

EXELIXIS INC
Form 424B5
August 17, 2005

Filed Pursuant to Rule 424(b)(5)
Registration No. 333-66134

Prospectus Supplement to Prospectus dated August 7, 2001.

6,500,000 Shares

Common Stock

Exelixis, Inc. is selling 6,500,000 shares of its common stock by this prospectus supplement.

The common stock is quoted on the Nasdaq National Market under the symbol EXEL. The last reported sale price of the common stock on August 16, 2005 was \$8.20 per share.

See Risk Factors beginning on page S-5 and Cautionary Note Regarding Forward-Looking Statements on page S-23 to read about factors you should consider before buying shares of the common stock.

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

	Per Share	Total
Initial price to public	\$ 7.75	\$ 50,375,000
Underwriting discount	\$ 0.10	\$ 650,000
Proceeds, before expenses, to Exelixis	\$ 7.65	\$ 49,725,000

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

Goldman, Sachs & Co. expects to deliver the shares against payment in New York, New York on August 19, 2005.

Goldman, Sachs & Co.

Prospectus Supplement dated August 16, 2005.

ABOUT THIS PROSPECTUS SUPPLEMENT

You should read this prospectus supplement along with the accompanying prospectus carefully before you invest in our common stock. Both documents contain important information you should consider when making your investment decision. This prospectus supplement may add, update or change information in the accompanying prospectus. You should rely only on the information provided in this prospectus supplement and the accompanying prospectus or incorporated by reference in the accompanying prospectus. We have not, and the underwriter has not, authorized anyone to provide you with different information. We are not, and the underwriter is not, making an offer to sell our common stock in any jurisdiction where the offer or sale is not permitted.

To the extent there is a conflict between the information contained in this prospectus supplement, on the one hand, and the information contained in the accompanying prospectus, on the other hand, the information contained in this prospectus supplement shall control.

PROSPECTUS SUPPLEMENT SUMMARY

This is a summary of the information contained elsewhere in this prospectus supplement and the accompanying prospectus or incorporated by reference into the accompanying prospectus. Investors should carefully consider the information set forth under Risk Factors in this prospectus supplement and in the accompanying prospectus.

Exelixis, Inc.

Exelixis, Inc. is a biopharmaceutical company whose primary mission is to use its biological expertise and integrated drug discovery capabilities to develop high-quality, differentiated pharmaceutical products for the treatment of cancer, metabolic disorders, cardiovascular disease and other serious diseases. Our clinical development pipeline currently includes the following compounds in cancer and renal disease: XL119 (becatecarin), for which a Phase 3 clinical trial is ongoing in patients with bile duct tumors and which has been exclusively licensed to Helsinn Healthcare S.A. with rights to reacquire the commercial rights for North America for the use in the indications of gall bladder cancer and bile duct tumors; XL784, initially an anticancer compound, currently being developed as a treatment for renal disease for which we anticipate initiating additional clinical studies in 2005; XL647, XL999, XL880 and XL820, anticancer compounds in ongoing Phase 1 clinical trials; and XL844 and XL184, anticancer compounds for which investigational new drug applications (or INDs) were filed in the second quarter of 2005. We have licensed to Symphony Evolution, Inc. (or SEI) our intellectual property rights related to XL784, XL647 and XL999, with rights to reacquire all or one of the programs. We continue to be primarily responsible for the clinical development of these product candidates. Pursuant to a product development and commercialization agreement between Exelixis and GlaxoSmithKline (or GSK), GSK has the option, after completion of Phase IIa clinical trials, to elect to develop two or three compounds in Exelixis' product candidate pipeline, including any of the cancer compounds identified above (other than XL119, but including XL784), thus potentially triggering milestone payments and royalties from GSK and co-promotion rights by Exelixis.

Our preclinical pipeline, which is comprised of six programs, includes three cancer programs (XL281, XL418 and XL228) focused on the inhibition of the RAF, Akt/S6k and insulin growth factor 1 receptor (or IGF1R) kinases and three programs in metabolic and cardiovascular disease that target the nuclear hormone receptors LXR (Liver X Receptor), FXR (Farnesoid X Receptor) and MR (Mineralocorticoid Receptor). We anticipate advancing at least some of these drug candidates in 2005, with the potential of filing INDs beginning in 2006.

We have established collaborations with major pharmaceutical and biotechnology companies based on the strength of our technologies and expertise in biology, drug discovery and development to support additional development of our proprietary products. Through these collaborations, we obtain license fees and research funding, together with the opportunity to receive milestone payments and royalties from research results and subsequent product development. In addition, many of our collaborations have been structured strategically to provide us access to technology to rapidly advance our internal programs.

We were incorporated in Delaware in November 1994 as Exelixis Pharmaceuticals, Inc. and we changed our name to Exelixis, Inc. in February 2000. Our principal executive offices are located at 170 Harbor Way, P.O. Box 511, South San Francisco, California 94083. Our telephone number is

(650) 837-7000 and our website is <http://www.exelixis.com>. We have not incorporated by reference into this prospectus supplement or the accompanying prospectus the information on our website, and you should not consider it to be a part of this document. Our website address is included in this document as an inactive textual reference only.

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

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The Offering

Common stock offered by Exelixis	6,500,000 shares
Common stock to be outstanding after the offering	83,013,223 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-5 and Cautionary Note Regarding Forward-Looking Statements on page S-23 for a discussion of factors you should consider before buying shares of our common stock.
Nasdaq National 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, 2005. As of that date, we had 76,513,223 shares of common stock outstanding, excluding:

12,002,951 shares of common stock underlying options and warrants outstanding as of June 30, 2005 at a weighted average exercise price of \$11.05 per share;

7,120,389 shares available for future grant under our 2000 Equity Incentive Plan, 1,308,022 shares available for future issuance under our 2000 Employee Stock Purchase Plan and 1,299,695 shares available for future grant under our 2000 Non-Employee Directors Stock Option Plan, all as of June 30, 2005; and

16,154,088 shares issuable upon conversion of our convertible debt (assuming that the debt had been converted as of June 30, 2005).

Summary Consolidated Financial Data**(in thousands, except per share data)**

We derived the following information from our audited consolidated financial statements for each of the three years ended December 31, 2004, 2003 and 2002, respectively, our unaudited condensed consolidated balance sheet as of June 30, 2005 and our unaudited condensed consolidated statements of operations for the six months ended June 30, 2005 and 2004. 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 the accompanying prospectus.

Operating results for the six months ended June 30, 2005 are not necessarily indicative of the results that may be expected for the year ending December 31, 2005. 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 About Exelixis*. The as adjusted consolidated balance sheet data gives effect to the sale of 6,500,000 shares of our common stock in this offering, at the public offering price of \$7.75 per share, after deducting the underwriting discounts and commissions and estimated offering expenses payable by us.

	Year Ended December 31,			Six Months Ended	
				June 30,	
	2002	2003	2004	2004	2005
Consolidated Statement of Operations Data					
Total revenues	\$ 44,322	\$ 51,540	\$ 52,857	\$ 24,451	\$ 47,184
Total operating expenses	\$ 132,146	\$ 147,799	\$ 188,059	\$ 81,921	\$ 83,787
Net loss	\$ (86,130)	\$ (94,774)	\$ (137,245)	\$ (58,134)	\$ (37,107)
Net loss per share, basic and diluted	\$ (1.52)	\$ (1.45)	\$ (1.89)	\$ (0.81)	\$ (0.49)
Shares used in computing basic and diluted net loss per share	56,615	65,387	72,504	71,762	76,162

	June 30, 2005	
	Actual	As Adjusted
Consolidated Balance Sheet Data		
Cash, cash equivalents and short-term investments (including restricted cash and investments of \$14.8 million and investments held by Symphony Evolution, Inc. of \$40.0 million)	\$ 202,261	\$ 251,871
Working capital	\$ 106,018	\$ 155,628
Total assets	\$ 325,145	\$ 374,755
Long-term obligations, less current portion	\$ 118,329	\$ 118,329
Accumulated deficit	\$ (556,481)	\$ (556,481)
Total stockholders' equity	\$ 28,485	\$ 78,095

RISK FACTORS

If you purchase shares of our common stock, you will take on financial risk. In deciding whether to invest, you should carefully consider the following factors and the information contained in this prospectus supplement and the accompanying prospectus, including the additional information in our reports and other documents on file with the Securities and Exchange Commission that are incorporated by reference in the accompanying prospectus. If any of these risks occur, our business could suffer, the market price of our common stock could decline and you could lose all or part of your investment in our common stock.

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.

