
**UNITED STATES
SECURITIES AND EXCHANGE COMMISSION**
Washington, D.C. 20549

**Amendment No. 1
to
FORM S-3
REGISTRATION STATEMENT
UNDER
THE SECURITIES ACT OF 1933**

EXELIXIS, INC.

(Exact name of registrant as specified in its charter)

Delaware
(State or other jurisdiction of incorporation or organization)

04-3257395
(I.R.S. Employer Identification No.)

**170 Harbor Way
P.O. Box 511
South San Francisco, CA 94083
(650) 837-7000**
(Address, including zip code, and telephone number, including area code, of registrant's principal executive offices)

**George A. Scangos, Ph.D.
President and Chief Executive Officer
Exelixis, Inc.
170 Harbor Way
P.O. Box 511
South San Francisco, CA 94083
(650) 837-7000**
(Name, address, including zip code, and telephone number, including area code, of agent for service)

Copy to:

**Christoph Pereira, Esq.
Vice President, Legal Affairs and Secretary
Exelixis, Inc.
170 Harbor Way
P.O. Box 511
South San Francisco, CA 94083
(650) 837-7000**

**Andrea Vachss, Esq.
Covington & Burling
One Front Street
San Francisco, CA 94111
(415) 591-6000**

Approximate date of proposed sale to the public: From time to time after the effective date of this Registration Statement.

If the only securities being registered on this form are being offered pursuant to dividend or interest reinvestment plans, please check the following box.

If any of the securities being registered on this form are to be offered on a delayed or continuous basis pursuant to Rule 415 under the Securities Act of 1933, other than securities offered only in connection with dividend or interest reinvestment plans, check the following box.

If this form is filed to register additional securities for an offering pursuant to Rule 462(b) under the Securities Act, please check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering.

If this form is a post-effective amendment filed pursuant to Rule 462(c) under the Securities Act, check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering.

If delivery of the Prospectus is expected to be made pursuant to Rule 434, please check the following box.

The registrant hereby amends this registration statement on such date or dates as may be necessary to delay its effective date until the registrant shall file a further amendment that specifically states that this registration statement shall thereafter become effective in accordance with Section 8(a) of the Securities Act of 1933 or until the registration statement shall become effective on such date as the Securities and Exchange Commission, acting pursuant to said Section 8(a), may determine.

The information in this prospectus is not complete and may be changed. We may not sell these securities until the registration statement filed with the Securities and Exchange Commission is effective. This prospectus is not an offer to sell these securities and it is not soliciting an offer to buy these securities in any state where the offer or sale is not permitted.

SUBJECT TO COMPLETION, DATED MARCH 28, 2005

PROSPECTUS



EXELIXIS, INC.

2,561,174 Shares

Common Stock

This prospectus relates to resales by selling stockholders of shares of common stock of Exelixis, Inc. We will not receive any proceeds from this offering. The selling stockholders, formerly security holders of X-Ceptor Therapeutics, Inc., acquired their shares of our common stock in connection with our acquisition of X-Ceptor.

Our common stock is traded on The Nasdaq National Market under the symbol "EXEL." On March 28, 2005, the last reported sale price of our common stock on The Nasdaq National Market was \$7.15 per share.

We will not be paying any underwriting discounts or commissions in connection with this offering.

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

INVESTING IN OUR SECURITIES INVOLVES A HIGH DEGREE OF RISK. SEE THE SECTION ENTITLED "[RISK FACTORS](#)" ON PAGE 3 OF THIS PROSPECTUS.

The date of this prospectus is March __, 2005.

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This prospectus is part of a registration statement 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. No dealer, salesperson or other person is authorized to give any information or to represent anything not contained in this prospectus. You must not rely on any unauthorized information or representation. This prospectus is an offer to sell only the securities offered hereby, but only under circumstances and in jurisdictions where it is lawful to do so. You should assume that the information in this prospectus or any prospectus supplement is accurate only as of the date on the front of the document and that any information we have incorporated by reference is accurate only as of the date of the document incorporated by reference, regardless of the time of delivery of this prospectus or any sale of a security.

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

EXELIXIS, INC.

