EXELIXIS INC
Form 424B5
March 07, 2011
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**Filed Pursuant to Rule 424(b)(5)**
**Registration No. 333-158792**

**The information in this preliminary prospectus supplement is not complete and may be changed. This preliminary prospectus supplement is not an offer to sell nor does it seek an offer to buy these securities in any jurisdiction where the offer or sale is not permitted.**

Subject to Completion. Dated March 7, 2011.

Prospectus Supplement to Prospectus dated May 8, 2009.

# 12,500,000 Shares

# Common Stock

Exelixis, Inc. is offering 12,500,000 shares to be sold in the offering.

The common stock is quoted on the Nasdaq Global Select Market under the symbol EXEL. The last reported sale price of the common stock on March 4, 2011 was $11.75 per share.

*See* Risk Factors *beginning on page S-8 of this prospectus supplement to read about factors you should consider before buying shares of the common stock.*

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

| | Per Share | Total |
|---|---|---|
| Initial price to public | $ | $ |
| Underwriting discount | $ | $ |
| Proceeds, before expenses, to Exelixis | $ | $ |

To the extent that the underwriters sell more than 12,500,000 shares of common stock, the underwriters have the option to purchase up to an additional 1,875,000 shares from Exelixis at the initial price to public less the underwriting discount.

The underwriters expect to deliver the shares against payment in New York, New York on March , 2011.

*Joint Book-Running Managers*

**Goldman, Sachs & Co.** **Cowen and Company**

*Co-Managers*

**Citi** **Lazard Capital Markets**

Prospectus Supplement dated March , 2011.

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## ABOUT THIS PROSPECTUS SUPPLEMENT

This document is in two parts. The first part is this prospectus supplement, which describes the specific terms of the common stock we are offering. The second part, the accompanying prospectus dated May 8, 2009, gives more general information about our common stock. You should read this prospectus supplement and the accompanying prospectus, including the information incorporated by reference and any free writing prospectuses we have authorized for use in connection with this offering, in their entirety before making an investment decision.

You should rely only on the information contained or incorporated by reference in this prospectus supplement and the accompanying prospectus, along with the information contained in any free writing prospectuses we have authorized for use in connection with this offering. If the description of the offering varies between this prospectus supplement and the accompanying prospectus, you should rely on the information in this prospectus supplement. We have not authorized anyone to provide you with different or additional information. Under no circumstances should the delivery to you of this prospectus supplement and the accompanying prospectus or any sale made pursuant to this prospectus supplement create any implication that the information contained in this prospectus supplement or the accompanying prospectus is correct as of any time after the respective dates of such information.

Unless the context requires otherwise, the words Exelixis, we, the company, us and our refer to Exelixis, Inc. and its subsidiaries, and the ter you refers to a prospective investor.

This prospectus supplement and the accompanying prospectus, including the information incorporated by reference into this prospectus supplement and the accompanying prospectus, include trademarks, service marks and trade names owned by us or others. Exelixis, Inc., the Exelixis, Inc. logo and all other Exelixis product and service names are trademarks of Exelixis, Inc. in the United States and in other selected countries. All other trademarks, service marks and trade names included or incorporated by reference in this prospectus supplement and the accompanying prospectus are the property of their respective owners.

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## PROSPECTUS SUPPLEMENT SUMMARY

*This summary highlights selected information appearing elsewhere or incorporated by reference in this prospectus supplement and accompanying prospectus and any free-writing prospectus that we have authorized for use in connection with this offering and may not contain all of the information that is important to you. This prospectus supplement and the accompanying prospectus include information about the shares we are offering as well as information regarding our business and financial data. You should read this prospectus supplement and the accompanying prospectus, including the information incorporated by reference and any free writing prospectuses we have authorized for use in connection with this offering, in their entirety. Investors should carefully consider the information set forth under Risk Factors in this prospectus supplement.*

### Exelixis, Inc.

We are a biotechnology company committed to developing small molecule therapies for the treatment of cancer. We are focusing our resources and development efforts exclusively on cabozantinib (XL184), our most advanced solely-owned product candidate, in order to maximize the therapeutic and commercial potential of this compound. We believe cabozantinib has the potential to be a high-quality, broadly active, differentiated pharmaceutical product that can make a meaningful difference in the lives of patients. We have also established a portfolio of other novel compounds that we believe have the potential to address serious unmet medical needs.