We anticipate that the net proceeds from this offering, our current cash and cash equivalents, short-term investments, investments in and expected to be made in Symphony Evolution, Inc. and funding that we expect to receive from collaborators, which includes a moderate level of business development activity, will enable us to maintain our operations through the end of 2006. This estimate includes the potential repayment of a \$30.0 million convertible promissory note to Protein Design Labs, Inc.

Our capital needs in 2006 may include the repayment of a \$30.0 million convertible promissory note that we issued in May 2001 to Protein Design Labs in connection with a collaboration agreement. The note matures in May 2006 and is convertible into our common stock at Protein Design Labs' option any time after the first anniversary of the note. The note is convertible into our common stock at a conversion price per share equal to the lower of (i) \$28.175 or (ii) 110% of the fair market value (as defined in the note) of a share of our common stock at the time of conversion. If the note is not converted by Protein Design Labs, we will have to repay the entire note in May 2006.

Our future capital requirements will be substantial and will depend on many factors, including:

payments received under collaborative agreements, licensing agreements and other arrangements;

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the progress and scope of our collaborative and independent clinical trials and other research and development projects;

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

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 establishing clinical and research supplies of our product candidates;

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our ability to remain in compliance with, or amend or cause to be waived, financial covenants contained in loan and lease agreements with third parties;

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, although we currently have no commitments relating to any such transactions; and

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

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

In addition, we must raise additional capital 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) must not be less than \$25.0 million and our cash and investments (total cash, cash equivalents and investments) must not be less than \$50.0 million. As of June 30, 2005, our working capital was \$106.0 million and our cash and investments were \$202.3 million, which includes restricted cash and investments of \$14.8 million and investments held by SEI of \$40.0 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. In addition, in connection with an equipment lease financing transaction with General Electric Capital Corporation, we entered into a lease agreement pursuant to which we are required to maintain minimum unrestricted cash, which is defined as cash on hand, including investments in marketable securities with maturities of less than 24 months, less cash pledged to other parties, of \$35.0 million. As of June 30, 2005, we had unrestricted cash of \$118.0 million. If we were to default on this financial covenant, we may be required to pay as liquidated damages the stipulated loss value of the equipment and all rents and other sums then due under the agreement. 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 or lessor exercises its remedies under the agreement, we would not be able to operate under our current operating plan.

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

We have incurred net losses each year since our inception, including a net loss of approximately \$37.1 million for the six months ended June 30, 2005. As of that date, we had an accumulated deficit of approximately \$556.5 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 product candidates and, consequently, have not generated revenues from the

sale of products. Our only revenues to date are license revenues and revenues under

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contracts with our partners. The size of our net losses will depend, in part, on the rate of growth, if any, in our license and contract revenues and on the level of our expenses. These losses have had and will continue to have an adverse effect on our stockholders equity and working capital. Our research and development expenditures and general and administrative expenses have exceeded our revenues to date, and we expect to spend significant additional amounts to fund research and development in order to enhance our technologies and undertake product development. We currently have numerous product candidates in various stages of clinical development and we anticipate filing IND applications for additional product candidates during the next 12 months. As a result, we expect that our operating expenses will increase significantly, and, consequently, we will need to generate significant additional revenues to achieve profitability. Because of the numerous risks and uncertainties associated with developing drugs, we are unable to predict the extent of any future losses or when we will become profitable, if at all. Even if we do increase our revenues and achieve profitability, we may not be able to maintain or increase profitability.

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

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

We have also received an exclusive program option from SEI allowing us under certain conditions to separately reacquire from SEI one of the three product candidates licensed to SEI. The program option is exercisable at any time, at our sole discretion, during a period beginning on June 9, 2005 and ending on December 9, 2006 at an exercise price equal to that portion of the funded capital expended on the development of the applicable product candidate being repurchased, plus a specified premium. The program option exercise price may be paid in cash only.

If we elect to exercise either one of the options, we will be required to make a substantial cash payment and/or to issue a substantial number of shares of our common stock, or enter into a financing arrangement or license arrangement with one or more third parties, or some combination of the foregoing. A payment in cash would reduce our capital resources. A payment in shares of our common stock could result in dilution to our stockholders at that time. Other financing or licensing alternatives may be expensive or impossible to obtain. If we do not exercise the purchase options prior to their expiration, our rights in and to SEI with respect to XL647, XL999 and XL784 will terminate. We may not have the financial resources to exercise the options, which may result in our loss of these rights. Additionally, we may not have sufficient clinical data in order to determine whether we should exercise the options.

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

Risks Related to Development of Product Candidates

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

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

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

our product candidates may not prove to be efficacious or may cause harmful side effects;

negative or inconclusive clinical trial results may require us to conduct further testing or to abandon projects that we had expected to be promising;

patient registration or enrollment in our clinical testing may be lower than we anticipate, resulting in the delay or cancellation of clinical testing; and

regulators or institutional review boards may not authorize, delay, suspend or terminate clinical research for various reasons, including noncompliance with regulatory requirements or their determination that participating patients are being exposed to unacceptable health risks.

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

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

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;

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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 discovered other compounds that we believe show significantly improved safety or efficacy compared to our product candidates, which could limit our ability to generate revenues, cause us to incur additional expense and cause the market price of our common stock to decline significantly.

Risks Related to Our Relationships With Third Parties

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

Under our exclusive license agreement with Helsinn, Helsinn is responsible for all aspects of clinical development of XL119 upon completion of the transfer of the IND for XL119 and all of its foreign equivalents. If XL119 receives regulatory approval, Helsinn will be responsible for the marketing and sale of the commercial product worldwide, unless and to the extent we require the commercialization rights for North America. Because Helsinn is responsible for these functions after the IND has been transferred, we have no control over the development schedule or, if XL119 receives regulatory approval, the marketing plan for XL119. If the clinical trials for XL119 are not successful, XL119 will not be commercialized. Moreover, beginning June 10, 2006, Helsinn may relinquish all rights and the license granted to it under the license agreement and thereby terminate the license agreement on at least six months prior written notice, if in Helsinn's reasonable business judgment based on scientific or economic evidence, it is impossible for Helsinn to carry out further development or marketing of XL119. In that event, the rights to develop and market XL119 will revert to us. If these rights revert to us, we will have to fund the clinical programs for XL119 on our own, seek a strategic partner or licensee for clinical development or abandon XL119.

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

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

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

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

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

If we are unable to deliver certain clinical trial materials to Helsinn for the ongoing Phase 3 clinical trial of XL119, milestone payments under our license agreement with Helsinn would be reduced and Helsinn could under certain

conditions terminate the license agreement or continue the agreement at reduced royalty rates.

Under our license agreement with Helsinn, we are required to supply to Helsinn certain clinical trial materials (at Helsinn's expense) by April 30, 2006 for the ongoing Phase 3 clinical trials of XL119. Our primary supplier of clinical materials for the ongoing XL119 trial previously informed us of an

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internal restructuring that impacted our ability to obtain drug substance from them. While we expect that we will be able to obtain clinical trial materials when necessary to satisfy our obligation to deliver the required materials to Helsinn, we cannot be certain that we will be able to obtain additional supplies in a timely manner. Our inability to obtain clinical trial materials would result in reduced milestone payments under the license agreement. Furthermore, if we fail to supply these materials and such failure prevents Helsinn from enrolling additional patients or from maintaining the then-current enrollment in the Phase 3 trials, then Helsinn may terminate the license agreement or elect to continue the agreement at a reduced royalty rate. If the license agreement is terminated, the rights to develop and market XL119 will revert to us and we would have to fund the clinical development of XL119 on our own. If Helsinn chooses to continue the agreement at a reduced royalty rate, potential future royalty payments by Helsinn will be reduced.

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 up to \$80.0 million to advance the clinical development of XL647, XL999 and XL784. We will be responsible for developing XL647, XL999 and XL784 in accordance with a specified development plan and related development budget. Our development activities will be supervised by SEI's development committee, which is comprised of an equal number of representatives from Exelixis and SEI. If the development committee cannot resolve a particular development issue, the issue will be referred to the chief executive officers of Exelixis and Symphony. 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 on 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 our research. If we are unable to successfully achieve milestones or our collaborators fail to develop successful products, we will not earn the revenues contemplated under such collaborative agreements. In addition, some of our collaborations are exclusive and preclude us from entering into additional collaborative 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 collaborative agreements on commercially acceptable terms, our revenues and product development efforts could suffer. For example, our agreement with Pharmacia Corporation terminated by mutual agreement in February 2002, which eliminated the opportunity for us to earn approximately \$9.0 million in research revenue in 2002 and 2003. Similarly, our collaboration with GlaxoSmithKline is scheduled to expire in October 2008 but is subject to earlier termination at the discretion of GlaxoSmithKline starting in 2005 if we fail to meet certain diligence requirements. 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 key business. We may not be able to enter into new collaborative 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 collaborative 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 collaborative 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 collaborative 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 take the position that our internal activities overlap with those areas that are exclusive to our collaborative 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 collaborative agreements may have provisions that give rise to disputes regarding the 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 obligations thereunder. Also, our collaboration agreements may be subject to early termination on the mutual agreement between us and our collaborators. Further, our collaborators may elect not to develop products arising out of our collaborative 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 and may fail to lead to commercialized products.

