

EXELIXIS INC
Form POS AM
May 08, 2009
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As filed with the Securities and Exchange Commission on May 8, 2009

Registration No. 333-152166

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

POST-EFFECTIVE AMENDMENT NO. 2

TO FORM S-1

ON 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.)

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249 East Grand Ave.

P.O. Box 511

South San Francisco, CA 94083-0511

(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.

249 East Grand Ave.

P.O. Box 511

South San Francisco, CA 94083-0511

(650) 837-7000

(Name, address, including zip code, and telephone number, including area code, of agent for service)

Copy to:

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Approximate date of commencement of proposed sale to the public:

From time to time after the effective date of this Registration Statement.

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If the only securities being registered on this Form are being offered pursuant to dividend or interest reinvestment plans, 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 this Form is a registration statement pursuant to General Instruction I.D. or a post-effective amendment thereto that shall become effective upon filing with the Commission pursuant to Rule 462(e) under the Securities Act, check the following box.

If this Form is a post-effective amendment to a registration statement filed pursuant to General Instruction I.D. filed to register additional securities or additional classes of securities pursuant to Rule 413(b) under the Securities Act, check the following box.

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer, or a smaller reporting company. See the definitions of large accelerated filer, accelerated filer and smaller reporting company in Rule 12b-2 of the Exchange Act.

| | |
|--|---|
| Large accelerated filer <input type="checkbox"/> | Accelerated filer <input checked="" type="checkbox"/> |
| Non-accelerated filer <input type="checkbox"/> (Do not check if a smaller reporting company) | Smaller reporting company <input type="checkbox"/> |

This filing constitutes a Post-Effective Amendment to the Registration Statement on Form S-1 (File No. 333-152166), which was declared effective on October 20, 2008. This Post-Effective Amendment shall hereafter become effective in accordance with Section 8(c) of the Securities Act of 1933, as amended, on such date as the Securities and Exchange Commission, acting pursuant to Section 8(c), may determine.

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EXPLANATORY NOTE

On July 7, 2008, the registrant filed a registration statement with the Securities and Exchange Commission (the Commission) on Form S-1 (Registration No. 333-152166), which was amended by Pre-Effective Amendment No. 1 to Form S-1 and Pre-Effective Amendment No. 2 to Form S-1 filed with the Commission on September 26, 2008 and October 16, 2008, respectively, and declared effective by the Commission on October 20, 2008 (as amended, the Form S-1), to register for resale by the selling security holders named in the prospectus up to 1,000,000 shares of the registrant's common stock, \$0.001 par value, issuable upon the exercise of warrants.

This Post-Effective Amendment No. 2 to Form S-1 on Form S-3 is being filed by the registrant to convert the Form S-1 into a registration statement on Form S-3, and contains an updated prospectus relating to the offering and sale of the shares that were registered for resale on the Form S-1.

All filing fees payable in connection with the registration of the shares of the common stock covered by the registration statement were paid by the registrant at the time of the initial filing of the Form S-1.

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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 jurisdiction where the offer or sale is not permitted.

PROSPECTUS

Subject to Completion, Dated May 8, 2009

1,000,000 Shares

EXELIXIS, INC.

Common Stock

This prospectus relates to the offer and sale of up to 1,000,000 shares of our common stock by the selling security holders listed on page 22, including their transferees, pledgees or donees or their respective successors, which shares of common stock are issuable upon the exercise of warrants issued pursuant to a facility agreement dated as of June 4, 2008 between us and the lenders identified therein. We are registering these shares on behalf of the selling security holders, to be offered and sold by them from time to time.

We will not receive any proceeds from any resale of the shares of common stock being offered by this prospectus. The selling security holders may sell the shares of common stock described in this prospectus in a number of different ways and at varying prices. We provide more information about how the selling security holders may sell their shares of common stock in the section entitled Plan of Distribution on page 23. We will not be paying any underwriting discounts or commissions in this offering.

Our common stock is traded on The NASDAQ Global Select Market under the trading symbol EXEL. On May 7, 2009, the last reported sale price of our common stock was \$4.59 per share.

Investing in our securities involves a high degree of risk. You should review carefully the risks and uncertainties described under the heading Risk Factors beginning on page 3, and under similar headings in the other documents that are incorporated by reference into this prospectus, before you decide whether to invest in shares of our common stock.

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

The date of this Prospectus is _____, 2009

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ABOUT THIS PROSPECTUS

This prospectus is part of a registration statement on Form S-3 that we filed with the Securities and Exchange Commission using the shelf registration process. Under this process, selling security holders may from time to time, in one or more offerings, sell up to 1,000,000 shares of our common stock.

You should rely only on the information contained in or incorporated by reference into this prospectus (as supplemented and amended). We have not authorized anyone to provide you with different information. This document may only be used where it is legal to sell these securities. The information contained in this prospectus is accurate only as of the date of this prospectus and 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 our common stock.

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

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

References in this prospectus to Exelixis, we, us and our refer to Exelixis, Inc., a Delaware corporation, and its subsidiaries. Our principal executive offices are located at 249 East Grand Ave, P.O. Box 511, South San Francisco, CA 94083-0511 and our telephone number is (650) 837-7000. Our web site address is <http://www.exelixis.com>. The information contained in, or that can be accessed through, our web site is not part of this prospectus.

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This summary may not contain all the information that may be important to you. You should read the entire prospectus, including the financial data and related notes, risk factors and other information incorporated by reference in this prospectus (as supplemented and amended), before making an investment decision.

Company Overview

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

Utilizing our library of more than 4.5 million compounds, we have integrated high-throughput processes, medicinal chemistry, bioinformatics, structural biology and early *in vivo* testing into a process that allows us to efficiently and rapidly identify highly qualified drug candidates that meet our extensive development criteria.

Since our inception, we have filed 16 investigational new drug applications, or INDs, with the United States Food and Drug Administration, or FDA. As our compounds advance into clinical development, we expect to generate a critical mass of data that will help us to understand the full clinical and commercial potential of our product candidates. In addition to guiding the potential commercialization of our innovative therapies, these data may contribute to the understanding of disease and help improve treatment outcomes.

Based on the strength of our expertise in biology, drug discovery and development, we have established collaborations with leading pharmaceutical and biotechnology companies, including SmithKline Beecham Corporation (which does business as GlaxoSmithKline), Bristol-Myers Squibb Company and Genentech, Inc., that allow us to retain economic participation in compounds and support additional development of our pipeline. Our collaborations generally fall into one of two categories: collaborations in which we co-develop compounds with a partner, share development costs and profits from commercialization and may have the right to co-promote products in the United States, and collaborations in which we out-license compounds to a partner for further development and commercialization, have no further unreimbursed cost obligations and are entitled only to receive milestones and royalties from commercialization. Under either form of collaboration, we may also be entitled to license fees, research funding and milestone payments from research results and subsequent product development activities. We maintain exclusive ownership of those compounds in our pipeline that we are developing ourselves. We are responsible for all development costs for these compounds and are entitled to 100% of profits if the compounds are commercialized.

The following table sets forth those compounds in clinical development that we are developing internally or are co-developing with a partner:

| Compound | Partner | Principal Targets | Indication | Stage of Development |
|-----------------|----------------------|--------------------------|-------------------|-----------------------------|
| XL184 | Bristol-Myers Squibb | MET, VEGFR2, RET | Cancer | Phase 3 |
| XL147 | Unpartnered | PI3K | Cancer | Phase 1b/2 |
| XL765 | Unpartnered | PI3K, mTOR | Cancer | Phase 1b/2 |
| XL518 | Genentech | MEK | Cancer | Phase 1 |
| XL228 | Unpartnered | IGF1R , ABL, SRC | Cancer | Phase 1 |
| XL019 | Unpartnered | JAK2 | Cancer | Phase 1 |
| XL139 | Bristol-Myers Squibb | Hedgehog | Cancer | Phase 1 |
| XL413 | Bristol-Myers Squibb | CDC7 | Cancer | Phase 1 |
| XL888 | Unpartnered | HSP90 | Cancer | Phase 1 |

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The following table sets forth those compounds in preclinical and clinical development that we have out-licensed to third parties for further development and commercialization:

| Compound | Partner | Principal Targets | Indication | Stage of Development |
|-----------------|-----------------------|--------------------------|---------------------------------------|-----------------------------|
| XL880 | GlaxoSmithKline | MET, VEGFR2 | Cancer | Phase 2 |
| XL281 | Bristol-Myers Squibb | RAF | Cancer | Phase 1 |
| XL652 | Bristol-Myers Squibb | LXR | Metabolic and cardiovascular diseases | Phase 1 |
| XL550 | Daiichi-Sankyo | MR | Metabolic and cardiovascular diseases | Preclinical |
| FXR | Wyeth Pharmaceuticals | FXR | Metabolic and liver disorders | Preclinical |

The Offering

The selling security holders named in this prospectus may offer up to 1,000,000 shares of our common stock, which shares of common stock are issuable upon the exercise of warrants issued pursuant to a facility agreement dated as of June 4, 2008, or the Facility Agreement, between us and Deerfield Private Design Fund, L.P., Deerfield Private Design International, L.P., Deerfield Partners, L.P. and Deerfield International Limited, which we collectively refer to as the Deerfield Entities. Our common stock currently is listed on The NASDAQ Global Select Market under the symbol EXEL. Shares of common stock that may be offered in this offering, when issued and paid for, will be fully paid and non-assessable. We will not receive any of the proceeds of sales by the selling security holders of any of the securities covered by this prospectus.