Our primary mission is to develop proprietary human therapeutics by leveraging our integrated discovery platform to increase the speed, efficiency and quality of pharmaceutical product discovery and development. We have generated a substantial development pipeline of small molecule compounds that we believe are therapeutically differentiated and commercially valuable. Our clinical pipeline includes compounds being developed to treat cancer and renal disease and is led by XL119, our Phase 3 cancer compound. We also have multiple compounds in preclinical development for diseases including cancer, metabolic disorders and cardiovascular disease.

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

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

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

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 or in any accompanying prospectus supplement, including the additional information in our reports and other documents we file with the Securities and Exchange Commission that are incorporated by reference in this prospectus. These documents may update the risk factors from time to time. 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 our current cash and cash equivalents, short-term investments and funding that we expect to receive from collaborators will enable us to maintain our currently planned operations for at least the next 15 months. 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;
- 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, including clinical development costs we intend to offload through financing vehicles or by partnering with other companies;
- 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

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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.

Our capital needs may also increase in 2006 if we have to repay a \$30 million convertible promissory note that we issued in May 2001 to Protein Design Labs, Inc. in connection with a collaboration agreement. The note matures in May 2006 and is convertible into our common stock at Protein Design Labs option. The note is convertible into Exelixis 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.

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 SmithKlineBeecham Corporation, 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 December 31, 2004, our working capital was \$100.2 million and our cash and investments were \$171.2 million. If we were to default on the financial covenants under the loan and security agreement, SmithKlineBeecham Corporation 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 December 31, 2004, we had unrestricted cash of \$86.4 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 \$137.2 million for the year ended December 31, 2004. As of that date, we had an accumulated deficit of approximately \$519.4 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 five product candidates in various stages of clinical development and we anticipate filing IND applications for

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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.

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 trial, including, among others:

- the number of patients that ultimately participate in the 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.

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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 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. 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.

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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 pre-clinical 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 our current compounds in clinical development, XL119, XL784, XL647, XL999 and XL880. We rely on collaborators and third-party contractors to produce our compounds for pre-clinical 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 pre-clinical 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,

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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. For example, our primary supplier for XL119 informed us of an internal restructuring that may impact our ability to obtain drug substance from them. While we do not expect that this restructuring will jeopardize the drug supply for the Phase 3 clinical studies for XL119 and expect that we will be able to obtain additional supplies of XL119 when necessary, we cannot be certain that we will be able to obtain additional supplies of XL119 in a timely manner and on terms as favorable as our current arrangement. Our inability to obtain critical materials for any reason could substantially impair our development activities or the production, marketing and distribution of any products that we may develop.

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 pre-clinical testing, and data obtained from pre-clinical 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.

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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

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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 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. 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

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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 pre-clinical 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.

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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 or 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

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

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

We have experienced a period of rapid and substantial growth that has placed, and our anticipated growth in the future will continue to place, a strain on our research, administrative and operational infrastructure. As our operations expand, we will need to continue to manage multiple locations and additional relationships with various collaborative partners, suppliers and other third parties. Our ability to manage our operations and growth effectively requires us to continue to improve our reporting systems and procedures as well as our operational, financial and management controls. In addition, 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

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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, 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 are considering regulations that ban 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

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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 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;

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- the timing and amount of expenses incurred for clinical development and manufacturing of our products;
- the impairment of acquired goodwill and other assets; and
- general and industry-specific economic conditions that may affect our collaborators' research and development expenditures.

A large portion of our expenses, including expenses for facilities, equipment and personnel, are relatively fixed in the short term. In addition, we expect operating expenses to increase significantly as we move more compounds into clinical development. Accordingly, if our revenues decline or do not grow as anticipated due to the expiration or termination of existing contracts 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;
- 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;
- 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.

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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.

For example, in October 2004, we completed our acquisition of X-Ceptor. If we are not successful in integrating X-Ceptor in our operations, the anticipated benefits of the acquisition may not be realized. The dedication of management resources to integration activities may detract attention from the day-to-day business. In addition, key officers and employees of X-Ceptor may leave the company at any time. The failure to retain such key officers and employees may decrease the likelihood of a successful integration.

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

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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.

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.