If third parties on whom 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 manufacturing capabilities or experience necessary to enable us to produce materials for clinical trials, including the trials for XL784, XL647, XL999, XL880 as well as XL119 for which we have a remaining obligation under our license agreement with Helsinn to deliver certain clinical trial materials to Helsinn for the ongoing Phase 3 clinical trials of XL119 by April 30, 2006. 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 significantly and adversely affect our business.

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

Some of the materials necessary for the manufacture of our compounds under development may, from time to time, be available either in limited quantities, or from a limited number of manufacturers, or both. Our contract manufacturers need to obtain these materials for our clinical trials and, potentially, for commercial distribution when and if we obtain marketing approval for these compounds. Suppliers may not sell us these materials at the time we need them or on commercially reasonable terms. If we are unable to obtain the materials needed for the conduct of our clinical trials, product testing and potential regulatory approval could be delayed, adversely impacting our ability to develop the product candidates. Similarly, if we are unable to obtain critical materials after regulatory approval has been obtained for a product candidate, the commercial launch of that product could be delayed or there would be a shortage in supply, which could materially affect our ability to generate revenues from that product. If suppliers increase the price of these materials, the price for one or more of our products may increase, which may make our product 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 in the facilities used to produce these materials, due to technical, regulatory or other problems, 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, often takes many years, if approval is obtained at all, and can vary substantially based upon the type, complexity and novelty of the product candidates involved. Before a new drug application can be filed with the FDA, the product candidate must undergo extensive clinical trials, which can take many years and may require substantial expenditures. Any clinical trial may fail to produce results satisfactory to the FDA. For example, the FDA could determine that the design of a clinical trial is inadequate to produce reliable results. The regulatory process also requires preclinical testing, and data obtained from preclinical and clinical activities are susceptible to varying interpretations, which could delay, limit or prevent regulatory approval. In addition, delays or rejections may be encountered based upon changes in regulatory policy for product approval during the period of product development and regulatory agency review. Changes in regulatory approval policy, regulations or statutes or the process for regulatory review during the development or approval periods of our product candidates may cause delays in the approval or rejection of an application. Even if the FDA or a comparable authority in another country approves a product candidate, the approval may impose significant restrictions on the indicated uses, conditions for use, labeling, advertising, promotion, marketing and/or production of such product and may impose ongoing requirements for post-approval studies, including additional research and development and clinical trials. These agencies also may impose various civil or criminal sanctions for failure to comply with regulatory requirements, including withdrawal of product approval.

Risks Related to Commercialization of Products

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

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

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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 to perform sales, marketing and distribution services with third parties, 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 their medical needs. If third-party payors do not provide coverage or reimbursement for any products that we may develop, our revenues and prospects for profitability will suffer. In addition, even if third-party payors provide some coverage or reimbursement for our products, the availability of such coverage or reimbursement for prescription drugs under private health insurance and managed care plans often varies based on the type of contract or plan purchased.

A primary trend in the United States health care industry is toward cost containment. In December 2003, the President signed into law legislation creating a prescription drug benefit program for Medicare recipients. The prescription drug program established by the legislation may have the effect of reducing the prices that we are able to charge for products we develop and sell through these plans. This prescription drug legislation 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 amount that they will pay.

Another development that may affect the pricing of drugs is the proposed Congressional action regarding drug reimportation into the United States. The Medicare Prescription Drug Plan legislation gives additional discretion to the Secretary of Health and Human Services to allow drug reimportation from foreign countries into the United States under some circumstances, including countries where the drugs are sold at a lower price than in the United States. Proponents of drug reimportation may attempt to pass

legislation, which would directly allow reimportation under certain circumstances. If legislation or regulations were passed allowing the reimportation of drugs, they 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 of the European Union, the pricing of prescription pharmaceuticals is subject to governmental control. In these countries, pricing negotiations with governmental authorities can take six to 12 months or longer after the receipt of regulatory marketing approval for a product. To obtain reimbursement or pricing approval in some countries, we may be required to conduct a clinical trial that compares the cost effectiveness of our product candidates or products to other available therapies. The conduct of such a clinical trial could be expensive and result in delays in the commercialization of our product candidates. Third-party payors are challenging the prices charged for medical products and services, and many third-party payors limit reimbursement for newly approved health care products. In particular, third-party payors may limit the indications for which they will reimburse patients who use any products that we may develop. Cost-control initiatives could decrease the price we might establish for products that we may develop, which would result in lower product revenues to us.

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

The biotechnology industry is highly fragmented and is characterized by rapid technological change. In particular, the area of kinase-targeted therapies is a rapidly evolving and competitive field. We face, and will continue to face, intense competition from large biotechnology and pharmaceutical 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 on 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 staffs and facilities, more experience in obtaining regulatory approvals and more extensive product manufacturing and marketing capabilities. As a result, our competitors may be able to more easily develop technologies and products that would render our technologies and products, and those of our collaborators, obsolete and noncompetitive. In addition, there may be product candidates of which we are not aware at an earlier stage of development that may compete with our product candidates.

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

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

Risks Related to Our Intellectual Property

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

Our success will depend in part on 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 on our ability to avoid infringing patents and proprietary rights of third parties and not breaching any licenses that we have entered into with regard to our technologies. Other parties have filed, and in the future are likely to file, patent applications covering genes and gene fragments, techniques and methodologies relating to model systems and products and technologies that we have developed or intend to develop. If patents covering technologies required by our operations are issued to others, we may have to obtain licenses from third parties, which may not be available on commercially reasonable terms, or at all, and may require us to pay

substantial royalties, grant a cross-license to some of our patents to another patent holder or redesign the formulation of a product candidate so that we do not infringe third-party patents, which may be impossible 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 these 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 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 on 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. However, we do not currently have sufficient executive management and technical personnel to fully execute our business plan. Recruiting and retaining qualified scientific and clinical personnel will be critical to support activities related to advancing our clinical and preclinical development programs, and supporting our collaborative arrangements and our internal proprietary research and development efforts. Although we believe that we will be successful in attracting and retaining qualified management, competition is intense for experienced technical personnel, and we may be unable to retain or recruit scientists with the expertise or experience necessary to allow us to pursue collaborations, develop our products and core technologies or expand our operations to the extent otherwise possible. Further, all of our employees are employed at will and, therefore, may leave our employment at any time.

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

We work with scientific and clinical advisors and collaborators at academic and other institutions that assist us in our research and development efforts. These advisors and collaborators are not our employees and may have other commitments that limit their

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availability to us. Although they generally agree not to do competing work, if a conflict of interest between their work for us and their work for another entity arises, we may lose their services. In addition, although our advisors and collaborators sign agreements not to disclose our confidential information, it is possible that valuable proprietary knowledge may become publicly known through them.

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

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

Our headquarters facilities are located near known earthquake fault zones, and the occurrence of an earthquake or other catastrophic disaster could cause damage to our facilities and equipment, which could require us to cease or curtail 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 worldwide to damage from other types of disasters, including fire, floods, power loss, communications failures, terrorism and similar events. If any disaster were to occur, our ability to operate our business at our facilities would 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. The insurance we maintain may not be adequate to cover our losses resulting from disasters or other business interruptions. Accordingly, an earthquake or other disaster could materially and adversely harm our ability to conduct business.

Risks Related to Environmental and Product Liability

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

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

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

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

We may be held liable if any product our collaborators or we 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,

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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 based on drugs that had unanticipated side effects. In addition, the pharmaceutical and biotechnology industries, in general, have been subject to significant medical malpractice litigation. A successful product liability claim or series of claims brought against us would decrease our cash reserves and could cause our stock price to fall.

Risks Related to Genetic Engineering of Products

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

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

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

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

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

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additives. Our product candidates may be subject to lengthy FDA reviews and unfavorable FDA determinations if they raise questions regarding safety or our products are deemed to be food additives.