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RISK FACTORS

In addition to the factors discussed elsewhere in this prospectus and in the documents incorporated by reference in this prospectus, the following are important factors that could cause actual results or events to differ materially from those contained in any forward-looking statements made by us or on our behalf. The risks and uncertainties described below are not the only ones facing the company. Additional risks and uncertainties not presently known to us or that we currently deem immaterial also may impair our business operations. If any of the following risks or such other risks actually occurs, our business could be harmed.

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

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

We will need to raise additional capital to:

fund our operations and clinical trials;

continue our research and development efforts; and

commercialize our product candidates, if any such candidates receive regulatory approval for commercial sale.

As of March 31, 2009, we had \$237.7 million in cash and cash equivalents and short-term and long-term marketable securities, which included investments held by Symphony Evolution, Inc., or SEI, of \$12.6 million and restricted cash and investments of \$4.9 million. We anticipate that our current cash and cash equivalents, short-term and long-term marketable securities, investments held by SEI, funds available under the Facility Agreement with the Deerfield Entities, and other funding that we expect to receive from collaborators, which assumes a moderate level of business development activity, will enable us to maintain our operations for a period of at least 12 months following the filing date of the registration statement of which this prospectus is a part. Our goal is to be able to operate independently of the capital markets for a substantial period of time. However, our future capital requirements will be substantial and will depend on many factors that may require us to use available capital resources significantly earlier than we currently anticipate. These factors include:

repayment of our loan from GlaxoSmithKline In October 2002, we entered into a collaboration with GlaxoSmithKline, to discover and develop novel therapeutics in the areas of vascular biology, inflammatory disease and oncology. As part of the collaboration, we entered into a loan and security agreement with GlaxoSmithKline, pursuant to which we borrowed \$85.0 million for use in our efforts under the collaboration. The loan bears interest at a rate of 4.0% per annum and is secured by certain intellectual property, technology and equipment created or utilized pursuant to the collaboration. Principal and accrued interest under the loan becomes due in three annual installments, beginning on October 27, 2009. Repayment of all or any of the amounts advanced to us under this agreement may, at our election, be in the form of our common stock at fair market value, subject to certain conditions. As of March 31, 2009, the aggregate principal and interest outstanding under our GlaxoSmithKline loan was \$103.1 million. Following the conclusion on October 27, 2008 of the development term under our collaboration with GlaxoSmithKline, we are no longer eligible to receive selection milestone payments from GlaxoSmithKline to credit against outstanding loan amounts, and in the event the market price for our common stock is depressed, we may not be able to repay the loan in full using shares of our common stock due to restrictions in the agreement on the number of shares we may issue. In addition, the issuance of shares of our common stock to repay the loan may result in significant dilution to our stockholders. As a result, we may need to obtain additional funding, including from funds available under the Facility Agreement with the Deerfield Entities, to satisfy our repayment obligations, including the payment that is due on October 27, 2009. There can be no assurance that we will have sufficient funds to repay amounts outstanding under the loan when due or that we will satisfy the conditions to our ability to repay the loan in shares of our common stock;

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whether and when we draw funds under our Facility Agreement with the Deerfield Entities In June 2008, we entered into the Facility Agreement with the Deerfield Entities pursuant to which the Deerfield Entities agreed to loan to us up to \$150.0 million, subject to certain conditions. We may draw down on the facility in \$15.0 million increments at any time until December 2009. The outstanding principal and interest under the loan, if any, is due by June 4, 2013, and, at our option, can be repaid at any time with shares of our common stock, subject to certain restrictions, or in cash. Interest under the loan does not accrue until we draw down on the facility, at which time interest will begin to accrue at a rate of 6.75% per annum compounded annually on the outstanding principal amount of the facility. The Deerfield Entities also have limited rights to accelerate repayment of the loan upon certain changes of control of Exelixis or an event of default. Pursuant to the Facility Agreement, we paid the Deerfield Entities a one time transaction fee of \$3.8 million, or 2.5% of the loan facility, and we are obligated to pay an annual commitment fee of \$3.4 million, or 2.25% of the loan facility, payable quarterly. If we draw funds under the Facility Agreement, we would be required to issue to the Deerfield Entities additional warrants to purchase shares of our common stock. If we draw down under the Facility Agreement, there is no assurance that the conditions to our ability to repay the loan in shares of our common stock would be satisfied at the time that any outstanding principal and interest under the loan is due, in which case we would be obligated to repay the loan in cash, or that events permitting acceleration of the loan will not occur, in which event we would be required to repay any outstanding principal and interest sooner than anticipated;

the progress and scope of our collaborative and independent clinical trials and other research and development projects, including with respect to XL184, our most advanced asset. We expect to particularly focus our later stage development efforts on XL184, which is being studied in a variety of tumor types, with the goal of rapidly commercializing the compound. As described under Item 2. Management's Discussion and Analysis of Financial Condition and Results of Operations Certain Factors Important to Understanding Our Financial Condition and Results of Operations 2008 Cancer Collaboration with Bristol-Myers Squibb in our Quarterly Report on Form 10-Q for the fiscal quarter ended April 3, 2009, in December 2008, we entered into a worldwide co-development collaboration with Bristol-Myers Squibb for the development and commercialization of XL184. The companies will share worldwide (except for Japan) development costs for XL184. We are responsible for 35% of such costs and Bristol-Myers Squibb is responsible for 65% of such costs, except that we are responsible to fund the initial \$100 million of combined costs and have the option to defer payments for development costs above certain thresholds. In return, we will share 50% of the commercial profits and losses (including pre-launch commercialization expenses) in the United States and have the option to co-promote XL184 in the United States. We have the right to defer payment for certain early commercialization and other related costs above certain thresholds. During the term of the collaboration, so long as we have not opted out of the co-development of XL184, there may be periods during which Bristol-Myers Squibb will partially reimburse us for certain research and development expenses, and other periods during which we will owe Bristol-Myers Squibb for research and development expenses that Bristol-Myers Squibb incurred on joint development projects, less amounts reimbursable to us by Bristol-Myers Squibb on these projects. On an annual basis, to the extent that net research and development funding payments are received from Bristol-Myers Squibb, these payments will be presented as collaboration revenue. In annual periods when net research and development funding payments are payable to Bristol-Myers Squibb, these payments will be presented as collaboration cost sharing expense. Generally, the direction of cash flows will depend on the level of development activity by either party, which may change during the development term. Our capital requirements will be impacted by the level of our expenses for the development activity conducted by us and the degree to which we will be required to make payments to, or we will receive payments from, Bristol-Myers Squibb. If we opt out of the co-development of XL184, we would have no further unreimbursed cost obligations;

the level of payments received under existing collaboration agreements, licensing agreements and other arrangements as well as our ability to enter into new collaboration agreements, licensing agreements and other arrangements that provide additional payments;

our ability to control costs;

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

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the amount of our cash and cash equivalents and marketable securities that serve as collateral for bank lines of credit;

future clinical trial results;

our need to expand our product and clinical development efforts;

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

the cost and timing of regulatory approvals;

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

the effect of competing technological and market developments;

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

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

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

One or more of these factors or changes to our current operating plan may require us to use available capital resources significantly earlier than we anticipate. If our capital resources are insufficient to meet future capital requirements, we will have to raise additional funds. We may seek to raise funds through the sale of equity or debt securities or through external borrowings. In addition, we may enter into strategic partnerships for the development and commercialization of our compounds. However, 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 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 not favorable 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 or we may be required to relinquish rights to technology or product candidates or to grant licenses on terms that are unfavorable to us.