SPECIAL 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. Examples of these statements include, but are not limited to, statements regarding the following: our business and scientific strategies; the progress of our product development programs, including clinical testing; our corporate collaborations, including revenues received from these collaborations; our drug discovery technologies; our research and development expenses; protection of our intellectual property; sufficiency of our cash resources; and our operations and legal risks. 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" in documents incorporated by reference in this prospectus. The forward-looking statements made in this prospectus relate only to events as of the date on which the statements are made. We do not intend to update any forward-looking statement to reflect events or circumstances after the date on which the statement is made or to reflect the occurrence of unanticipated events.

USE OF PROCEEDS

The proceeds from the sale of the common stock offered pursuant to this prospectus are solely for the account of the selling stockholders. We will not receive any proceeds from the sale of these shares of common stock.

SELLING STOCKHOLDERS

We are registering the shares of common stock covered by this prospectus on behalf of the selling stockholders named in the table below. We issued the shares to the selling stockholders in a private placement transaction in connection with our acquisition of X-Ceptor Therapeutics, Inc. on October 18, 2004. On that date we entered into a Registration Rights Agreement with the selling stockholders, in which we agreed to register the shares to permit the selling stockholders and their pledgees, donees, transferees or other successors-in-interest that receive their shares from a selling stockholder as a gift, partnership distribution or other non-sale related transfer after the date of this prospectus, to resell the shares.

The following table sets forth certain information provided to us by the selling stockholders, including the name of each selling stockholder, the number of shares of our common stock beneficially owned by each selling stockholder as of March 15, 2005, the number of shares that may be offered under this prospectus and the number of shares of our common stock beneficially owned by each selling stockholder after this offering is completed. Except as set forth in the table below, none of the selling stockholders has had a material relationship with us within the past three years. The number of shares in the column “Number of Shares Being Offered” represents all of the shares that each selling stockholder may offer under this prospectus. The selling stockholders may sell some, all or none of their shares.

Name	Number of Shares Beneficially Owned Prior to Offering	Number of Shares Being Offered	Number of Shares Beneficially Owned After Offering (1)
A.M. Pappas Life Science Ventures I, LP ⁽²⁾	208,796	208,796	—
Capital Technologies CDPQ Inc.	206,056	206,056	—
Cubitt, Andrew ⁽³⁾	1,257	1,257	—
Domain Partners IV, L.P. ⁽⁴⁾	516,469	516,469	—
DP IV Associates, L.P. ⁽⁴⁾	12,375	12,375	—
Evans, Ronald M. ⁽⁵⁾	7,494	7,494	—
Farallon Capital Institutional Partners II, L.P. ⁽⁶⁾	126,208	126,208	—
Farallon Capital Institutional Partners III, L.P. ⁽⁶⁾	54,089	54,089	—
Farallon Capital Institutional Partners, L.P. ⁽⁶⁾	302,902	302,902	—
Farallon Capital Partners, L.P. ⁽⁶⁾	201,934	201,934	—
Giargiari, Robert P.	274	274	—
GIMV NV	195,753	195,753	—
Heyman, Richard A. ⁽⁷⁾	23,311	23,311	—
Kinsella, Kevin J. ⁽³⁾	6,852	6,852	—
Lazard Frères & Co. L.L.C. ⁽⁸⁾	18,656	18,656	—
Ligand Pharmaceuticals Incorporated	618,169	618,169	—
Mangelsdorf, David ⁽⁵⁾	5,850	5,850	—
Mohan, Raju ⁽⁷⁾	7,542	7,542	—
Naeve, Janis Corey ⁽³⁾	2,514	2,514	—
O’Malley, Bert W. ⁽⁵⁾	2,055	2,055	—
RR Capital Partners, L.P. ⁽⁶⁾	36,059	36,059	—
Schulman, Ira ⁽⁷⁾	5,028	5,028	—
Tran, Donna Dau-Thi ⁽³⁾	1,257	1,257	—
Wang, Ming Wei	274	274	—

⁽¹⁾ Assumes the sale of all shares being offered.