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

Risks Related to Our Common Stock

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

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

recognition of upfront licensing or other fees;

payments of non-refundable upfront or licensing fees to third parties;

acceptance of our technologies and platforms;

the success rate of our discovery efforts leading to milestone payments and royalties;

the introduction of new technologies or products by our competitors;

the timing and willingness of collaborators to commercialize our products;

our ability to enter into new collaborative relationships;

the termination or non-renewal of existing collaborations;

the timing and amount of expenses incurred for clinical development and manufacturing of our products;

the impairment of acquired goodwill and other assets; and

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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 or our failure to obtain new contracts, our inability to meet milestones or 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 stock.

Our stock price may be extremely volatile.

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

adverse results or delays in clinical trials;

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

the announcement of new products by us or our competitors;

quarterly variations in our or our competitors' results of operations;

litigation, including intellectual property infringement lawsuits, involving us;

failure to achieve operating results projected by securities analysts;

changes in earnings estimates or recommendations by securities analysts;

financing transactions;

developments in the biotechnology or pharmaceutical industry;

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

departures of key personnel;

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 and fluctuations, 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 deemed appropriate. For example, following an acquisition, a significant number of shares of our common stock held by new stockholders may become freely tradable or holders of registration rights could cause us to register their shares for resale. Sales of these shares of common stock held by existing stockholders could cause the market price of our common stock to decline.

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

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

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 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 us, 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; and

limitations on the removal of directors.

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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. Finally, these provisions establish advance notice requirements for nominations for election to our Board of Directors or for proposing matters that can be acted upon at stockholder meetings. These provisions would apply even if the offer may be considered beneficial by some stockholders.

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CAUTIONARY NOTE REGARDING FORWARD-LOOKING STATEMENTS

Some of the statements in this prospectus supplement, the accompanying prospectus and the documents incorporated by reference are forward-looking statements. 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, predict, potential and continue, terms or other similar expressions, identify forward-looking statements. 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 several factors more fully described under the caption Risk Factors beginning on page S-5 of this prospectus supplement and in the documents incorporated by reference in the accompanying prospectus. 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 will receive approximately \$49.6 million in net proceeds from the sale of 6,500,000 shares of common stock in this offering, after deducting underwriting discounts and commissions and estimated offering expenses payable by us.

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.

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PRICE RANGE OF OUR COMMON STOCK

Since April 11, 2000, our common stock has been quoted and traded on the Nasdaq 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 National Market:

	<u>High</u>	<u>Low</u>
Year ended December 31, 2003		
First Quarter	\$ 8.03	\$ 5.01
Second Quarter	9.75	6.52
Third Quarter	9.40	5.99
Fourth Quarter	8.21	5.99
Year ended December 31, 2004		
First Quarter	\$ 9.50	\$ 6.81
Second Quarter	10.64	8.04
Third Quarter	10.10	6.11
Fourth Quarter	9.79	7.97
Year ended December 31, 2005		
First Quarter	\$ 9.69	\$ 6.02
Second Quarter	8.57	6.51
Third Quarter (through August 16, 2005)	9.37	7.12

The reported last sale price of our common stock on the Nasdaq National Market on August 16, 2005 was \$8.20 per share. As of August 9, 2005, there were approximately 815 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.

DILUTION

Our net tangible book value on June 30, 2005 was approximately \$(9.1) million, or approximately \$(0.12) per share. Net tangible book value 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, 2005. Dilution in net tangible book value 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 per share of our common stock immediately after this offering. After giving effect to the sale of 6,500,000 shares of common stock in this offering at the public offering price of \$7.75 per share, and after deducting underwriting discounts and commissions and estimated offering expenses payable by us, our net tangible book value on June 30, 2005 would have been approximately \$40.5 million, or approximately \$0.49 per share. This represents an immediate dilution of \$7.26 per share to new investors purchasing shares of common stock in this offering. The following table illustrates this dilution:

Public offering price per share	\$ 7.75
Net tangible book value per share as of June 30, 2005	\$ (0.12)
Increase per share attributable to new investors	0.61
	<hr/>
Net tangible book value per share as of June 30, 2005 after giving effect to this offering	0.49
	<hr/>
Dilution per share to new investors	\$ 7.26
	<hr/>

The foregoing table does not take into account further dilution to new investors that could occur upon the exercise of outstanding options and warrants having a per share exercise price less than the per share offering price to the public in this offering. As of June 30, 2005, there were:

12,002,951 shares of common stock underlying options and warrants outstanding at a weighted average exercise price of \$11.05 per share;

7,120,389 shares available for future grant under our 2000 Equity Incentive Plan, 1,308,022 shares available for future issuance under our 2000 Employee Stock Purchase Plan and 1,299,695 shares available for future grant under our 2000 Non-Employee Directors Stock Option Plan; and

16,154,088 shares issuable upon conversion of our convertible debt (assuming that the debt had been converted as of June 30, 2005).

UNDERWRITING

Exelixis 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 6,500,000 shares offered hereby.

Shares sold by Goldman, Sachs & Co. to the public will initially be offered at the initial price to public set forth on the cover of this prospectus supplement. In addition, Goldman, Sachs & Co. may receive from purchasers of the shares normal brokerage commissions in amounts agreed with such purchasers. If all of the shares are not sold at the initial price to public, Goldman, Sachs & Co. may change the offering price and the other selling terms.

The following table shows the per share and total underwriting discounts and commissions to be paid to Goldman, Sachs & Co. by Exelixis.

Paid by Exelixis

Per share	\$0.10
Total	\$ 650,000

Exelixis and each 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. This agreement does not apply to any Rule 10b5-1 sales plan of Exelixis' chief executive officer (under which approximately 2,500 shares are expected to be sold each week during the 90-day lock-up period), to the issuance of shares by Exelixis pursuant to its existing equity incentive plans or to 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 5% of Exelixis' outstanding shares of common stock if such shares are issued in connection with a strategic transaction that includes a commercial relationship involving Exelixis, or if such shares are issued as direct consideration for any business, products or technologies; provided that the recipients of these shares agree to be bound by the 90 day lock-up agreement described above. Goldman, Sachs & Co., in its sole discretion, may release any of the securities subject to these lock-up agreements at any time without notice.

In connection with this offering, Goldman, Sachs & Co. may purchase and sell shares of the 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 & Co. of a greater number of shares than it is required to purchase in the offering. Goldman, Sachs & Co. will need to close out any short sale by purchasing shares in the open market. Goldman, Sachs & Co. is likely to create a short position if it 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 or purchases 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 may have the effect of preventing or retarding a decline in the market price of the common 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 by Goldman, Sachs & Co. at any time. These transactions may be effected on the Nasdaq National Market, in the over-the-counter market or otherwise.

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Goldman, Sachs & Co. has represented, warranted and agreed that: (i) it has not offered or sold and, prior to the expiry of a period of six months from the closing date, will not offer or sell any shares to persons in the United Kingdom except to persons whose ordinary activities involve them in acquiring, holding, managing or disposing of investments (as principal or agent) for the purposes of their businesses or otherwise in circumstances which have not resulted and will not result in an offer to the public in the United Kingdom within the meaning of the Public Offers of Securities Regulations 1995; (ii) it has only communicated or caused to be communicated and will only communicate or cause to be communicated any invitation or inducement to engage in investment activity (within the meaning of section 21 of the Financial Services and Markets Act 2000, or FSMA) received by it in connection with the issue or sale of any shares in circumstances in which section 21(1) of the FSMA does not apply to Exelixis; and (iii) it has complied and will comply with all applicable provisions of the FSMA with respect to anything done by it in relation to the shares in, from or otherwise involving the United Kingdom.

The shares may not be offered or sold, transferred or delivered, as part of their initial distribution or at any time thereafter, directly or indirectly, to any individual or legal entity in the Netherlands other than to individuals or legal entities who or which trade or invest in securities in the conduct of their profession or trade, which includes banks, securities intermediaries, insurance companies, pension funds, other institutional investors and commercial enterprises which, as an ancillary activity, regularly trade or invest in securities.

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, the accompanying prospectus and any other document or material in connection with the offer or sale, or invitation or 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 under circumstances in which such offer, sale or invitation does not constitute an offer or sale, or invitation for subscription or purchase, of the shares to the public in Singapore.

Goldman, Sachs & Co. has acknowledged and agreed that the shares have not been registered under the Securities and Exchange Law of Japan and are not being offered or sold and may not be offered or sold, directly or indirectly, in Japan or to or for the account of any resident of Japan, except (i) pursuant to an exemption from the registration requirements of the Securities and Exchange Law of Japan and (ii) in compliance with any other applicable requirements of Japanese law. As part of the offering, Goldman, Sachs & Co. may offer shares in Japan to a list of 49 offerees in accordance with the above provisions.