We will have to obtain additional funding in order to stay in compliance with financial covenants contained in agreements with third parties. For example, as part of our collaboration with GlaxoSmithKline, we entered into the loan and security agreement, which, as amended, contains financial covenants pursuant to which our working capital (the amount by which our current assets exceed our current liabilities as defined by the agreement, which excludes restricted cash and deferred revenue, but includes amounts available for borrowing under the Facility Agreement with the Deerfield Entities) must not be less than \$25.0 million and our cash and investments (total cash, cash equivalents and investments as defined by the agreement, which excludes restricted cash) must not be less than \$50.0 million. As of March 31, 2009, our working capital was \$287.6 million (including \$150.0 million available for borrowing under the Facility Agreement) and our cash and investments were \$232.9 million. If we were to default on the financial covenants under the loan and security agreement, GlaxoSmithKline may, among other remedies, declare immediately due and payable all obligations under the loan and security agreement. Outstanding borrowings and accrued interest under the loan and security agreement totaled \$103.1 million at March 31, 2009. Principal and accrued interest under the loan becomes due in three annual installments beginning on October 27, 2009. In addition, if our cash and cash equivalents and marketable securities on the last day of any calendar quarter are less than \$75.0 million, then we would be in default under the Facility Agreement with the Deerfield Entities, and the Deerfield Entities would have the right, among other remedies, to cancel our right to request disbursements and declare immediately due and payable any amounts accrued or payable under the Facility Agreement. If our cash reserves fall below \$80.0 million and we are unable to increase such cash reserves to \$80.0 million or more within 90 days, our co-development and co-promotion rights with respect to XL184 under

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our 2008 collaboration agreement with Bristol-Myers Squibb may be terminated. Cash reserves for purposes of our 2008 collaboration agreement with Bristol-Myers Squibb includes our total cash, cash equivalents and investments (excluding any restricted cash), plus the amount then available for borrowing by us under the Facility Agreement with the Deerfield Entities, as the same may be amended from time to time, and any other similar financing arrangements.

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

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

We have incurred net losses since inception, including a net loss attributable to Exelixis, Inc. of \$36.2 million for the three months ended March 31, 2009. As of that date, we had an accumulated deficit of \$990.7 million. We expect our losses in 2009 to increase as compared to 2008 and anticipate negative operating cash flow for the foreseeable future. We have not yet completed the development, including obtaining regulatory approval, of any of our pharmaceutical product candidates and, consequently, have not generated revenues from the sale of pharmaceutical products. Except for revenues associated with the transgenic mouse business of our former German subsidiary, Artemis Pharmaceuticals, GmbH, or Artemis, our only revenues to date are license revenues and revenues under contracts with our partners. In November 2007, we sold 80.1% of our ownership interest in Artemis. The amount of our net losses will depend, in part, on the rate of growth, if any, in our license and contract revenues and on the level of our expenses. These losses have had and will continue to have an adverse effect on our stockholders' equity and working capital. Our research and development expenditures and general and administrative expenses have exceeded our revenues to date, and we expect to spend significant additional amounts to fund research and development in order to enhance our technologies and undertake product development. We currently have numerous product candidates in various stages of clinical development and we anticipate filing additional IND applications for additional product candidates within the next 12 months. As a result, we expect to continue to incur substantial operating expenses, and, consequently, we will need to generate significant additional revenues to achieve profitability. Because of the numerous risks and uncertainties associated with developing drugs, we are unable to predict the extent of any future losses or when we will become profitable, if at all. Even if we do increase our revenues and achieve profitability, we may not be able to maintain or increase profitability.

We may not realize the expected benefits of our initiatives to control costs.

Managing costs is a key element of our business strategy. Consistent with this element of our strategy, in November 2008 we implemented a restructuring that resulted in the reduction of approximately 10% of our workforce. We anticipate that we will incur some level of restructuring charges through the end of 2009 as we continue to implement this restructuring.

If we experience excessive unanticipated inefficiencies or incremental costs in connection with restructuring activities, such as unanticipated inefficiencies caused by reducing headcount, we may be unable to meaningfully realize cost savings and we may incur expenses in excess of what we anticipate. Either of these outcomes could prevent us from meeting our goal of being able to operate independently of the capital markets for a substantial period of time, and could adversely impact our results of operations or financial condition.

Global credit and financial market conditions could negatively impact the value of our current portfolio of cash equivalents or short-term investments and our ability to meet our financing objectives.

Our cash and cash equivalents are maintained in highly liquid investments with remaining maturities of 90 days or less at the time of purchase. Our short-term and long-term investments consist primarily of readily marketable debt securities with remaining maturities of more than 90 days at the time of purchase. While as of the date of this prospectus, we are not aware of any downgrades, material losses, or other significant deterioration in the fair value of our cash equivalents, short-term investments, or long-term investments since March 31, 2009, no assurance can be given that further deterioration in conditions of the global credit and financial markets would not negatively impact our current portfolio of cash equivalents or investments or our ability to meet our financing objectives.

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Risks Related to Development of Product Candidates

Clinical testing of our product candidates is a lengthy, costly, complex and uncertain process and may fail to demonstrate safety and efficacy.

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;

we or our competitors may subsequently discover other compounds that we believe show significantly improved safety or efficacy compared to our product candidates;

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 or our ability to generate revenue from the affected product candidates could be impaired, either of which could 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 United States Food and Drug Administration, or FDA. We do not know whether our planned clinical trials will begin on time, will be completed on schedule, or at all, will be sufficient for registration of these compounds or will result in approvable products.

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

the number of patients that ultimately participate in the clinical trial;

the duration of patient follow-up that is appropriate in view of the results;

the number of clinical sites included in the trials; and

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the length of time required to enroll suitable patient subjects.

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

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

If any of these agreements is not renewed or is terminated early, whether unilaterally or by mutual agreement, or if we are unable to enter into new collaboration agreements on commercially acceptable terms, our revenues and product development efforts could suffer. Our agreements with Bristol-Myers Squibb, Genentech, Daiichi-Sanko and Wyeth Pharmaceuticals contain early termination provisions. In addition, from time to time we review and assess certain aspects of our collaborations, partnerships and agreements and may amend or terminate, either by mutual agreement or pursuant to any applicable early termination provisions, such collaborations, partnerships or agreements if we deem them to be no longer in our economic or strategic interests. We may not be able to enter into new collaboration agreements on similar or superior financial terms to offset the loss of revenue from the termination or expiration of any of our existing arrangements, and the timing of new collaboration agreements may have a material adverse effect on our ability to continue to successfully meet our objectives.

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

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

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collaborators develop competing products, preclude us from entering into collaborations with their competitors, fail to obtain necessary regulatory approvals, terminate their agreements with us prematurely or fail to devote sufficient resources to the development and commercialization of our products, our product development efforts could be delayed or otherwise adversely effected and may fail to lead to commercialized products.

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

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

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

We currently do not have the manufacturing capabilities or experience necessary to enable us to produce materials for our clinical trials. We rely on collaborators and third-party contractors to produce our compounds for preclinical and clinical testing. These suppliers must comply with applicable regulatory requirements, including the FDA's current Good Manufacturing Practices, or GMP. Our current and anticipated future dependence upon these third-party manufacturers may adversely affect our future profit margins and our ability to develop and commercialize product candidates on a timely and competitive basis. These manufacturers may not be able to produce material on a timely basis or manufacture material at the quality level or in the quantity required to meet our development timelines and applicable regulatory requirements. We may not be able to maintain or renew our existing third-party manufacturing arrangements, or enter into new arrangements, on acceptable terms, or at all. Our third-party manufacturers could terminate or decline to renew our manufacturing arrangements based on their own business priorities, at a time that is costly or inconvenient for us. If we are unable to contract for the production of materials in sufficient quantity and of sufficient quality on acceptable terms, our clinical trials may be delayed. Delays in preclinical or clinical testing could delay the filing of our INDs and the initiation of clinical trials.