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- (2) AMP&A Management, LLC is the General Partner of A.M. Pappas Life Science Ventures I, LP. Arthur M. Pappas, in his capacity as Chairman of the Investment Committee of AMP&A Management, LLC, has voting and dispositive power over the shares being offered by A.M. Pappas Life Science Ventures I, LP.
- (3) Mr. Cubitt, Mr. Kinsella, Ms. Naeve and Ms. Tran were employees of X-Ceptor Therapeutics, Inc. a wholly owned subsidiary of the Company, prior to its acquisition by the Company.
- (4) One Palmer Square Associates IV, LLC is the General Partner of Domain Partners IV, LP and DP IV Associates, LP. James C. Blair, Brian H. Dovey, Jesse I. Treu and Kathleen K. Schoemaker, the Managing Members of One Palmer Square Associates IV, LLP, have voting and dispositive power over the shares being offered by Domain Partners IV, LP and DP IV Associates, LP.
- (5) Messrs. Evans, Mangelsdorf and O'Malley were consultants to X-Ceptor Therapeutics, Inc. prior to its acquisition by the Company. The Company expects to enter into a consulting agreement with Mr. Evans.
- (6) As the general partner of each of the noted partnerships, Farallon Partners, L.L.C., may, for purposes of Rule 13d-3 under the Securities Exchange Act of 1934, as amended, be deemed to own beneficially the shares held by the Farallon partnerships. As the managing members of Farallon Partners, L.L.C., each of Chun R. Ding, Joseph F. Downes, William F. Duhamel, Charles E. Ellwein, Richard B. Fried, Monica R. Landry, William F. Mellin, Rajiv A. Patel, Stephen L. Millham, Derek C. Schrier, Thomas F. Steyer and Mark C. Wehrly may, for purposes of Rule 13d-3 under the Exchange Act, be deemed to own beneficially the shares held by the Farallon partnerships. As investment sub-advisers to Farallon Partners, L.L.C., each of Noonday G.P. (U.S.), L.L.C. and Noonday Asset Management, L.P. may, for purposes of Rule 13d-3 under the Exchange Act, be deemed to own beneficially the shares held by the Farallon partnerships. Noonday Capital, L.L.C., as the general partner of Noonday Asset Management, L.P., may, for purposes of Rule 13d-3 under the Exchange Act, be deemed to own beneficially the shares held by the Farallon partnerships. David I. Cohen, as the managing member of Noonday G.P. (U.S.), L.L.C. and Noonday Capital, L.L.C., may, for purposes of Rule 13d-3 under the Exchange Act, be deemed to own beneficially the shares held by the Farallon partnerships. Each of Farallon Partners, L.L.C., Noonday G.P. (U.S.), L.L.C., Noonday Asset Management, L.P. and Noonday Capital, L.L.C., the managing members of Farallon Partners, L.L.C. and Cohen disclaim any beneficial ownership of such shares. All of the above-mentioned entities and persons disclaim group attribution.
- (7) Messrs. Heyman, Mohan, and Schulman are employees of X-Ceptor Therapeutics, Inc.
- (8) Lazard Frères & Co. L.L.C., a broker-dealer, received its shares of common stock as compensation for investment banking services provided in connection with our acquisition of X-Ceptor Therapeutics, Inc. We also paid Lazard Frères & Co. L.L.C. \$1,350,000 in connection with the transaction.

PLAN OF DISTRIBUTION

The selling stockholders may sell the shares from time to time. The selling stockholders will act independently of us in making decisions regarding the timing, manner and size of each sale. The sales may be made on the Nasdaq Stock Market, on one or more exchanges or in the over-the-counter market or otherwise, at prices and at terms then prevailing or at prices related to the then current market price, or in privately negotiated transactions. The selling stockholders may effect these transactions by selling the shares to or through broker-dealers. The selling stockholders may also sell their shares in one or more of, or a combination of:

- ordinary brokerage transactions and transactions in which the broker solicits purchasers;
- a block trade in which the broker-dealer will attempt to sell the shares as agent but may position and resell a portion of the block as principal to facilitate the transaction;
- a purchase by a broker-dealer as principal and resale by a broker-dealer for its account under this prospectus; and
- an exchange distribution in accordance with the rules of an exchange.

To the extent required, this prospectus may be amended or supplemented from time to time to describe a specific plan of distribution. If the plan of distribution involves an arrangement with a broker-dealer for the sale of shares through a block trade, special offering, exchange distribution or secondary distribution or a purchase by a broker or dealer, the amendment or supplement will disclose:

- the name of each selling stockholder and of the participating broker-dealer(s);
- the number of shares involved;
- the price at which the shares were sold;
- the commissions paid or discounts or concessions allowed to the broker-dealer(s), where applicable;

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- that a broker-dealer(s) did not conduct any investigation to verify the information set out or incorporated by reference in this prospectus; and
- other facts material to the transaction.