Exelixis estimates that its share of the total expenses of this offering, excluding underwriting discounts and commissions, will be approximately \$115,000.

Exelixis has agreed to indemnify Goldman, Sachs & Co. against certain liabilities, including liabilities under the Securities Act of 1933.

In the ordinary course of its business, Goldman, Sachs & Co. and its affiliates have from time to time performed, and may in the future perform, certain investment banking and financial advisory services for Exelixis for which it has received, and may 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 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 31, 2004, and management's assessment of the effectiveness of our internal control over financial reporting as of December 31, 2004, as set forth in their reports, which are incorporated by reference in this 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 report, given on their authority as experts in accounting and auditing.

PROSPECTUS

\$150,000,000

Exelixis, Inc.

COMMON STOCK

Exelixis, Inc. may offer from time to time, in one or more issuances, shares of common stock under this prospectus. We will offer the shares of our common stock in an amount and on terms that market conditions will determine at the time of the offering. Please read any prospectus supplements and this prospectus carefully before you invest in our common stock. This prospectus may not be used to sell shares of our common stock unless accompanied by a prospectus supplement.

Our common stock trades on the Nasdaq National Market under the symbol EXEL. On July 27, 2001, the last reported sale price of our common stock was \$18.60 per share.

See *Risk Factors* beginning on page 3 to read about factors you should consider before buying shares of our common stock.

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

Prospectus dated August 7, 2001

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This prospectus is part of a registration statement that we filed with the Securities and Exchange Commission. You should rely only on the information we have provided or incorporated by reference in this prospectus or any prospectus supplement. We have not authorized anyone to provide you with additional or different information. We are not making an offer of these shares of common stock in any jurisdiction where the offer is not permitted. You should assume that the information contained in this prospectus or any prospectus supplement is accurate only as of the date on the front of document and that any information we have incorporated by reference is accurate only as of the date of the document incorporated by reference.

Exelixis, Artemis Pharmaceuticals, ACTTAG, the Exelixis, Inc. logos and all other Exelixis product and service names are registered trademarks or trademarks of Exelixis, Inc. in the U.S. and in other selected countries. All other brand names or trademarks appearing in this prospectus are the property of their respective holders.

ABOUT THIS PROSPECTUS

This prospectus is part of a registration statement on Form S-3 that we filed with the Securities and Exchange Commission utilizing a shelf registration process. Under this shelf process, we may offer from time to time the shares of our common stock described in this prospectus in one or more offerings for up to a total amount of \$150,000,000. This prospectus provides you with a general description of our common stock that we may offer. Each time we use this prospectus to offer shares of our common stock, we will provide a prospectus supplement that will contain specific information about the terms of that offering. The prospectus supplements may also add, update or change information contained in this prospectus. You should read both this prospectus and any prospectus supplement together with additional information described below under the heading **Where You Can Find More Information About Exelixis**.

EXELIXIS

We believe that we are a leader in the discovery and validation of high-quality novel targets for several major human diseases, and a leader in the discovery of potential new drug therapies, specifically for cancer and other proliferative diseases. Our mission is to develop proprietary products by leveraging our integrated discovery platform to increase the speed, efficiency and quality of pharmaceutical and agricultural product discovery and development.

Through our expertise in biology and drug discovery built upon a foundation of comparative genomics and model system genetics, we are able to find new drug targets that we believe would be difficult or impossible to uncover using other experimental approaches. Our pharmaceutical research identifies novel genes and proteins expressed by those genes that, when changed, either decrease or increase the activity in a specific disease pathway in a therapeutically relevant manner. These genes and proteins then represent either potential product targets or drugs that may treat disease, or prevent disease initiation or progression.

Specifically in cancer, the remarkable evolutionary conservation of the biochemical pathways between humans and lower organisms strongly supports the use of simple model systems, such as fruit flies, nematode worms, zebrafish and mice to identify key members of critical cancer pathways that can then be targeted for drug discovery. We expect to develop new cancer drugs by exploiting the underlying genetic liabilities of tumor cells to provide specificity in targeting these cells for destruction, while leaving normal cells unharmed. We have discovered and are further developing a number of small molecule drug targets in addition to monoclonal antibody drug targets. Molecules developed

against these targets may selectively kill cancer cells while leaving normal cells unharmed, and may provide alternatives to current cancer therapies.

While our proprietary programs focus on drug discovery and development, we believe that our proprietary technologies are valuable to all other industries whose products can be enhanced by an understanding of DNA or proteins, including the agrochemical, agricultural and diagnostic industries. Many of these industries have shorter product development cycles and lower risk than the pharmaceutical industry, while at the same time generating significant sales with double-digit product margins. By partnering with leading companies in multiple industries, we are able to diversify our business risk, while at the same time maximizing our future revenue stream.

We are a Delaware corporation. Our principal executive offices are located at 170 Harbor Way, South San Francisco, California 94080, and our telephone number is (650) 837-7000. In this prospectus, Exelixis, we, us, and our refer to Exelixis, Inc., unless the context otherwise requires.

RISK FACTORS

You should carefully consider the following risk factors, in addition to other information included or incorporated by reference in this prospectus, before making an investment decision. The risks described below are not the only risks we face. Additional risks that we do not yet know of or that we currently think are immaterial may also impair our business operations. If any of the events or circumstances described in the following risks actually occurs, our business may suffer, the trading price of our common stock could decline and you may lose all or part of your investment.

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

We have incurred net losses each year since our inception, including a net loss of approximately \$12.7 million for the three months ended March 31, 2001. As of that date, we had an accumulated deficit of approximately \$142.8 million. We expect these losses to continue and anticipate negative cash flow for the foreseeable future. The size of these 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. Our research and development expenditures and general and administrative costs have exceeded our revenues to date, and we expect to spend significant additional amounts to fund research and development in order to enhance our core technologies and undertake product development. As a result, we expect that our operating expenses will increase significantly in the near term and, consequently, we will need to generate significant additional revenues to achieve profitability. Even if we do increase our revenues and achieve profitability, we may not be able to sustain or increase profitability.

We will need additional capital in the future, which may not be available to us.

Our future capital requirements will be substantial, and will depend on many factors including:

payments received under collaborative agreements;

the progress and scope of our collaborative and independent research and development projects;

our ability to successfully continue development of a recently acquired cancer compound;

our need to expand our other proprietary product development efforts as well as develop manufacturing and marketing capabilities to commercialize products; and

the filing, prosecution and enforcement of patent claims.

We anticipate that our current cash and cash equivalents, short-term investments and funding to be received from collaborators will enable us to maintain our currently planned operations for at least the next two years. Changes to our current operating plan may require us to consume available capital resources significantly sooner than we expect. For example, our newly acquired cancer product from our recent relationship with Bristol Myers-Squibb will require significant resources for development that were not in our

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operation plans prior to acquiring the cancer product. We may be unable to raise sufficient additional capital when we need it, on favorable terms, or at all. If our capital resources are insufficient to meet future capital requirements, we our capital resources are insufficient to meet future capital requirements, we will have to raise additional funds. The sale of equity or convertible debt securities in the future may be dilutive to our stockholders, and debt financing arrangements may require us to pledge certain assets and enter into covenants that would restrict our ability to incur further indebtedness. If we are unable to obtain adequate funds on reasonable terms, we may be required to curtail operations significantly or to obtain funds by entering into financing, supply or collaboration agreements on unattractive terms.

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 administrative and operational infrastructure. As our operations expand, we expect that we will need to manage multiple locations, including locations outside the United States, 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 operational, financial and management controls, reporting systems and procedures. We may not be able to successfully implement improvements to our management information and control systems in an efficient or timely manner and may discover deficiencies in existing systems and controls. In addition, acquisitions involve the integration of different financial and management reporting systems. We may not be able to successfully integrate the administrative and operational infrastructure without significant additional improvements and investments in management systems and procedures.

We are dependent on 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.