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

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

Some of the materials necessary for the manufacture of our compounds under development may, from time to time, be available either in limited quantities, or from a limited number of manufacturers, or both. Our contract manufacturers need to obtain these materials for our clinical trials and, potentially, for commercial distribution when and if we obtain marketing approval for these compounds. Suppliers may not sell us these materials at the time we need them or on commercially reasonable terms. If we are unable to obtain the materials needed to conduct our

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clinical trials, product testing and potential regulatory approval could be delayed, adversely affecting our ability to develop the product candidates. Similarly, if we are unable to obtain critical manufacturing materials after regulatory approval has been obtained for a product candidate, the commercial launch of that product candidate could be delayed or there could be a shortage in supply, which could materially affect our ability to generate revenues from that product candidate. If suppliers increase the price of manufacturing materials, the price for one or more of our products may increase, which may make our products less competitive in the marketplace. If it becomes necessary to change suppliers for any of these materials or if any of our suppliers experience a shutdown or disruption at the facilities used to produce these materials, due to technical, regulatory or other reasons, it could harm our ability to manufacture our products.

Risks Related to Regulatory Approval of Our Product Candidates

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

Our product candidates, as well as the activities associated with their research, development and commercialization, are subject to extensive regulation by the FDA and other regulatory agencies in the United States and by comparable authorities in other countries. Failure to obtain regulatory approval for a product candidate would prevent us from commercializing that product candidate. We have not received regulatory approval to market any of our product candidates in any jurisdiction and have only limited experience in preparing and filing the applications necessary to gain regulatory approvals. The process of obtaining regulatory approvals is expensive, and often takes many years, if approval is obtained at all, and can vary substantially based upon the type, complexity and novelty of the product candidates involved. Before a new drug application can be filed with the FDA, the product candidate must undergo extensive clinical trials, which can take many years and may require substantial expenditures. Any clinical trial may fail to produce results satisfactory to the FDA. For example, the FDA could determine that the design of a clinical trial is inadequate to produce reliable results. The regulatory process also requires preclinical testing, and data obtained from preclinical and clinical activities are susceptible to varying interpretations, which could delay, limit or prevent regulatory approval. In addition, delays or rejections may be encountered based upon changes in regulatory policy for product approval during the period of product development and regulatory agency review. Changes in regulatory approval policy, regulations or statutes or the process for regulatory review during the development or approval periods of our product candidates may cause delays in the approval or rejection of an application. Even if the FDA or a comparable authority in another country approves a product candidate, the approval may impose significant restrictions on the indicated uses, conditions for use, labeling, advertising, promotion, marketing and/or production of such product and may impose ongoing requirements for post-approval studies, including additional research and development and clinical trials. These agencies also may impose various civil or criminal sanctions for failure to comply with regulatory requirements, including withdrawal of product approval.

Risks Related to Commercialization of Products

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

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

the effectiveness, or perceived effectiveness, of our products in comparison to competing products;

the existence of any significant side effects, as well as their severity in comparison to any competing products;

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potential advantages over alternative treatments;

the ability to offer our products for sale at competitive prices;

relative convenience and ease of administration;

the strength of marketing and distribution support; and

sufficient third-party coverage or reimbursement.

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

We have no experience as a company in the sales, marketing and distribution of pharmaceutical products and do not currently have a sales and marketing organization. Developing a sales and marketing force would be expensive and time-consuming, could delay any product launch, and we may never be able to develop this capacity. To the extent that we enter into arrangements with third parties to provide sales, marketing and distribution services, our product revenues are likely to be lower than if we market and sell any products that we develop ourselves. If we are unable to establish adequate sales, marketing and distribution capabilities, independently or with others, we may not be able to generate product revenues.

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

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

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

State Medicaid programs generally have outpatient prescription drug coverage, subject to state regulatory restrictions, for the population eligible for Medicaid. The availability of coverage or reimbursement for prescription drugs under private health insurance and managed care plans varies based on the type of contract or plan purchased.

Another development that may affect the pricing of drugs is proposed congressional action regarding drug reimportation into the United States. The Medicare Prescription Drug, Improvement and Modernization Act of 2003 gives discretion to the Secretary of Health and Human Services to allow drug reimportation into the United States under some circumstances from foreign countries, 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 allow direct reimportation under certain circumstances. If legislation or regulations were passed allowing the reimportation of drugs, it could decrease the price we receive for any products that we may develop, thereby negatively affecting our revenues and prospects for profitability.

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

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

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

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

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

Risks Related to Our Intellectual Property

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

Our success will depend in part upon our ability to obtain patents and maintain adequate protection of the intellectual property related to our technologies and products. The patent positions of biotechnology companies, including our patent position, are generally uncertain and involve complex legal and factual questions. We will be able to protect our intellectual property rights from unauthorized use by third parties only to the extent that our

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technologies are covered by valid and enforceable patents or are effectively maintained as trade secrets. We will continue to apply for patents covering our technologies and products as and when we deem appropriate. However, these applications may be challenged or may fail to result in issued patents. In addition, because patent applications can take many years to issue, there may be currently pending applications, unknown to us, which may later result in issued patents that cover the production, manufacture, commercialization or use of our product candidates. Our existing patents and any future patents we obtain may not be sufficiently broad to prevent others from practicing our technologies or from developing competing products. Furthermore, others may independently develop similar or alternative technologies or design around our patents. In addition, our patents may be challenged or invalidated or may fail to provide us with any competitive advantages, if, for example, others were the first to invent or to file patent applications for these inventions.

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

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

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

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

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

Many of our employees and independent contractors were previously employed at universities, other biotechnology or pharmaceutical companies, including our competitors or potential competitors. We may be subject to claims that these employees, independent contractors or we have inadvertently or otherwise used or disclosed trade secrets or other proprietary information of their former employers. Litigation may be necessary to defend against these claims. Even if we are successful in defending against these claims, litigation could result in substantial costs and divert management's attention. If we fail in defending such claims, in addition to paying money claims, we may lose valuable intellectual property rights or personnel. A loss of key research personnel and/or their work product could hamper or prevent our ability to commercialize certain product candidates, which could severely harm our business.

Risks Related to Employees, Growth and Location

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

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

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

We work with scientific and clinical advisors and collaborators at academic and other institutions that assist us in our research and development efforts. These advisors and collaborators are not our employees and may have other commitments that limit their availability to us. Although these advisors and collaborators generally agree not to do competing work, if a conflict of interest between their work for us and their work for another entity arises, we may lose their services. In such a circumstance, we may lose work performed by them, and our development efforts with respect to the matters on which they were working may be significantly delayed or otherwise adversely affected. In addition, although our advisors and collaborators sign agreements not to disclose our confidential information, it is possible that valuable proprietary knowledge may become publicly known through them.

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

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

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

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

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

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

Risks Related to Environmental and Product Liability

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

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

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

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

We may be held liable if any product we or our collaborators develop causes injury or is found otherwise unsuitable during product testing, manufacturing, marketing or sale. Regardless of merit or eventual outcome, product liability claims could result in decreased demand for our product candidates, injury to our reputation, withdrawal of patients from our clinical trials, substantial monetary awards to trial participants and the inability to commercialize any products that we may develop. These claims might be made directly by consumers, health care providers, pharmaceutical companies or others selling or testing our products. We have obtained limited product liability insurance coverage for our clinical trials in the amount of \$10.0 million per occurrence and \$10.0 million in the aggregate. However, our insurance may not reimburse us or may not be sufficient to reimburse us for expenses or losses we may suffer. Moreover, if insurance coverage becomes more expensive, we may not be able to maintain

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insurance coverage at a reasonable cost or in sufficient amounts to protect us against losses due to liability. If we obtain marketing approval for any of our product candidates, we intend to expand our insurance coverage to include the sale of commercial products, but we may be unable to obtain commercially reasonable product liability insurance for any products approved for marketing. On occasion, juries have awarded large judgments in class action lawsuits for claims based on drugs that had unanticipated side effects. In addition, the pharmaceutical and biotechnology industries, in general, have been subject to significant medical malpractice litigation. A successful product liability claim or series of claims brought against us could harm our reputation and business and would decrease our cash reserves.

Risks Related to Our Common Stock

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

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

recognition of upfront licensing or other fees or revenue;

payments of non-refundable upfront or licensing fees, or payment for cost-sharing expenses, to third parties;

acceptance of our technologies and platforms;

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

the introduction of new technologies or products by our competitors;

the timing and willingness of collaborators to commercialize our products;

our ability to enter into new collaborative relationships;

the termination or non-renewal of existing collaborations;

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

the impairment of acquired goodwill and other assets; and

general and industry-specific economic conditions that may affect our collaborators' research and development expenditures.