From time to time, a selling stockholder may transfer, pledge, donate or assign its shares of common stock to lenders or others, and each of such persons will be deemed to be a “selling stockholder” for purposes of this prospectus. The number of shares of common stock beneficially owned by the selling stockholder will decrease as and when it takes such actions. The plan of distribution for the selling stockholders’ shares of common stock sold under this prospectus will otherwise remain unchanged, except that the transferees, pledgees, donees or other successors will be selling stockholders hereunder. Upon being notified by a selling stockholder that a donee or pledgee intends to sell more than 500 shares, we will file a supplement to this prospectus.

The selling stockholders may enter into option or other transactions with broker-dealers which require the delivery to the broker-dealer of the shares. The broker-dealer may then resell or otherwise transfer the shares under this prospectus. The selling stockholders also may loan or pledge the shares to a broker-dealer. The broker-dealer may sell the loaned shares, or upon a default the broker-dealer may sell the pledged shares under this prospectus.

In effecting sales, broker-dealers engaged by the selling stockholders may arrange for other broker-dealers to participate in the resales. Broker-dealers or agents may receive compensation in the form of commissions, discounts or concessions from selling stockholders. Broker-dealers or agents may also receive compensation from the purchasers of the shares for whom they act as agents or to whom they sell as principals, or both. Compensation as to a particular broker-dealer might be in excess of customary commissions and will be in amounts to be negotiated in connection with the sale. Broker-dealers or agents and any other participating broker-dealers or the selling stockholders may be deemed to be “underwriters” within the meaning of Section 2(11) of the Securities Act of 1933, as amended, in connection with sales of the shares. Accordingly, any commission, discount or concession received by them and any profit on the resale of the shares purchased by them may be deemed to be underwriting discounts or commissions under the Securities Act. Because selling stockholders may be deemed to be “underwriters” within the meaning of Section 2(11) of the Securities Act, the selling stockholders will be subject to the prospectus delivery requirements of the Securities Act. In addition, any securities covered by this prospectus that qualify for sale under Rule 144 promulgated under the Securities Act may be sold under Rule 144 rather than under this prospectus. The selling stockholders have advised that they have not entered into any agreements, understandings or arrangements with any underwriters or broker-dealers regarding the sale of their securities. There is no underwriter or coordinating broker acting in connection with the proposed sale of shares by the selling stockholders.

The shares will be sold only through registered or licensed brokers or dealers if required under applicable state securities laws. In addition, in some states the shares may not be sold unless they have been registered or qualified for sale in the applicable state or an exemption from the registration or qualification requirement is available and is complied with.

In the event of a distribution of the shares, the selling stockholders, any selling broker or dealer and any affiliated purchasers may be subject to Regulation M under the Exchange Act, which would generally prohibit these persons from bidding for or purchasing any security that is the subject of the distribution until his or her participation in that distribution is completed. In addition, Regulation M also prohibits any bid or purchase for the purpose of pegging, fixing or stabilizing the price of our common stock in connection with this offering.

We will bear all printing, registration and filing fees and our own legal and accounting fees and in connection with the registration of the shares. The selling stockholders will bear their own legal fees and costs and all commissions, discounts and expenses of underwriters or brokers, if any, attributable to the sales of the shares. We and the selling stockholders have agreed to indemnify each other against certain liabilities that could arise from the registration and sale of the shares.

Holders of 2,050,875 shares being offered pursuant to this prospectus have agreed to restrictions regarding the sale of their shares of common stock. Until April 16, 2005, none of the shares subject to these restrictions may be sold. Commencing on April 16, 2005, up to 410,171 of the shares subject to these restrictions may be sold in each subsequent three-month period. Commencing on October 18, 2006, up to 820,346 of the shares subject to these restrictions may be sold in each subsequent three-month period. All of the foregoing restrictions are subject to expiration in the event of certain merger or tender offer transactions.