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

We currently have collaborative research agreements with Bayer, Bristol-Myers Squibb (two agreements), Dow AgroSciences, Aventis and Protein Design Labs. Our current collaborative agreement with Bayer is scheduled to expire in 2008, after which it will automatically be extended for one-year terms unless terminated by either party upon 12-month written notice. Our agreement permits Bayer to terminate our collaborative activities prior to 2008 upon the occurrence of specified conditions, such as the failure to agree on key strategic issues after a period of years or the acquisition of Exelixis by certain specified third parties. In addition, our agreements with Bayer are subject to termination at an earlier date if two or more of our Chief Executive Officer, Chief Scientific Office, Agricultural Biotechnology Program Leader and Chief Informatics Officer cease to have a relationship with us within six months of each other and we are unable to find replacements acceptable to Bayer. The first of our collaborative agreements with Bristol-Myers Squibb expires in September 2002. The funded research term of second arrangement, entered into July 2002, expires in July 2005. Our collaborative agreement with Dow AgroSciences is scheduled to expire in July 2003, after which Dow AgroSciences has the option to renew on an annual basis. Our collaborative research arrangement with Aventis is scheduled to expire in June 2004. Aventis has the right to terminate the research arrangement prior to the expiration date, provided that it pays the annual research funding amount due for the year following termination. Thereafter, the arrangement renews annually unless Aventis terminates automatic renewal prior to the scheduled date of renewal. The Aventis arrangement is conducted through a limited liability company, Agrinomics, which is owned equally by Aventis and Exelixis. Aventis may surrender its interest in Agrinomics and terminate the related research collaboration prior to the scheduled expiration upon the payment of the subsequent year's funding commitment. Bayer and Aventis recently announced an exclusive negotiation period for acquisition were to occur. Our agreement with Protein Design Labs is scheduled to expire in May 2003. Protein Design Labs has a unilateral right to renew for 12 and six month periods thereafter. The five-year term of the convertible promissory note entered

into as part of this arrangement is unaffected by whether or not Protein Design Labs renews. If these existing agreements are not renewed or if we are unable to enter into new collaborative may be adversely affected.

We recently announced the reacquisition, effective February 2002, of future rights to research programs in metabolism and alzheimer's disease previously licensed exclusively to Pharmacia Corporation. Pharmacia will retain rights to targets under the existing agreement selected prior to the reacquisition date, subject to the payment of milestones for certain of those targets selected and royalties for future development of products against or using those targets but will have no other obligations to make payments to the Company, including approximately \$9 million in annual funding that would otherwise be payable for two years if the Company had not elected to reacquire rights to the research at this time. Although we anticipate entering into future collaborations involving either or both of these programs, there can be no assurance that we will be able to enter into new collaborative agreements or that such collaborations will provide revenues equal to or exceeding those otherwise obtainable under the Pharmacia collaboration.

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

We intend to conduct proprietary research programs in specific disease and agricultural product areas that are not covered by our collaborative agreements. Our pursuit of opportunities in agricultural and pharmaceutical markets could, however, 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 collaborative 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 collaborative agreements may have provisions that give rise to disputes regarding the rights and obligations of the parties. Any conflict with our collaborators could lead to the termination of our collaborative agreements, delay collaborative activities, reduce 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.

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 obligations thereunder. Further, our collaborators may elect not to develop products arising out of our collaborative arrangements or may fail to devote sufficient resources to the development, manufacture, market or sale of such products. Certain of our collaborators could also become our 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 and may fail to lead to commercialized products.

We are deploying unproven technologies, and we may not be able to develop commercially successful products.

You must evaluate us in light of the uncertainties and complexities affecting a biotechnology company. Our technologies are still in the early stages of development. Our research and operations thus far have allowed us to identify a number of product targets for use by our collaborators and our own internal development programs. We are not certain, however, of the commercial value of any of our current or future targets, and we may not be successful in expanding the scope of our research into new fields of pharmaceutical or pesticide research, or other agricultural applications such as enhancing plant traits to produce superior crop yields, disease resistance or increased nutritional content.

Significant research and development, financial resources and personnel will be required to capitalize on our technology, develop commercially viable products and obtain regulatory approval for such products.

We have no experience in developing, manufacturing and marketing products and may be unable to commercialize proprietary products.

We recently acquired a product (Rebeccamycin) directed against cancer under our recent collaborative agreement with Bristol Myers-Squibb. Clinical development of Rebeccamycin to date has been conducted by the National Cancer Institute, or the NCI, and manufacturing of this product has been the responsibility of Bristol Myers-Squibb. Rebeccamycin has recently completed Phase I clinical studies and is in early Phase II clinical trials being conducted by the NCI. We are currently in negotiations with the NCI to use the results of the clinical studies they have conducted to date and to determine what additional studies, if any, will be conducted by the NCI or us. There can be no assurance that we will successfully agree upon further development plans, the respective rights and obligations of the parties to conduct additional clinical studies or the timing of such studies. In addition, there can be no assurance that the clinical studies conducted to date will support further clinical development or be accepted by the FDA in conjunction with any application for product approval submitted to the FDA for RebeccamycinS. Moreover, although Bristol Myers-Squibb has provided the NCI with sufficient quantities of Rebeccamycin, development necessary for product approval will require us to either develop internal manufacturing capabilities or retain a third party to manufacture the product. In addition, we have recently hired a new Senior Vice President responsible for clinical development of this product, as well as any new potential products that we may develop. As a result, we have limited experience in clinical development and no experience in manufacturing potential drug products. Accordingly, the development of Rebeccamycin is subject to significant risk and uncertainty, particularly with respect to our ability to successfully develop, manufacture and market Rebeccamycin as a product.

With respect to products developed against our proprietary drug targets, we will rely on our collaborators to develop and commercialize products based on our research and development efforts. We have limited or no experience in using the targets that we identify to develop our own proprietary products. Our recent success in applying our drug development capabilities to our proprietary targets in cancer are subject to significant risk and uncertainty, particularly with respect to our ability to meet currently estimated timelines and goals for completing preclinical development efforts and filing an Investigational New Drug Application for compounds developed. In order for us to commercialize products, we would need to significantly enhance our capabilities with respect to product development, and establish manufacturing and marketing capabilities, either directly or through outsourcing or licensing arrangements. We may not be able to enter into such outsourcing or licensing agreements on commercially reasonable terms, or at all.

Since our technologies have many potential applications and we have limited resources, our focus on a particular area may result in our failure to capitalize on more profitable areas.

We have limited financial and managerial resources. This requires us to focus on product candidates in specific industries and forego opportunities with regard to other products and industries. For example, depending on our ability to allocate resources, a decision to concentrate on a particular agricultural program may mean that we will not have resources available to apply the same technology to a pharmaceutical project. While our technologies may permit us to work in both areas, resource commitments may require trade-offs resulting in delays in the development of certain programs or research areas, which may place us at a competitive disadvantage. Our decisions impacting resource allocation may not lead to the development of viable commercial products and may divert resources from more profitable market opportunities.

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

The biotechnology industry is highly fragmented and is characterized by rapid technological change. In particular, the area of gene research is a rapidly evolving field. We face, and will continue to face, intense competition from large 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. Our future success will depend on 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 staffs 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.

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 on 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. The laws of some foreign countries do not protect intellectual property rights to the same extent as the laws of the U.S., and many companies have encountered significant problems in protecting and defending such rights in foreign jurisdictions. 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. 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, invalidated or fail to provide us with any competitive advantages.

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 on our ability to avoid infringing patents and proprietary rights of third parties, and not breaching any licenses that we have entered into with regard to our technologies. Other parties have filed, and in the future are likely to file, patent applications covering genes and gene fragments, techniques and methodologies relating to model systems, and

products

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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 rely on licenses from third parties, which may not be available on commercially reasonable terms, or at all.

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 these 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.

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 on 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. In addition, recruiting and retaining qualified scientific personnel to perform future research and development work will be critical to our success. We do not currently have sufficient executive management and technical personnel to fully execute our business plan. There is currently a shortage of skilled executives and employees with technical expertise, and this shortage is likely to continue. As a result, competition for skilled personnel is intense and turnover rates are high. Although we believe we will be successful in attracting and retaining qualified personnel, competition for experienced scientists from numerous companies, academic and other research institutions may limit our ability to do so.

Our business operations will require additional expertise in specific industries and areas applicable to products identified and developed through our technologies. These activities will require the addition of new personnel, including management and technical personnel and the development of additional expertise by existing employees. The inability to attract such personnel or to develop this expertise could prevent us from expanding our operations in a timely manner, or at all.

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

We work with scientific advisors and collaborators at academic and other institutions that assist us in our research and development efforts. These scientists are not our employees and may have other commitments that would limit their availability to us. Although our scientific 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 addition, although our scientific advisors and collaborators sign agreements not to disclose our confidential information, it is possible that valuable proprietary knowledge may become publicly known through them.

Our potential therapeutic products 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.