***Cabozantinib***

Cabozantinib inhibits MET, VEGFR2 and RET, proteins that are key drivers of tumor growth and/or vascularization. Cabozantinib is the most advanced inhibitor of MET in clinical development and is being evaluated in a broad development program encompassing multiple cancer indications. The current clinical program for cabozantinib is focused on the treatment of metastatic castration-resistant prostate cancer and ovarian cancer, based on encouraging interim data that has emerged from a randomized discontinuation trial, or RDT, investigating cabozantinib in nine distinct tumor types. Data from the RDT were released at Annual Meeting of the American Society of Clinical Oncology, or ASCO, Annual Meeting, in June 2010 and demonstrated broad activity for cabozantinib across multiple tumor types, in particular, metastatic castration-resistant prostate, ovarian, non-small cell lung and hepatocellular cancers and melanoma. Updated interim data presented at the 22nd EORTC-NCI-AACR Symposium on Molecular Targets and Cancer Therapeutics in November 2010, or the 2010 EORTC Symposium, and at the ASCO 2011 Genitourinary Cancers Symposium in February 2011, suggest that cabozantinib has a novel and differentiated clinical profile in metastatic castration-resistant prostate cancer and ovarian cancer. The data presented indicate that cabozantinib has shown novel activity against metastatic bone and soft tissue lesions in metastatic castration-resistant prostate cancer. In addition, we have observed resolution of metastatic bone lesions on bone scan in patients with metastatic breast cancer, renal cell carcinoma, thyroid cancer and melanoma. Another priority for us will be to generate additional data in the various other cohorts of the RDT, including melanoma, breast cancer, non-small cell lung cancer and hepatocellular cancer, to support further prioritization of our clinical and commercial options. In addition, we are conducting ongoing exploratory clinical trials for cabozantinib in other tumor types, including renal cell carcinoma. Objective tumor responses have been observed in patients with cabozantinib in 12 of 13 unique tumor types investigated to date, reflecting the broad potential clinical activity and commercial opportunity with this new agent.

Cabozantinib is also being studied in an ongoing global phase 3 registration trial in medullary thyroid cancer. We expect to release top-line results from the phase 3 trial in the first half of 2011 and

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to potentially submit a new drug application, or NDA, for cabozantinib as a treatment for medullary thyroid cancer in the United States in the second half of 2011.

In January 2011, we announced that the U.S. Food and Drug Administration, or the FDA, granted orphan drug designation to cabozantinib for the treatment of follicular, medullary, and anaplastic thyroid carcinoma, and metastatic or locally advanced papillary thyroid cancer. Orphan drug status is granted to treatments for diseases that affect fewer than 200,000 people in the U.S. and provides the benefits of potential market exclusivity for the orphan-designated product for the orphan designated indication for seven years, tax credits of up to 50% of the qualified clinical trial expenses and a waiver of FDA application user fees.

***Strategy***

Our strategy is to aggressively advance cabozantinib through development toward commercialization. In doing so, we will pursue a pragmatic development plan focused on those cancer indications where we believe cabozantinib has the greatest near-term therapeutic and commercial potential. We are aggressively managing our expenses to preserve our cash resources and ensure we are appropriately dedicating those resources towards successfully executing our strategy.

We also have five proprietary compounds (in addition to cabozantinib and our partnered pipeline) that are of potential value. Consistent with focusing our resources on cabozantinib, we are discontinuing efforts with respect to all of our compounds and programs that are not funded by partners pursuant to collaboration agreements and are actively pursuing collaborations or other external opportunities for the continued development of these compounds and programs.

***Recent Events***

In furtherance of our decision to focus on cabozantinib and aggressively manage our expenses, in December 2010 we implemented a restructuring plan that resulted in a reduction of our workforce by 143 employees. Personnel reductions were made across our entire organization, including discovery, development and general & administrative, or G&A, departments. Further personnel reductions are expected to be made through the end of 2012 as we complete our obligations under collaboration agreements and withdraw resources from completed projects. Discovery and clinical activities under various collaborations will continue at funded levels until we complete our contractual obligations.

***Collaborations***

Based on the strength of our expertise in biology, drug discovery and development, we have established collaborations with leading pharmaceutical and biotechnology companies, including Bristol-Myers Squibb Company, or Bristol-Myers Squibb, sanofi-aventis, Genentech, Inc. (a wholly owned member of the Roche Group), or Genentech, Boehringer Ingelheim GmbH, GlaxoSmithKline and Daiichi Sankyo Company Limited for the remaining compounds and programs in our portfolio. Pursuant to these collaborations, we have out-licensed compounds or programs to a partner for further development and commercialization, generally have no further unfunded cost obligations related to such compounds or programs and may be entitled to receive research funding, milestones and royalties or a share of profits from commercialization. With respect to our partnered compounds, we are eligible to receive potential milestone payments under our collaborations totaling approximately $3.7 billion in the aggregate, on a non-risk adjusted basis, of which 13% are related to clinical development milestones, 47% are related to regulatory milestones and 40% are related to commercial milestones.