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

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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 securities analysts and investors, which could result in a decline in the price of our common stock.

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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 , many of which we cannot control:

adverse results or delays in clinical trials;

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

the announcement of new products by us or our competitors;

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

conflicts or litigation with our collaborators;

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

failure to achieve operating results projected by securities analysts;

changes in earnings estimates or recommendations by securities analysts;

financing transactions;

developments in the biotechnology or pharmaceutical industry;

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

departures of key personnel or board members;

developments concerning current or future collaborations;

FDA or international regulatory actions;

third-party reimbursement policies;

acquisitions of other companies or technologies;

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

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

These factors, as well as general economic, political and market conditions, may materially adversely affect the market price of our common stock. As with the stock of many other public companies, the market price of our common stock has been particularly volatile during the recent period of upheaval in the capital markets and world economy. This excessive volatility may continue for an extended period of time following the date of this prospectus.

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

We are exposed to risks associated with acquisitions.

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

difficulties and increased costs in connection with integration of the personnel, operations, technologies and products of acquired companies;

diversion of management's attention from other operational matters;

the potential loss of key employees;

the potential loss of key collaborators;

lack of synergy, or the inability to realize expected synergies, resulting from the acquisition; and

acquired intangible assets becoming impaired as a result of technological advancements or worse-than-expected performance of the acquired company.

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

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

If our stockholders sell substantial amounts of our common stock (including shares issued upon the exercise of options and warrants and shares issued under our employee stock purchase plan) in the public market, the market price of our common stock could fall. These sales also might make it more difficult for us to sell equity or equity-related securities in the future at a time and price that we deem appropriate.

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

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

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

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

members of our management team. These provisions include:

a classified Board of Directors;

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a prohibition on actions by our stockholders by written consent;

the inability of our stockholders to call special meetings of stockholders;

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

limitations on the removal of directors; and

advance notice requirements for director nominations and stockholder proposals.

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

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FORWARD-LOOKING STATEMENTS

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

our business strategy and our expectations with respect to the implementation of our business strategy;

our expectations with respect to the potential therapeutic and commercial value of our product candidates;

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

our expectations with respect to our intellectual property position; and

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

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

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

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USE OF PROCEEDS

The selling security holders will receive all of the net proceeds from sales of the common stock sold pursuant to this prospectus. However, upon the exercise of the warrants issued to the selling security holders on June 4, 2008 for cash, the selling security holders would pay us an exercise price of \$7.40 per share of common stock, or an aggregate of \$7.4 million if the warrants are exercised in full. The proceeds to us of such warrant exercises, if any, will not be subject to any restrictions. Under certain conditions set forth in all of the warrants issued to the selling security holders, the warrants are exercisable on a cashless basis. If the warrants are exercised on a cashless basis, we would not receive any cash payment from the selling security holders upon any exercise of the warrants.

SELLING SECURITY HOLDERS

An aggregate of 1,000,000 shares of common stock are being registered in this offering for the account of the selling security holders. All of the shares of common stock being offered and sold under this prospectus are shares issuable upon the exercise of warrants issued pursuant to the Facility Agreement dated June 4, 2008, by and between us and the Deerfield Entities.

Under the Facility Agreement, the Deerfield Entities have agreed to loan to us up to \$150.0 million, subject to certain conditions. We may draw down on the facility in \$15.0 million increments at any time during the 18 months following the effective date of the Facility Agreement and are not subject to any limitations on the number of incremental draw downs we can make at any one time. Upon execution of the Facility Agreement, we issued to the Deerfield Entities warrants to purchase an aggregate of 1,000,000 shares of our common stock at an exercise price of \$7.40 per share. Subject to certain conditions and limitations, we have the right to request one or more cash disbursements from the Deerfield Entities pursuant to the Facility Agreement, which disbursements would be accompanied by our issuance to the Deerfield Entities of: (1) for each of the first through fifth disbursements, warrants to purchase an aggregate of 400,000 shares of our common stock at an exercise price equal to the then prevailing exercise price under the warrants issued on June 4, 2008 and (2) for each disbursement, warrants to purchase an aggregate of 800,000 shares of our common stock at an exercise price equal to 120% of the average of the Volume Weighted Average Price, as defined in the Facility Agreement, of our common stock for each of the 15 trading days beginning with the trading day following receipt by the Deerfield Entities of a disbursement request. The warrants are exercisable for a term of six years from the date of issuance and contain certain limitations that prevent the holder of the warrants from acquiring shares upon exercise of a warrant that would result in the number of shares beneficially owned by it to exceed 9.98% of the total number of shares of our common stock then issued and outstanding. The number of shares for which the warrants are exercisable and the associated exercise prices are subject to certain adjustments as set forth in the warrants. In addition, upon certain changes in control of our company, to the extent the warrants are not assumed by the acquiring entity, or upon certain defaults under the warrants, the holder has the right to net exercise the warrants for shares of our common stock, or, in certain circumstances, be paid an amount in cash, equal to the Black-Scholes value of the shares of our common stock issuable under warrants that are outstanding.

The outstanding principal and interest under the Facility Agreement, if any, is due by June 4, 2013, and, at our option, can be repaid at any time with shares of our common stock that have been registered under the Securities Act, with certain restrictions, or in cash.

We also entered into a registration rights agreement with the Deerfield Entities dated June 4, 2008, or the Registration Rights Agreement. Pursuant to the terms of the Registration Rights Agreement, we agreed to file a registration statement, of which this prospectus is a part, with the SEC on or prior to 45 days from the effective date of the Registration Rights Agreement. Such registration statement is intended to cover the resale of shares of our common stock subject to issuance upon the exercise of the warrants. We have additional obligations under the Registration Rights Agreement, subject to SEC rules and regulations, to register either on a primary or resale basis, any shares issuable in connection with the Facility Agreement not included in the registration statement of which this prospectus is a part.

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The foregoing summaries of the Facility Agreement, the warrants and the Registration Rights Agreement are not complete and are qualified in their entirety by reference to these agreements. A copy of the Facility Agreement was previously filed as an exhibit to the registration statement of which this prospectus is a part, and copies of the warrants and the Registration Rights Agreement were previously filed as exhibits to our Current Report on Form 8-K filed with the SEC on June 9, 2008, each of which are incorporated herein by reference.

The shares offered by this prospectus may be offered from time to time, in whole or in part, by the selling security holders or their transferees, pledgees or donees or their respective successors. The following table sets forth the name of each selling security holder, the number of shares of common stock the selling security holder will beneficially own prior to this offering, the maximum number of shares which may be offered for resale pursuant to this prospectus and the number of shares and percentage that would be owned by the selling security holder after the completion of this offering. The selling security holders may sell some, all or none of their shares. We do not know how long the selling security holders will hold the shares before selling them. For purposes of the table below, we have assumed that the selling security holders exercised the warrants in full pursuant to a cash exercise (without giving effect to any limitations on exercise) and the selling security holders sold all of such shares. The table does not give effect to the issuance of additional warrants in connection with the drawings on the facility or shares used to repay any borrowings under the Facility Agreement. This table is prepared based on information supplied to us by the selling security holders and reflects holdings as of April 6, 2009.

| Selling Security Holder (1) | Number of Shares of Common Stock Owned Before the Offering (2) | Shares Available for Sale Under This Prospectus (3) | Number of Shares of Common Stock to Be Owned After Completion of the Offering (4) | Percent of Common Stock to be Owned After Completion of the Offering (5) |
|--|--|--|--|---|
| Deerfield Private Design Fund, L.P. | 306,400 | 306,400 | 0 | * |
| Deerfield Private Design International, L.P. | 493,600 | 493,600 | 0 | * |
| Deerfield Partners, L.P. | 152,925 | 72,800 | 80,125 | * |
| Deerfield International Limited | 256,267 | 127,200 | 129,067 | * |

* Represents less than 1%.

- (1) James E. Flynn has the power to vote or dispose of the shares held by the selling security holders through Deerfield Capital L.P., in the case of shares owned by Deerfield Partners, L.P., and through Deerfield Management Company, L.P., in the case of the other Deerfield Entities.
- (2) Includes 80,125 shares and 129,067 shares of common stock owned by Deerfield Partners, L.P. and Deerfield International Limited, respectively.
- (3) Represents shares of common stock issuable upon exercise of warrants issued pursuant to the Facility Agreement.
- (4) Assumes sale of all shares available for sale under this prospectus and no further acquisitions of shares by the selling security holders.
- (5) Calculated pursuant to Rule 13d-3 of the Securities Exchange Act of 1934, as amended. Under Rule 13d-3(d), shares not outstanding which are subject to options, warrants, rights or conversion privileges exercisable within 60 days are deemed outstanding for the purpose of calculating the number and percentage owned by such person, but not deemed outstanding for the purpose of calculating the percentage owned by each other person listed. As of April 6, 2009, we had 107,448,343 shares of common stock outstanding.