We have agreed to use commercially reasonable efforts to keep the registration statement effective until the earliest of (i) such time as all shares of common stock offered pursuant to this prospectus may be sold in a three

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month period pursuant to Rule 144 under the Securities Act (taking into consideration volume limitations under Rule 144(e) relating to one percent of the shares outstanding of Exelixis but not taking into consideration the average weekly trading volume), (ii) such time as all of the shares of common stock offered pursuant to this prospectus have been sold or otherwise disposed of by the selling stockholders and (iii) October 18, 2006.

LEGAL MATTERS

The validity of the securities being offered hereby will be passed upon by Covington & Burling, San Francisco, California.

EXPERTS

Ernst & Young LLP, independent registered public accounting firm, have audited our consolidated financial statements included in our Annual Report on Form 10-K for the year ended December 31, 2004, and Exelixis, Inc. management's assessment of the effectiveness of internal control over financial reporting as of December 31, 2004 included therein, as set forth in their reports, which are incorporated by reference in this prospectus and elsewhere in this registration statement. Our financial statements and management's assessment are incorporated by reference in reliance on Ernst & Young LLP's reports, given on their authority as experts in accounting and auditing.

WHERE YOU CAN FIND MORE INFORMATION

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

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

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

1. Our annual report on Form 10-K for the year ended December 31, 2004, filed with the Securities and Exchange Commission on March 15, 2005;

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2. Our current report on Form 8-K, filed with the Securities and Exchange Commission on January 7, 2005;
3. Our current report on Form 8-K, filed with the Securities and Exchange Commission on January 10, 2005;
4. Our current report on Form 8-K, filed with the Securities and Exchange Commission on January 19, 2005;
5. Our current report on Form 8-K, filed with the Securities and Exchange Commission on February 16, 2005 (except for information contained in Item 2.02 or any related exhibit); and
6. The description of our common stock set forth in our registration statement on Form 8-A, filed with the Securities and Exchange Commission on April 6, 2000, including any amendments or reports filed for the purposes of updating this description.

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

PART II
INFORMATION NOT REQUIRED IN THE PROSPECTUS

Item 14. Other Expenses of Issuance and Distribution

The following table sets forth the estimated costs and expenses payable by the registrant in connection with the offering of the securities being registered. All the amounts shown are estimates, except for the registration fee.

Securities and Exchange Commission registration fee	\$ 2,572
Accounting fees and expenses	12,000
Legal fees and expenses	50,000
Printing and miscellaneous expenses	3,428
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Total	\$68,000
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Item 15. Indemnification of Officers and Directors

Our amended and restated certificate of incorporation provides that we must indemnify our directors to the fullest extent under applicable law. Pursuant to Delaware law, this includes elimination of liability for monetary damages for breach of the directors' fiduciary duty of care to Exelixis and its stockholders. However, our directors may be personally liable for liability:

- for any breach of duty of loyalty to us or to our stockholders;
- for acts or omissions not in good faith or that involve intentional misconduct or a knowing violation of law;
- for unlawful payment of dividends or unlawful stock repurchases or redemptions under Section 174 of the Delaware General Corporation Law; or
- for any transaction from which the director derived an improper personal benefit.

In addition, our amended and restated bylaws provide that:

- we are required to indemnify our directors and executive officers to the fullest extent not prohibited by Delaware law or any other applicable law, subject to limited exceptions;
- we may indemnify our other officers, employees and other agents as set forth in Delaware law or any other applicable law;
- we are required to advance expenses to our directors and executive officers as incurred in connection with legal proceedings against them for which they may be indemnified; and
- the rights conferred in the amended and restated bylaws are not exclusive.

We have also provided for liability insurance for each director and officer for certain losses arising from claims or charges made against them while acting in their capacities as directors or officers of Exelixis.

We have entered into indemnification agreements with each of our directors and certain officers. These agreements, among other things, require us to indemnify each director and officer to the fullest extent permitted by Delaware law, including indemnification for expenses such as attorneys' fees, judgments, fines and settlement amounts incurred by the director or officer in any action or proceeding, including any action by or in the right of Exelixis, arising out of the person's services as a director or officer of us, any subsidiary of ours or any other company or enterprise to which the person provides services at our request. At present, we are not aware of any pending or threatened litigation or proceeding involving any of our directors, officers, employees or agents in which indemnification would be required or permitted. We believe that our charter provisions and indemnification agreements are necessary to attract and retain qualified persons as directors and officers.