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***Corporate Information***

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

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**The Offering**

| | |
|---|---|
| Common stock offered by Exelixis | 12,500,000 shares |
| Common stock to be outstanding after the offering | 121,787,160 shares |
| Use of proceeds | We currently expect to use the net proceeds from this offering for general corporate purposes, including for research and development, capital expenditures and working capital. |
| Risk factors | See Risk Factors beginning on page S-8 for a discussion of factors you should consider before buying shares of our common stock. |
| Nasdaq Global Select Market Symbol | EXEL |

The number of shares of common stock to be outstanding after the offering is based on the number of shares outstanding as of December 31, 2010. As of that date, we had 109,287,160 shares of common stock outstanding, excluding:

- 19,630,030 shares of common stock underlying options outstanding as of December 31, 2010 at a weighted average exercise price of $7.52 per share;
- 2,250,000 shares of common stock underlying warrants outstanding as of December 31, 2010 at a weighted average exercise price of $7.60 per share;
- 2,172,431 unvested restricted stock units as of December 31, 2010; and
- 3,060,505 shares available for future grant under our 2000 Employee Stock Purchase Plan, 2,727,656 shares available for future grant under our 2000 Non-Employee Directors Stock Option Plan, 861,050 shares available for future grant under our 2010 Inducement Award Plan and 755,781 shares available for future grant under our 401(k) Retirement Plan, all as of December 31, 2010.

Unless we specifically state otherwise, the information in this prospectus supplement assumes that the underwriters do not exercise their option to purchase up to 1,875,000 additional shares of our common stock within 30 days after the date of this prospectus supplement.

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**Summary Consolidated Financial Data**

We derived the following information from our audited consolidated financial statements for each of the three years ended December 31, 2008, 2009 and 2010. The following information should be read in conjunction with our consolidated financial statements and related notes incorporated by reference in this prospectus supplement and the accompanying prospectus.

For more details on how you can obtain our SEC reports and other information, you should read the section of the accompanying prospectus entitled Where You Can Find More Information.

We have adopted a 52- or 53-week fiscal year that ends on the Friday closest to December 31st. Fiscal year 2008, a 53-week year, ended on January 2, 2009, fiscal year 2009, a 52-week year, ended on January 1, 2010, and fiscal year 2010, a 52-week year, ended on December 31, 2010. For convenience, references in this prospectus supplement as of and for the fiscal years ended January 2, 2009, January 1, 2010 and December 31, 2010 are indicated on a calendar year basis, ended December 31, 2008, 2009 and 2010, respectively.

| | Year Ended December 31, | | |
|---|---|---|---|
| | 2008 | 2009 | 2010 |
| | (in thousands, except per share data) | | |
| **Consolidated Statement of Operations Data** | | | |
| Total revenues | $ 117,859 | $ 151,759 | $ 185,045 |
| Total operating expenses | $ 297,172 | $ 273,666 | $ 276,442 |
| Consolidated net loss | $ (175,570) | $ (139,557) | $ (92,330) |
| Loss attributed to noncontrolling interest | $ 12,716 | $ 4,337 | $ |
| Net loss attributable to Exelixis, Inc. | $ (162,854) | $ (135,220) | $ (92,330) |
| Net loss per share, basic and diluted attributable to Exelixis, Inc. | $ (1.54) | $ (1.26) | $ (0.85) |
| Shares used in computing basic and diluted net loss per share | 105,498 | 107,073 | 108,522 |

| | As of December 31, 2010 | |
|---|---|---|
| | Actual | As Adjusted(1)(2) (unaudited) |
| | (in thousands) | |
| **Consolidated Balance Sheet Data** | | |
| Cash and cash equivalents, marketable securities, restricted cash and investments and long-term investments | $ 256,377 | $ 395,191 |
| Working capital (deficit) | $ (16,455) | $ 122,359 |
| Total assets | $ 360,790 | $ 499,604 |
| Long-term obligations, less current portion | $ 186,702 | $ 186,702 |
| Accumulated deficit | $ (1,182,054) | $ (1,182,054) |
| Total stockholders (deficit) equity | $ (228,325) | $ (89,511) |

(1) Each $1.00 increase or decrease in the assumed offering price per share would increase or decrease the as adjusted figure shown above for each of cash and cash equivalents, marketable securities, restricted cash and investments and long-term investments, working capital (deficit), total assets and total stockholders (deficit) equity by approximately $11.8 million, assuming that the number of shares offered by us, as set forth on the cover page of this prospectus supplement, remains the same and after deducting the estimated underwriting discount and estimated offering expenses payable by us. We may also increase or decrease the number of shares we are offering. An increase or decrease of 500,000 shares in the number of shares offered by us at the assumed offering price would increase or decrease the as adjusted figure

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above for each of cash and cash equivalents, marketable securities, restricted cash and investments and long-term investments, working capital (deficit), total assets and total stockholders (deficit) equity by approximately $5.6 million, after deducting the estimated underwriting discounts and estimated offering expenses payable by us.