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PLAN OF DISTRIBUTION

We are registering the shares of common stock offered in this prospectus on behalf of the selling security holders. The selling security holders, which as used herein includes pledgees, donees, transferees or other successors-in-interest selling shares received from the selling security holders as a gift, pledge, partnership distribution or other transfer after the date of this prospectus, may, from time to time, sell, transfer or otherwise dispose of any or all of their shares of common stock or interests in shares of common stock on any stock exchange, market or trading facility on which the shares are traded or in private transactions. The selling security holders will pay any brokerage commissions and similar selling expenses attributable to the sale of the shares. We will not receive any of the proceeds from the sale of the shares by the selling security holders. However, upon the exercise of the warrants issued to the selling security holders on June 4, 2008 for cash, we will receive the exercise price of \$7.40 per share of common stock exercised. If the warrants are exercised in a cashless exercise, we will not receive any proceeds from the exercise of the warrants.

These dispositions may be at fixed prices, at prevailing market prices at the time of sale, at prices related to the prevailing market price, at varying prices determined at the time of sale, or at negotiated prices. To the extent any of the selling security holders gift, pledge or otherwise transfer the shares offered hereby, such transferees may offer and sell the shares from time to time under this prospectus, provided that this prospectus has been amended under Rule 424(b)(3) or other applicable provision of the Securities Act of 1933, as amended, or the Securities Act, to include the name of such transferee in the list of selling security holders under this prospectus.

The selling security holders may use any one or more of the following methods when disposing of shares or interests therein:

ordinary brokerage transactions and transactions in which the broker-dealer solicits purchasers;

block trades 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;

purchases by a broker-dealer as principal and resale by the broker-dealer for its account;

an exchange distribution in accordance with the rules of the applicable exchange;

privately negotiated transactions;

short sales;

through the writing or settlement of options or other hedging transactions, whether through an options exchange or otherwise;

broker-dealers may agree with the selling security holders to sell a specified number of such shares at a stipulated price per share;

a combination of any such methods of sale; and

any other method permitted pursuant to applicable law.

The selling security holders may, from time to time, pledge or grant a security interest in some or all of the shares of common stock owned by them and, if they default in the performance of their secured obligations, the pledgees or secured parties may offer and sell the shares of common

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stock, from time to time, under this prospectus or under an amendment to this prospectus under Rule 424(b)(3) or other applicable provision of the Securities Act, by amending the list of selling security holders to include the pledgee, transferee or other successors in interest as selling security holders under this prospectus.

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In connection with the sale of our common stock or interests therein, the selling security holders may enter into hedging transactions with broker-dealers or other financial institutions, which may in turn engage in short sales of the common stock in the course of hedging the positions they assume. The selling security holders may also sell shares of our common stock short and deliver these securities to close out their short positions, or loan or pledge the common stock to broker-dealers that in turn may sell these securities. The selling security holders may also enter into option or other transactions with broker-dealers or other financial institutions or the creation of one or more derivative securities which require the delivery to such broker-dealer or other financial institution of shares offered by this prospectus, which shares such broker-dealer or other financial institution may resell pursuant to this prospectus (as supplemented or amended to reflect such transaction).

The aggregate proceeds to the selling security holders from the sale of the common stock offered by them will be the purchase price of the common stock less discounts or commissions, if any. Each of the selling security holders reserves the right to accept and, together with their agents from time to time, to reject, in whole or in part, any proposed purchase of common stock to be made directly or through agents.

To the extent required, the shares of our common stock to be sold, the names of the selling security holders, the respective purchase prices and public offering prices, the names of any agent, dealer or underwriter, and any applicable commissions or discounts with respect to a particular offer will be set forth in an accompanying prospectus supplement or, if appropriate, a post-effective amendment to the registration statement that includes this prospectus.

In order to comply with the securities laws of some states, if applicable, the common stock may be sold in these jurisdictions only through registered or licensed brokers or dealers. In addition, in some states the common stock may not be sold unless it has been registered or qualified for sale or an exemption from registration or qualification requirements is available and is complied with.

We have advised the selling security holders that the anti-manipulation rules of Regulation M under the Securities Exchange Act of 1934, as amended, or the Exchange Act, may apply to sales of shares in the market and to the activities of the selling security holders and their affiliates. In addition, we will make copies of this prospectus (as it may be supplemented or amended from time to time) available to the selling security holders for the purpose of satisfying the prospectus delivery requirements of the Securities Act. The selling security holders may indemnify any broker-dealer that participates in transactions involving the sale of the shares against certain liabilities, including liabilities arising under the Securities Act.

We have agreed to indemnify the selling security holders against liabilities, including liabilities under the Securities Act, the Exchange Act and state securities laws, relating to the registration of the shares offered by this prospectus.

We have agreed with the selling security holders to keep the registration statement that includes this prospectus effective until the earlier of (1) such time as all of the shares covered by this prospectus have been disposed of pursuant to and in accordance with the registration statement that contains this prospectus and (2) the date on which the shares cease to be registrable securities a such term is defined in the Registration Rights Agreement.

The selling security holders and any broker dealers that act in connection with the sale of the shares might be deemed to be underwriters as the term is defined in Section 2(11) of the Securities Act. Consequently, any commissions received by these broker dealers and any profit on the resale of the shares sold by them while acting as principals might be deemed to be underwriting discounts or commissions under the Securities Act. Because the selling security holders may be deemed to be underwriters as defined in Section 2(11) of the Securities Act, the selling security holders may be subject to the prospectus delivery requirements of the Securities Act.

The selling security holders also may resell all or a portion of the shares in open market transactions in reliance upon Rule 144 under the Securities Act, provided that they meet the criteria and conform to the requirements of that rule.

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VALIDITY OF COMMON STOCK

The validity of the common stock being offered hereby has been passed upon for us by Cooley Godward Kronish LLP, Palo Alto, California. As of the date of this prospectus, certain partners and associates of Cooley Godward Kronish LLP own an aggregate of approximately 5,291 shares of our common stock, either individually or through investment partnerships.

EXPERTS

Ernst & Young LLP, an independent registered public accounting firm, has audited our consolidated financial statements included in our Annual Report on Form 10-K for the fiscal year ended January 2, 2009, and the effectiveness of our internal control over financial reporting as of January 2, 2009, as set forth in their reports, which are incorporated by reference in this prospectus and elsewhere in the registration statement. Our consolidated financial statements and our management's assessment of the effectiveness of internal control over financial reporting as of January 2, 2009 are incorporated by reference in reliance on Ernst & Young LLP's reports, given on their authority as experts in accounting and auditing.

WHERE YOU CAN FIND MORE INFORMATION

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

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

Our current report on Form 8-K, filed with the SEC on March 3, 2009;

Our annual report on Form 10-K for the fiscal year ended January 2, 2009, filed with the SEC on March 10, 2009 (the 2008 Form 10-K);

Our quarterly report on Form 10-Q for the fiscal quarter ended April 3, 2009, filed with the SEC on May 7, 2009;

The information specifically incorporated by reference into the 2008 Form 10-K from our definitive proxy statement on Schedule 14A filed with the SEC on April 13, 2009; and

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

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

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

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deemed to modify and supersede any information in any document we previously filed with the SEC that is incorporated or deemed to be incorporated herein by reference to the extent that statements in the later filed document modify or replace such earlier statements.

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We will furnish without charge to you, upon written or oral request, a copy of any or all of the documents incorporated by reference, including exhibits to these documents. You should direct any requests for documents to Exelixis, Inc., Attention: Corporate Secretary, 249 East Grand Ave, P.O. Box 511, South San Francisco, California 94083-0511. Our phone number is (650) 837-7000. In addition, all of the documents incorporated by reference into this prospectus may be accessed via the Internet at our website: <http://www.exelixis.com>.