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The Food and Drug Administration, or FDA, must approve any drug or biologic product before it can be marketed in the U.S. Any products resulting from our research and development efforts must also be approved by the regulatory agencies of foreign governments before the product can be sold outside the U.S. Before a new drug application or biologics license 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. The regulatory process also requires preclinical testing. 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. The clinical development and regulatory approval process is expensive and time consuming. Any failure to obtain regulatory approval could delay or prevent us from commercializing products.

Our efforts to date have been primarily limited to identifying targets. Significant research and development efforts will be necessary before any products resulting from such targets can be commercialized. If regulatory approval is granted to any of our products, this approval may impose limitations on the uses for which a product may be marketed. Further, once regulatory approval is obtained, a marketed product and its manufacturer are subject to continual review, and discovery of previously unknown problems with a product or manufacturer may result in restrictions and sanctions with respect to the product, manufacturer and relevant manufacturing facility, including withdrawal of the product from the market.

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

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

The subject of genetically modified organisms has received negative publicity, which has aroused public debate. For example, certain countries in Europe are considering regulations that may ban products or require express labeling of products that contain genetic modifications or are genetically modified. Adverse publicity has resulted in greater regulation internationally and trade restrictions on imports of genetically altered products. If similar action is taken in the U.S., genetic research and genetically engineered products could be subject to greater domestic regulation, including stricter labeling requirements. To date, our business has not been hampered by these activities. However, such publicity in the future may prevent any products resulting from our research from gaining market acceptance and reduce demand for our products.

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

Our collaborators or we may develop genetically engineered agricultural and animal products. The field-testing, production and marketing of genetically engineered products are subject to regulation by federal, state, local and foreign governments. Regulatory agencies administering existing or future regulations or legislation may prevent us from producing and marketing genetically engineered products in a timely manner or under technically or commercially feasible conditions. In addition, regulatory action or private litigation could result in expenses, delays or other impediments to our product development programs and the commercialization of products.

The FDA has released a policy statement stating that it will apply the same regulatory standards to foods developed through genetic engineering as it applies to foods developed through traditional

plant breeding. Genetically engineered food products will be subject to premarket review, however, if these products raise safety questions or are deemed to be food additives. Our products may be subject to lengthy FDA reviews and unfavorable FDA determinations if they raise questions regarding safety or our products are deemed to be food additives.

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

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

In addition, our collaborators may use hazardous materials in connection with our collaborative efforts. To our knowledge, their work is performed in accordance with applicable biosafety regulations. In the event of a lawsuit or investigation, however, we could be held responsible for any injury caused to persons or property by exposure to, or release of, these hazardous materials use 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 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 license, milestone or other fees;

payments of licensing fees to third parties;

acceptance of our technologies and platforms;

the success rate of our discovery efforts leading to milestones 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; 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 during the next year. Accordingly, if our revenues decline or do not grow as anticipated due to the expiration of existing contracts or our failure to obtain new contracts, our inability to meet milestones or 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 stock.

Our stock price may be extremely volatile.

We believe the trading price of our common stock will remain highly volatile and may fluctuate substantially due to factors such as the following:

the announcement of new products or services by us or our competitors;

quarterly variations in our or our competitors' results of operations;

failure to achieve operating results projected by securities analysts;

changes in earnings estimates or recommendations by securities analysts;

developments in the biotechnology industry;

acquisitions of other companies or technologies; and

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

These factors and fluctuations, 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 of acquired companies;

the potential loss of key collaborators of the acquired companies;

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.

Currency fluctuations may impair our financial results.

With our acquisition of Artemis, some of our operating expenses are denominated in foreign currencies. To the extent that our operating expenses are denominated in foreign currencies, our operating results may be adversely affected by changes in exchange rates. Given the substantial volatility of currency exchange rates, and constantly changing currency exposures, we cannot predict the effect of exchange rate fluctuations on our future operating results. Although we engage in foreign currency hedging transactions from time to time, these hedging transactions can be costly, and therefore, we do not attempt to cover all potential foreign currency exposures. These hedging techniques do not eliminate all of the effects of foreign currency fluctuations on anticipated revenue.

If product liability lawsuits are successfully brought against us, we could face substantial liabilities that exceed our resources.

We may be held liable if any product our collaborators or we develop causes injury or is found otherwise unsuitable during product testing, manufacturing, marketing or sale. Although we intend to obtain general liability and product liability insurance, this insurance may be prohibitively expensive, or may not fully cover our potential liabilities. Inability to obtain sufficient insurance coverage at an acceptable cost or to otherwise protect ourselves against potential product liability claims could prevent or inhibit the commercialization of products developed by our collaborators or us.

Our facilities are located near known earthquake fault zones, and the occurrence of an earthquake or other catastrophic disaster could cause damage to our facilities and equipment, which could require us to cease or curtail operations.

Given our location, our facilities are vulnerable to damage from earthquakes. We are also vulnerable to damage from other types of disasters, including fire, floods, power loss, communications failures and similar events. If any disaster were to occur, our ability to operate our business at our facilities would 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. The insurance we maintain may not be adequate to cover our losses resulting from disasters or other business interruptions. Accordingly, an earthquake or other disaster could materially and adversely harm our ability to conduct business.

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 outstanding 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 deemed appropriate. In October 2000, a significant number of shares of our common stock held by existing stockholders became freely tradable, subject in some instances to the volume and other limitations of Rule 144. Sales of these shares and other shares of common stock held by existing stockholders could cause the market price of our common stock to decline. In addition, up to 1.7 million shares of our common stock held by former investors in Artemis will become freely tradable in August 2001 following the expiration of a 90-day lock-up for shares acquired in the Artemis acquisition.

Some of our existing stockholders can exert control over us, and may not make decisions that are in the best interests of all 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 you would not approve.

CAUTIONARY NOTE REGARDING FORWARD-LOOKING STATEMENTS

Some of the statements in this prospectus and the documents incorporated by reference are forward-looking statements. 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, predict, potential, continue, or the negative of such terms or other similar expressions, identify forward-looking statements. 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 several factors more fully described under the caption "Risk Factors" and in the documents incorporated by reference. The forward-looking statements made in this prospectus relate only to events as of the date on which the statements are made.

USE OF PROCEEDS

Unless otherwise indicated in the prospectus supplement, the net proceeds from the sale of common stock offered by this prospectus will be used for general corporate purposes, including capital expenditures and to meet working capital needs. These purposes may also include repaying indebtedness. In addition, from time to time we may evaluate the acquisition of businesses, products and technologies for which a portion of the net proceeds may be used; however, we currently are not planning or negotiating any such transactions. Pending such uses, we may invest the net proceeds in interest-bearing securities.

PLAN OF DISTRIBUTION

We may sell the common stock offered under this prospectus:

through one or more underwriters or dealers in a public offering and sale by them;

directly to investors; or

through agents.

We may sell the common stock offered under this prospectus from time to time in one or more transactions:

at a fixed price or prices, which may be changed from time to time;

at market prices prevailing at the times of sale;

at prices related to such prevailing market prices; or

at negotiated prices.

We will describe the method of distribution of the securities in the prospectus supplement.

Underwriters, dealers or agents may receive compensation in the form of discounts, concessions or commissions from us or our purchasers (as their agents in connection with the sale of securities). These underwriters, dealers or agents may be considered to be underwriters under the Securities Act. As a result, discounts, commissions or profits on resale received by the underwriters, dealers or agents may be treated as underwriting discounts and commissions. The prospectus supplement will identify any such underwriter, dealer or agent, and describe any compensation received by them from us. Any public offering price and any discounts or concessions allowed or reallocated or paid to dealers may be changed from time to time.

Underwriters, dealers and agents may be entitled to indemnification by us against certain civil liabilities, including liabilities under the Securities Act, or to contribution with respect to payments made by the underwriters, dealers or agents, under agreements between us and the underwriters, dealers and agents.

We may grant underwriters who participate in the distribution of our common stock an option to purchase additional shares of common stock to cover over-allotments, if any, in connection with the distribution.

Underwriters or agents and their associates may be customers of, engage in transactions with or perform services for us in the ordinary course of business.

DESCRIPTION OF CAPITAL STOCK

Our authorized capital stock consists of 100,000,000 shares of common stock, \$0.001 par value per share, and 10,000,000 shares of preferred stock, \$0.001 par value per share.

