

WHERE YOU CAN FIND MORE INFORMATION

We file annual, quarterly and special reports, proxy statements and other information with the SEC. You may read and copy any document we file at the SEC's Public Reference Room at 100 F Street, N.E., Washington, D.C. 20549. Please call the SEC at 1-800-SEC-0330 for more information about the operation of the public reference room. The SEC maintains an Internet site that contains reports, proxy and information statements, and other information regarding issuers that file electronically with the SEC, including Exelixis. The SEC's Internet site can be found at <http://www.sec.gov>.

The SEC allows us to incorporate by reference the information we file with it, which means that we can disclose important information to you by referring you to another document that we have filed separately with the SEC. You should read the information incorporated by reference because it is an important part of this prospectus. We incorporate by reference the following information or documents that we have filed with the SEC (Commission File No. 0-30235):

The following documents filed with the SEC are incorporated by reference in this prospectus:

Our current report on Form 8-K, filed with the SEC on January 5, 2007;

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Our current report on Form 8-K, filed with the SEC on January 22, 2007;

Our current report on Form 8-K relating to Item 5.02 of Form 8-K, filed with the SEC on February 13, 2007;

Our annual report on Form 10-K for the fiscal year ended December 29, 2006, filed with the SEC on February 27, 2007 (the 2006 10-K);

The information specifically incorporated by reference into our 2006 10-K from our definitive proxy statement on Schedule 14A filed with the SEC on March 29, 2007;

Our current report on Form 8-K, filed with the SEC on April 25, 2007;

Our quarterly report on Form 10-Q for the quarter ended March 30, 2007, filed with the SEC on May 3, 2007;

Our current report on Form 8-K, filed with the SEC on July 10, 2007;

Our current report on Form 8-K, filed with the SEC on July 26, 2007;

Our quarterly report on Form 10-Q for the quarter ended June 29, 2007, filed with the SEC on August 7, 2007;

Our current report on Form 8-K, filed with the SEC on August 24, 2007;

Our current report on Form 8-K, filed with the SEC on September 4, 2007;

Our current report on Form 8-K, filed with the SEC on September 10, 2007; and

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

Any information in any of the foregoing documents will automatically be deemed to be modified or superseded to the extent that information in this prospectus or in a later filed document that is incorporated or deemed to be incorporated herein by reference modifies or replaces such information.

We also incorporate by reference any future filings (other than current reports furnished under Item 2.02 or Item 7.01 of Form 8-K and exhibits filed on such form that are related to such items) made with the SEC pursuant to Sections 13(a), 13(c), 14 or 15(d) of the Exchange Act, until we file a post-effective amendment which indicates the termination of the offering of the securities made by this prospectus. Information in such future filings updates and supplements the information provided in this prospectus. Any statements in any such future filings will automatically be deemed to modify and supersede any information in any document we previously filed with the SEC that is incorporated or deemed to be incorporated herein by reference to the extent that statements in the later filed document modify or replace such earlier statements.

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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: Investor Relations, 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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7,000,000 Shares

Exelixis, Inc.

Common Stock

PROSPECTUS SUPPLEMENT

Goldman, Sachs & Co.