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

| | |
|-------------------------------------|-------------------|
| SEC registration fee | \$ 251 |
| Accounting fees and expenses | 30,000 |
| Legal fees and expenses | 50,000 |
| Printing and miscellaneous expenses | 21,749 |
| Total | \$ 102,000 |

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 our 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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The Registration Rights Agreement that we entered into with the Deerfield Entities provides for cross-indemnification in connection with registration of our common stock on behalf of the selling security holders pursuant to the Registration Rights Agreement. In this regard, the Registration Rights Agreement provides that the selling security holders are obligated, under certain circumstances, to indemnify our directors, officers and controlling persons against specified liabilities, including liabilities under the Securities Act.

Item 16. Exhibits

| Exhibit Number | Description |
|-----------------------|---|
| 2.1 | Agreement and Plan of Merger, dated September 27, 2004, by and among Exelixis, Inc., XBO Acquisition Corp., and X-Ceptor Therapeutics, Inc. (1) |
| 2.2* | Asset Purchase and License Agreement, dated as of September 4, 2007, by and among Agrigenetics, Inc., Mycogen Corporation, Exelixis Plant Sciences, Inc., Agrinomics, LLC and Exelixis, Inc. (2) |
| 2.3* | Share Sale and Transfer Agreement, dated November 20, 2007, by and between Taconic Farms, Inc. and Exelixis, Inc. (3) |
| 3.1 | Amended and Restated Certificate of Incorporation of Exelixis, Inc. (4) |
| 3.2 | Certificate of Amendment of Amended and Restated Certificate of Incorporation of Exelixis, Inc. (5) |
| 3.3 | Amended and Restated Bylaws of Exelixis, Inc. (6) |
| 4.1 | Specimen Common Stock Certificate. (7) |
| 4.2 | Form of Warrant, dated June 9, 2005, to purchase 750,000 shares of Exelixis, Inc. common stock in favor of Symphony Evolution Holdings LLC. (8) |
| 4.3 | Form of Warrant, dated June 13, 2006, to purchase 750,000 shares of Exelixis, Inc. common stock in favor of Symphony Evolution Holdings LLC. (9) |
| 4.4* | Warrant Purchase Agreement, dated June 9, 2005, between Exelixis, Inc. and Symphony Evolution Holdings LLC. (8) |
| 4.5 | Fourth Amended and Restated Registration Rights Agreement, dated February 26, 1999, among Exelixis, Inc. and certain Stockholders of Exelixis, Inc. (7) |
| 4.6 | Registration Rights Agreement, dated October 18, 2004, by and among Exelixis, Inc., X-Ceptor Therapeutics, Inc., and certain holders of capital stock of X-Ceptor Therapeutics, Inc. listed in Annex I thereto. (10) |
| 4.7 | Registration Rights Agreement, dated October 18, 2004, by and among Exelixis, Inc., X-Ceptor Therapeutics, Inc., and certain holders of capital stock of X-Ceptor Therapeutics, Inc. listed in Annex I thereto. (10) |
| 4.8* | Registration Rights Agreement, dated June 9, 2005, between Exelixis, Inc. and Symphony Evolution Holdings LLC. (8) |
| 4.9* | Form Warrant to Purchase Common Stock of Exelixis, Inc. issued or issuable to Deerfield Private Design Fund, L.P., Deerfield Private Design International, L.P., Deerfield Partners, L.P. and Deerfield International Limited. (11) |
| 4.10 | Registration Rights Agreement between Exelixis, Inc. and Deerfield Private Design Fund, L.P., Deerfield Private Design International, L.P., Deerfield Partners, L.P. and Deerfield International Limited dated June 4, 2008. (11) |
| 5.1 | Opinion of Cooley Godward Kronish LLP (previously filed with the Registrant's Form S-1/A filed with the SEC on September 26, 2008). |
| 23.1 | Consent of Independent Registered Public Accounting Firm. |
| 23.2 | Consent of Cooley Godward Kronish LLP (included in Exhibit 5.1). |

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Exhibit

Number Description

24.1 Power of Attorney (included in the signature page of Registrant's Form S-1 filed with the SEC on July 7, 2008).

* Confidential treatment granted for certain portions of this exhibit.

1. Filed as an Exhibit to Exelixis, Inc.'s Current Report on Form 8-K, as filed with the Securities and Exchange Commission on September 28, 2004 and incorporated herein by reference.
2. Filed as an Exhibit to Exelixis, Inc.'s Quarterly Report on Form 10-Q for the quarter ended September 28, 2007, filed with the Securities Exchange Commission on November 5, 2007 and incorporated herein by reference.
3. Filed as an Exhibit to Exelixis, Inc.'s Annual Report on Form 10-K for the fiscal year ended December 28, 2007, filed with the Securities and Exchange Commission on February 25, 2008 and incorporated herein by reference.
4. Filed as an Exhibit to Exelixis, Inc.'s Registration Statement on Form S-3 (File No. 333-152166), as filed with the Securities and Exchange Commission on April 24, 2009 and incorporated herein by reference.
5. Filed as an Exhibit to Exelixis, Inc.'s Quarterly Report on Form 10-Q for the quarter ended June 30, 2004, filed with the Securities and Exchange Commission on August 5, 2004 and incorporated herein by reference.
6. Filed as an Exhibit to Exelixis, Inc.'s Current Report on Form 8-K, as filed with the Securities and Exchange Commission on October 4, 2007 and incorporated herein by reference.
7. Filed as an Exhibit to Exelixis, Inc.'s Registration Statement on Form S-1 (File No. 333-96335), as filed with the Securities and Exchange Commission on February 7, 2000, as amended, and incorporated herein by reference.
8. Filed as an Exhibit to Exelixis, Inc.'s Quarterly Report on Form 10-Q for the quarter ended June 30, 2005, filed with the Securities and Exchange Commission on August 9, 2005 and incorporated herein by reference.
9. Filed as an Exhibit to Exelixis, Inc.'s Current Report on Form 8-K, as filed with the Securities and Exchange Commission on June 15, 2006 and incorporated herein by reference.
10. Filed as an Exhibit to Exelixis, Inc.'s Current Report on Form 8-K, as filed with the Securities and Exchange Commission on October 21, 2004 and incorporated herein by reference.
11. Filed as an Exhibit to Exelixis, Inc.'s Current Report on Form 8-K, as filed with the Securities and Exchange Commission on June 9, 2008 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;

(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 SEC 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), (1)(ii) and (1)(iii) of this section do not apply if the information required to be included in a post-effective amendment by those paragraphs is contained in reports filed with or furnished to the Commission by the registrant pursuant to section 13 or section 15(d) of the Securities Exchange Act of 1934 that are incorporated by reference in the registration statement, or is contained in a form of prospectus filed pursuant to Rule 424(b) that is part of the registration statement.

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(2) That, for the purpose of determining any liability under the Securities Act, each such post-effective amendment 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.

(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 the purpose of determining liability under the Securities Act of 1933 to any purchaser:

(i) If the registrant is relying on Rule 430B:

(A) Each prospectus filed by the registrant pursuant to Rule 424(b)(3) shall be deemed to be part of the registration statement as of the date the filed prospectus was deemed part of and included in the registration statement; and

(B) Each prospectus required to be filed pursuant to Rule 424(b)(2), (b)(5), or (b)(7) as part of a registration statement in reliance on Rule 430B relating to an offering made pursuant to Rule 415(a)(1)(i), (vii), or (x) for the purpose of providing the information required by Section 10(a) of the Securities Act of 1933 shall be deemed to be part of and included in the registration statement as of the earlier of the date such form of prospectus is first used after effectiveness or the date of the first contract of sale of securities in the offering described in the prospectus. As provided in Rule 430B, for liability purposes of the issuer and any person that is at that date an underwriter, such date shall be deemed to be a new effective date of the registration statement relating to the securities in the registration statement to which that prospectus relates, and the offering of such securities at that time shall be deemed to be the initial bona fide offering thereof. Provided, however, that no statement made in a registration statement or prospectus that is part of the registration statement or made in a document incorporated or deemed incorporated by reference into the registration statement or prospectus that is part of the registration statement will, as to a purchaser with a time of contract of sale prior to such effective date, supersede or modify any statement that was made in the registration statement or prospectus that was part of the registration statement or made in any such document immediately prior to such effective date; or

(ii) If the registrant is subject to Rule 430C, each prospectus filed pursuant to Rule 424(b) as part of a registration statement relating to an offering, other than registration statements relying on Rule 430B or other than prospectuses filed in reliance on Rule 430A, shall be deemed to be part of and included in the registration statement as of the date it is first used after effectiveness. Provided, however, that no statement made in a registration statement or prospectus that is part of the registration statement or made in a document incorporated or deemed incorporated by reference into the registration statement or prospectus that is part of the registration statement will, as to a purchaser with a time of contract of sale prior to such first use, supersede or modify any statement that was made in the registration statement or prospectus that was part of the registration statement or made in any such document immediately prior to such date of first use.