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Item 16. Exhibits and Financial Statement Schedules

(a) Exhibits

<u>Exhibit Number</u>	<u>Description of Document</u>
4.1	Amended and Restated Certificate of Incorporation of the Company.(1)
4.2	Amended and Restated Bylaws of the Company.(2)
4.3	Specimen Common Stock Certificate.(3)
5.1	Opinion of Covington & Burling.*
23.1	Consent of independent registered public accounting firm.
23.2	Consent of Covington & Burling (included in Exhibit 5.1).
24.1	Power of Attorney.*

* Previously filed.

- (1) Filed as an Exhibit to Exelixis, Inc.'s Quarterly Report on Form 10-Q for the quarter ended June 30, 2004 and incorporated herein by reference.
- (2) Filed as an Exhibit to Exelixis, Inc.'s current report on Form 8-K, as filed with the Securities and Exchange Commission on December 15, 2004 and incorporated herein by reference.
- (3) Filed as an Exhibit to Exelixis, Inc.'s Registration Statement on Form S-1 (File No. 333-30978), as filed with the Securities and Exchange Commission on February 7, 2000, as amended, and incorporated herein by reference.

Item 17. Undertakings

The undersigned registrant hereby undertakes:

(1) To file, during any period in which offers or sales are being made, a post-effective amendment to this registration statement:

(i) to include any prospectus required by section 10(a)(3) of the Securities Act of 1933;

(ii) to reflect in the prospectus any facts or events arising after the effective date of the registration statement (or the most recent post-effective amendment thereof) which, individually or in the aggregate, represent a fundamental change in the information set forth in the registration statement. Notwithstanding the foregoing, any increase or decrease in volume of securities offered (if the total dollar value of securities offered would not exceed that which was registered) and any deviation from the low or high end of the estimated maximum offering range may be reflected in the form of prospectus filed with the Securities and Exchange Commission pursuant to Rule 424(b) if, in the aggregate, the changes in volume and price represent no more than a 20 percent change in the maximum aggregate offering price set forth in the "Calculation of Registration Fee" table in the effective registration statement; and

(iii) to include any material information with respect to the plan of distribution not previously disclosed in the registration statement or any material change to such information in the registration statement.

provided, however, that paragraphs (1)(i) and (1)(ii) do not apply if the registration statement is on Form S-3, Form S-8 or Form F-3, and the information required to be included in a post-effective amendment by those paragraphs is contained in periodic reports filed with or furnished to the Securities and Exchange Commission by the registrant pursuant to section 13 or 15(d) of the Securities Exchange Act of 1934 that are incorporated by reference in the registration statement.

(2) That, for the purpose of determining any liability under the Securities Act of 1933, each post-effective amendment shall be deemed to be a new registration statement relating to the securities offered therein, and the offering of the securities at that time shall be deemed to be the initial bona fide offering thereof.

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(3) To remove from registration by means of a post-effective amendment any of the securities being registered which remain unsold at the termination of this offering.

(4) That, for purposes of determining any liability under the Securities Act of 1933, each filing of the registrant's annual report pursuant to section 13(a) or section 15(d) of the Securities Exchange Act of 1934 (and, where applicable, each filing of an employee benefit plan's annual report pursuant to section 15(d) of the Securities Exchange Act of 1934) that is incorporated by reference in the registration statement shall be deemed to be a new registration statement relating to the securities offered therein, and the offering of such securities at that time shall be deemed to be the initial bona fide offering thereof.

Insofar as indemnification for liabilities arising under the Securities Act of 1933 may be permitted to directors, officers and controlling persons of the registrant pursuant to the foregoing provisions, or otherwise, the registrant has been advised that in the opinion of the Securities and Exchange Commission this form of indemnification is against public policy as expressed in the Securities Act of 1933 and is, therefore, unenforceable. In the event that a claim for indemnification against these liabilities (other than the payment by the registrant of expenses incurred or paid by a director, officer or controlling person of the registrant in the successful defense of any action, suit or proceeding) is asserted by a director, officer or controlling person in connection with the securities being registered, the registrant will, unless in the opinion of its counsel the matter has been settled by controlling precedent, submit to a court of appropriate jurisdiction the question whether such indemnification by it is against public policy as expressed in the Securities Act of 1933 and will be governed by the final adjudication of this issue.

