EXELIXIS INC
Form 424B5
August 17, 2005

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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.

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 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;

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;

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 lendor 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

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;

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 reaquire 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

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;

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 confidentia