The undersigned registrant hereby undertakes 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 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 SEC this form of indemnification is against public policy as expressed in the Securities Act 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

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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 and will be governed by the final adjudication of this issue.

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Pursuant to the requirements of the Securities Act of 1933, the registrant certifies that it has reasonable grounds to believe that it meets all of the requirements for filing on Form S-3 and has duly caused this Post-Effective Amendment No. 2 on Form S-3 to the Registration Statement on Form S-1 to be signed on its behalf by the undersigned, thereunto duly authorized, in the city of South San Francisco, state of California, on May 8, 2009.

EXELIXIS, INC.

By: */s/ GEORGE A. SCANGOS, Ph.D.*
George A. Scangos, Ph.D.
President and Chief Executive Officer

Pursuant to the requirements of the Securities Act of 1933, this Post-Effective Amendment No. 2 on Form S-3 to the Registration Statement on Form S-1 has been signed below by the following persons in the capacities and on the dates indicated.

| Signatures | Title | Date |
|---|---|-------------|
| <i>/s/ GEORGE A. SCANGOS, Ph.D.</i> George A. Scangos, Ph.D. | Director, President and Chief Executive Officer (Principal Executive Officer) | May 8, 2009 |
| <i>/s/ FRANK KARBE</i> Frank Karbe | Chief Financial Officer (Principal Financial and Accounting Officer) | May 8, 2009 |
| <i>/s/ *</i> Stelios Papadopoulos, Ph.D. | Chairman of the Board | May 8, 2009 |
| <i>/s/ *</i> Charles Cohen, Ph.D. | Director | May 8, 2009 |
| <i>/s/ *</i> Carl B. Feldbaum, Esq. | Director | May 8, 2009 |
| <i>/s/ *</i> Alan M. Garber, M.D., Ph.D. | Director | May 8, 2009 |
| <i>/s/ *</i> Vincent Marchesi, M.D., Ph.D. | Director | May 8, 2009 |
| <i>/s/ *</i> Frank McCormick, Ph.D. | Director | May 8, 2009 |
| <i>/s/ *</i> George Poste, DVM, Ph.D. | Director | May 8, 2009 |

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|---|--|-------------|
| /s/ * Lance Willsey, M.D. | Director | May 8, 2009 |
| /s/ * Jack L. Wyszomierski | Director | May 8, 2009 |
| *By: /s/ GEORGE A. SCANGOS, PH.D. George A. Scangos, Ph.D. | Director, President and Chief Executive Officer | May 8, 2009 |

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Exhibit

| Number | Description |
|---------------|---|
| 2.1 | Agreement and Plan of Merger, dated September 27, 2004, by and among Exelixis, Inc., XBO Acquisition Corp., and X-Ceptor Therapeutics, Inc. (1) |
| 2.2* | Asset Purchase and License Agreement, dated as of September 4, 2007, by and among Agrigenetics, Inc., Mycogen Corporation, Exelixis Plant Sciences, Inc., Agrinomics, LLC and Exelixis, Inc. (2) |
| 2.3* | Share Sale and Transfer Agreement, dated November 20, 2007, by and between Taconic Farms, Inc. and Exelixis, Inc. (3) |
| 3.1 | Amended and Restated Certificate of Incorporation of Exelixis, Inc. (4) |
| 3.2 | Certificate of Amendment of Amended and Restated Certificate of Incorporation of Exelixis, Inc. (5) |
| 3.3 | Amended and Restated Bylaws of Exelixis, Inc. (6) |
| 4.1 | Specimen Common Stock Certificate. (7) |
| 4.2 | Form of Warrant, dated June 9, 2005, to purchase 750,000 shares of Exelixis, Inc. common stock in favor of Symphony Evolution Holdings LLC. (8) |
| 4.3 | Form of Warrant, dated June 13, 2006, to purchase 750,000 shares of Exelixis, Inc. common stock in favor of Symphony Evolution Holdings LLC. (9) |
| 4.4* | Warrant Purchase Agreement, dated June 9, 2005, between Exelixis, Inc. and Symphony Evolution Holdings LLC. (8) |
| 4.5 | Fourth Amended and Restated Registration Rights Agreement, dated February 26, 1999, among Exelixis, Inc. and certain Stockholders of Exelixis, Inc. (7) |
| 4.6 | Registration Rights Agreement, dated October 18, 2004, by and among Exelixis, Inc., X-Ceptor Therapeutics, Inc., and certain holders of capital stock of X-Ceptor Therapeutics, Inc. listed in Annex I thereto. (10) |
| 4.7 | Registration Rights Agreement, dated October 18, 2004, by and among Exelixis, Inc., X-Ceptor Therapeutics, Inc., and certain holders of capital stock of X-Ceptor Therapeutics, Inc. listed in Annex I thereto. (10) |
| 4.8* | Registration Rights Agreement, dated June 9, 2005, between Exelixis, Inc. and Symphony Evolution Holdings LLC. (8) |
| 4.9* | Form Warrant to Purchase Common Stock of Exelixis, Inc. issued or issuable to Deerfield Private Design Fund, L.P., Deerfield Private Design International, L.P., Deerfield Partners, L.P. and Deerfield International Limited. (11) |
| 4.10 | Registration Rights Agreement between Exelixis, Inc. and Deerfield Private Design Fund, L.P., Deerfield Private Design International, L.P., Deerfield Partners, L.P. and Deerfield International Limited dated June 4, 2008. (11) |
| 5.1 | Opinion of Cooley Godward Kronish LLP (previously filed with the Registrant's Form S-1/A filed with the SEC on September 26, 2008). |
| 23.1 | Consent of Independent Registered Public Accounting Firm. |
| 23.2 | Consent of Cooley Godward Kronish LLP (included in Exhibit 5.1). |
| 24.1 | Power of Attorney (included in the signature page of Registrant's Form S-1 filed with the SEC on July 7, 2008). |

* Confidential treatment granted for certain portions of this exhibit.

1. Filed as an Exhibit to Exelixis, Inc.'s Current Report on Form 8-K, as filed with the Securities and Exchange Commission on September 28, 2004 and incorporated herein by reference.
2. Filed as an Exhibit to Exelixis, Inc.'s Quarterly Report on Form 10-Q for the quarter ended September 28, 2007, filed with the Securities Exchange Commission on November 5, 2007 and incorporated herein by reference.

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3. Filed as an Exhibit to Exelixis, Inc. s Annual Report on Form 10-K for the fiscal year ended December 28, 2007, filed with the Securities and Exchange Commission on February 25, 2008 and incorporated herein by reference.
4. Filed as an Exhibit to Exelixis, Inc. s Registration Statement on Form S-3 (File No. 333-152166), as filed with the Securities and Exchange Commission on April 24, 2009 and incorporated herein by reference.
5. Filed as an Exhibit to Exelixis, Inc. s Quarterly Report on Form 10-Q for the quarter ended June 30, 2004, filed with the Securities and Exchange Commission on August 5, 2004 and incorporated herein by reference.
6. Filed as an Exhibit to Exelixis, Inc. s Current Report on Form 8-K, as filed with the Securities and Exchange Commission on October 4, 2007 and incorporated herein by reference.
7. Filed as an Exhibit to Exelixis, Inc. s Registration Statement on Form S-1 (File No. 333-96335), as filed with the Securities and Exchange Commission on February 7, 2000, as amended, and incorporated herein by reference.
8. Filed as an Exhibit to Exelixis, Inc. s Quarterly Report on Form 10-Q for the quarter ended June 30, 2005, filed with the Securities and Exchange Commission on August 9, 2005 and incorporated herein by reference.
9. Filed as an Exhibit to Exelixis, Inc. s Current Report on Form 8-K, as filed with the Securities and Exchange Commission on June 15, 2006 and incorporated herein by reference.
10. Filed as an Exhibit to Exelixis, Inc. s Current Report on Form 8-K, as filed with the Securities and Exchange Commission on October 21, 2004 and incorporated herein by reference.
11. Filed as an Exhibit to Exelixis, Inc. s Current Report on Form 8-K, as filed with the Securities and Exchange Commission on June 9, 2008 and incorporated herein by reference.