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*	Director	March 28, 2005
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Alan M. Garber, M.D., Ph.D.		
*	Director	March 28, 2005
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Vincent Marchesi, M.D., Ph.D.		
*	Director	March 28, 2005
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Lance Willsey, MD		
*	Director	March 28, 2005
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Frank McCormick, Ph.D.		
*	Director	March 28, 2005
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George Poste, D.V.M., Ph.D.		
*	Director	March 28, 2005
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Jack L. Wyszomierski		

*By: /s/ CHRISTOPH PEREIRA

Christoph Pereira
Attorney-in-Fact

INDEX TO EXHIBITS

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CONSENT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

We consent to the reference to our firm under the caption "Experts" in Amendment No. 1 to the Registration Statement on Form S-3 (No. 333-122079) and related Prospectus of Exelixis, Inc., for the registration of 2,561,174 shares of its common stock and to the incorporation by reference therein of our reports dated March 2, 2005, with respect to the consolidated financial statements of Exelixis, Inc., Exelixis, Inc. management's assessment of the effectiveness of internal control over financial reporting, and the effectiveness of internal control over financial reporting of Exelixis, Inc., included in its Annual Report (Form 10-K) for the year ended December 31, 2004, filed with the Securities and Exchange Commission.

/s/ Ernst & Young LLP

Palo Alto, California
March 24, 2005

VIA EDGAR

Jeffrey Riedler, Esq.
Anne Nguyen, Esq.
Securities and Exchange Commission
450 Fifth Street, N.W.
Washington, DC 20549

RE: Exelixis, Inc.
Registration Statement on Form S-3
File No. 333-122079

Dear Mr. Riedler and Ms. Nguyen:

On behalf of Exelixis, Inc., we are submitting this letter, and Amendment No. 1 to the above-captioned registration statement, in response to the staff's comment letter dated January 21, 2005 regarding the above filing. For your convenience, the staff's comment is reproduced below in italics:

"Please tell us whether any of the selling security holders are broker-dealers or affiliates of a broker-dealer. If any selling security holders are broker-dealers, please revise to identify these security holders and clearly state that these security holders are underwriters unless the shares were issued as underwriting compensation. If any of the security holders are affiliates of a broker dealer, then revise to indicate whether these selling security holders purchased the shares in the ordinary course of business. We may have further comments upon review of your response."

With the exception of Lazard Frères & Co. L.L.C., each of the selling stockholders named in the registration statement has returned to Exelixis a completed and signed questionnaire indicating that such stockholder is neither a broker-dealer nor an affiliate of a broker-dealer. Lazard has indicated that it is a broker-dealer.

In June 2003, Lazard and X-Ceptor entered into an investment banking engagement pursuant to which Lazard assisted X-Ceptor in finding a buyer (Exelixis) for X-Ceptor and provided further assistance in negotiating and consummating such transaction. Upon consummation of X-Ceptor's sale to Exelixis on October 18, 2004, Lazard earned a fee of \$1,500,000, which was paid in a combination of \$1,350,000 and the 18,656 shares of Exelixis' common stock being registered for resale on Lazard's behalf.

Jeffrey Riedler, Esq.
Anne Nguyen, Esq.
March 28, 2005
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Because Lazard earned the shares as compensation for investment banking services and represented in its questionnaire that, at the time it acquired such shares, it had no agreement or understanding, written or otherwise, with any person to distribute such shares, Exelixis respectfully submits that Lazard did not act as an underwriter in the acquisition transaction, is not acting as an underwriter in the resale of its compensatory shares of common stock and is not required to be identified as such in the registration statement.

We have added disclosure to the registration statement to clarify the foregoing and enclose for your convenience a marked copy of Amendment No. 1 to the registration statement, which is being filed simultaneously with this letter.

Thank you for your attention to this matter. Please direct any questions regarding this response to me at (415) 591-7069.

Sincerely,

/s/ Andrea Vachss
Andrea Vachss

Cc: Christoph Pereira, Esq.
Ken Ebanks, Esq.
Paul Rose, Esq.