Common Stock

As of May 31, 2001, there were 48,533,903 shares of Exelixis common stock outstanding, held of record by approximately 923 stockholders. The holders of common stock are entitled to one vote for each share held of record on all matters submitted to a vote of the stockholders. Accordingly, holders of a majority of the shares of common stock entitled to vote in any election of directors may elect all of the directors standing for election. Subject to preferences that may be applicable to any preferred stock outstanding at the time, the holders of outstanding shares of common stock are entitled to receive ratably any dividends out of assets legally available therefor as our board of directors may from time to time determine. Upon liquidation, dissolution or winding up of Exelixis, holders of common stock are entitled to share ratably in all assets remaining after payment of liabilities and the liquidation preference of any then outstanding shares of preferred stock. Holders of common stock have no preemptive or conversion rights or other subscription rights. There are no redemption or sinking fund provisions applicable to the common stock. All outstanding shares of Exelixis common stock are, and all shares of Exelixis common stock to be outstanding upon the closing of this offering will be, fully paid and nonassessable.

Preferred Stock

Our board of directors has the authority to issue up to 10,000,000 shares of Exelixis preferred stock, in one or more series and to determine the rights, preferences, privileges and restrictions of the preferred stock, including dividend rights, conversion rights, voting rights, terms of redemption, liquidation preferences, sinking fund terms and the number of shares constituting any series or the

designation of any series. The issuance of Exelixis preferred stock could diminish the voting power of holders of Exelixis common stock, and the likelihood that holders of Exelixis preferred stock will receive dividend payments and payments upon liquidation may have the effect of delaying, deferring or preventing a change in control of Exelixis. We have no present plans to issue any shares of Exelixis preferred stock.

Warrants

As of May 31, 2001, the following warrants to purchase an aggregate of 496,220 shares of Exelixis common stock were outstanding:

a warrant to purchase 71,428 shares of common stock at an exercise price of \$1.13 per share. The warrant expires on April 14, 2005;

three warrants to purchase an aggregate of 106,875 shares of common stock at an exercise price of \$4.00 per share. The warrants expire on April 14, 2005;

three warrants to purchase an aggregate of 78,750 shares of common stock at an exercise price of \$13.00 per share. The warrants expire on April 14, 2005;

13 warrants to purchase an aggregate of 166,251 shares of common stock at an exercise price of \$20.00 per share. The warrants expire on December 31, 2001;

a warrant to purchase 29,167 shares of common stock at an exercise price of \$20.98 per share. The warrant expires on December 31, 2001; and

two warrants to purchase an aggregate of 43,750 shares of common stock at an exercise price of \$20.00 per share. The warrants expire on September 30, 2004.

The warrants contain provisions for the adjustment of the exercise price and the aggregate number of shares that may be issued upon the exercise of the warrants if a stock dividend, stock split, reorganization, reclassification or consolidation occurs.

Registration Rights

Holders of an aggregate of 23,199,818 shares of common stock and holders of warrants to purchase an aggregate of 71,428 shares of common stock will be entitled to rights to register these shares under the Securities Act. These rights are provided under the fourth amended and restated securityholders agreement, dated January 28, 1999, under the fourth amended and restated registration rights agreement, dated February 26, 1999, and under agreements with similar registration rights. If we propose to register any of our securities under the Securities Act, either for our own account or for the account of others, the holders of these shares with registration rights are entitled to notice of the registration and are entitled to include, at our expense, their shares of common stock in the registration and any related underwriting, provided, among other conditions, that the underwriters may limit the number of shares to be included in the registration and in some cases, exclude these shares entirely. In addition, the holders of these shares may require us, at our expense and on not more than two occasions, to file a registration statement under the

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Securities Act with respect to their shares of common stock, and we will be required to use our best efforts to effect the registration. Further, the holders may require us, at our expense, to register their shares on Form S-3 when this form is available. In addition, in connection with our sale of shares of common stock to Bristol-Myers Squibb on July 17, 2001 we have agreed to file a resale registration statement on Form S-3 for the 600,600 shares purchased by Bristol-Myers Squibb within 45 days of the purchase date.

Delaware General Corporation Law and Certain Charter Provisions.

In general, Section 203 of the Delaware General Corporation Law prohibits a publicly-held Delaware corporation from engaging in any business combination with any interested stockholder for a period of three years following the date that the stockholder became an interested stockholder unless:

prior to that date, the corporation's board of directors approved either the business combination or the transaction that resulted in the stockholder becoming an interested stockholder;

upon consummation of the transaction that resulted in the stockholder becoming an interested stockholder, the interested stockholder owned at least 85% of the voting stock of the corporation outstanding at the time the transaction commenced, excluding those shares owned by persons who are directors and also officers, and by employee stock plans in which shares held subject to the plan will be tendered in a tender or exchange offer; or

on or subsequent to that date, the business combination is approved by the corporation's board of directors and is authorized at an annual or special meeting of stockholders, and not by written consent, by the affirmative vote of at least two-thirds of the outstanding voting stock not owned by the interested stockholder.

Section 203 defines "business combination" to include:

any merger or consolidation involving the corporation and the interested stockholder;

any sale, transfer, pledge or other disposition involving the interested stockholder of 10% or more of the assets of the corporation;

subject to exceptions, any transaction that results in the issuance or transfer by the corporation of any stock of the corporation to the interested stockholder; and

the receipt by the interested stockholder of the benefit of any loans, advances, guarantees, pledges or other financial benefits provided by or through the corporation.

In general, Section 203 defines an interested stockholder as any entity or person beneficially owning 15% or more of the outstanding voting stock of the corporation and any entity or person affiliated with or controlling or controlled by the entity or person.

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

substantially limits the use of cumulative voting in the election of directors;

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provides that the authorized number of directors may be changed only by resolution of its board of directors; and

authorizes its board of directors to issue blank check preferred stock to increase the amount of outstanding shares.

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

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

Transfer Agent and Registrar

The transfer agent and registrar for Exelixis common stock is Mellon Investor Services LLC.

LEGAL MATTERS

The validity of the shares of common stock offered hereby will be passed upon by Cooley Godward LLP, Palo Alto, California.

EXPERTS

The consolidated financial statements incorporated in this prospectus by reference to the Annual Report on Form 10-K for the year ended December 31, 2000, have been so incorporated in reliance on the report of PricewaterhouseCoopers LLP, independent accountants, given on the authority of said firm as experts in auditing and accounting.

WHERE YOU CAN FIND MORE INFORMATION ABOUT EXELIXIS

You should rely only on the information provided or incorporated by reference in this prospectus or any prospectus supplement. We have authorized no one to provide you with different information. We are not making an offer of these securities in any state where the offer is not permitted. You should not assume that the information in this prospectus or any prospectus supplement is accurate as of any date other than the date on the front of the document.

We have filed with the SEC a registration statement on Form S-3 to register the common stock offered by this prospectus. However, this prospectus does not contain all of the information contained in the registration statement and the exhibits and schedules to the registration statement. We strongly encourage you to carefully read the registration statement and the exhibits and schedules to the registration statement.

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 450 Fifth Street, N.W., Washington, DC 20549 or at the SEC's other public reference rooms located in New York, New York and Chicago, Illinois. You can request copies of these documents by contacting the SEC and paying a fee for the copying cost. Please call the SEC at 1-800-SEC-0330 for further information on the public reference rooms. Our SEC filings are also available to the public from the SEC's website at www.sec.gov.

The SEC allows us to incorporate by reference the information contained in documents that we file with them, which means that we can disclose important information to you by referring to those documents. The information incorporated by reference is considered to be part of this prospectus. Information in this prospectus supersedes information incorporated by reference that we filed with the SEC prior to the date of this prospectus, while information that we file later with the SEC will automatically update and supersede this information. We incorporate by reference the documents listed below and any future filings we will make with the SEC under

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Sections 13(a), 13(c), 14 or 15(d) of the Securities Exchange Act of 1934.

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

1. Our Annual Report on Form 10-K for the year ended December 31, 2000;

2. Our Quarterly Report on Form 10-Q for the quarter ended March 31, 2001;

3. Our Current Reports on Form 8-K, filed on May 15, 2001 pursuant to Item 2 of such report, on July 18, 2001 and on July 26, 2001 pursuant to Item 5 of such report; and

4. The description of our common stock set forth in our registration statement on Form 8-A, filed with the SEC on April 6, 2000.

We will furnish without charge to you, on 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, telephone: (650) 837-7000.

No dealer, salesperson or other person is authorized to give any information or to represent anything not contained in the prospectus and the prospectus supplement. You must not rely on any unauthorized information or representations. The prospectus and the prospectus supplement are 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 the prospectus and the prospectus supplement is current only as of their respective dates.

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6,500,000 Shares

Exelixis, Inc.

Common Stock

Goldman, Sachs & Co.