(2) As adjusted to reflect the sale of 12,500,000 shares being offered in this offering and the receipt of the estimated net proceeds of $138.8 million from the sale of these shares, assuming a public offering price of $11.75 per share and after deducting the estimated underwriting discounts and estimated offering expenses payable by us.

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## RISK FACTORS

*Investing in our common stock involves a high degree of risk. Before deciding whether to invest in our common stock, you should consider carefully the risk factors described below and in any free writing prospectus that we have authorized for use in connection with this offering. If any of these risks actually occur, it may materially harm our business, financial condition, operating results or cash flow. As a result, the market price of our common stock could decline, and you could lose all or part of your investment. Additional risks and uncertainties that are not yet identified or that we think are immaterial may also materially harm our business, operating results and financial condition and could result in a complete loss of your investment.*

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

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

We will need to raise additional capital to:

- fund our operations and clinical trials;
- continue our research and development efforts; and
- commercialize our product candidates, if any such candidates receive regulatory approval for commercial sale.

As of December 31, 2010, we had $256.4 million in cash and cash equivalents, marketable securities and long-term investments, which included restricted cash and investments of $6.4 million and approximately $96.9 million of cash and cash equivalents and marketable securities that we are required to maintain on deposit with Silicon Valley Bank pursuant to covenants in our loan and security agreement with Silicon Valley Bank. We anticipate that our current cash and cash equivalents, marketable securities, long-term investments and funding that we expect to receive from existing collaborators, together with the anticipated proceeds from this offering, will enable us to maintain our operations for a period of at least 12 months following the date of this prospectus supplement. However, our future capital requirements will be substantial and will depend on many factors that may require us to use available capital resources significantly earlier than we currently anticipate. These factors include:

- the cabozantinib development program  We are focusing our resources and development efforts on cabozantinib, our most advanced solely-owned product candidate, which is being studied in a variety of tumor types, with the goal of rapidly commercializing the compound. The current clinical program for cabozantinib is focused on the treatment of metastatic castration-resistant prostate cancer and ovarian cancer, based on encouraging interim data that has emerged from the RDT. Data from the RDT were released at the ASCO Annual Meeting in June 2010 and demonstrated broad activity for cabozantinib across multiple tumor types, in particular, metastatic castration-resistant prostate, ovarian, non-small cell lung and hepatocellular cancers and melanoma. Updated interim data presented at the 2010 EORTC Symposium in November 2010 and at the ASCO 2011 Genitourinary Cancers Symposium in February 2011, suggest that cabozantinib has a novel and differentiated clinical profile in metastatic castration-resistant prostate cancer and ovarian cancer. The data presented indicate that cabozantinib has shown novel activity against bone and soft tissue lesions in metastatic castration-resistant prostate cancer. Another priority for us will be to generate additional data in the various other cohorts of the RDT, including melanoma, breast cancer, non-small cell lung cancer and hepatocellular cancer, to support further prioritization of our clinical and commercial options. We also are focusing our efforts on our ongoing phase 3 clinical trial of cabozantinib as

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a potential treatment for medullary thyroid cancer that recently completed patient enrollment. In addition, we are conducting ongoing exploratory clinical trials for cabozantinib in other tumor types, including renal cell carcinoma. Our development plan for cabozantinib is dependent on the extent of our available financial resources. There can be no assurance that we will have sufficient financial resources independently or through other arrangements to fund a broad development plan for cabozantinib. If adequate funds are not available, we may be required to delay, discontinue or elect not to pursue one or more trials for cabozantinib;

repayment of our loan from GlaxoSmithKline In October 2002, we entered into a collaboration agreement with GlaxoSmithKline. 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. On October 27, 2010, we paid approximately $37.0 million in cash to GlaxoSmithKline as the second of three installments of principal and accrued interest due under the loan agreement. As of December 31, 2010, the aggregate principal and interest outstanding under the loan was $35.9 million. The final installment of principal and accrued interest under the loan is due on October 27, 2011. Repayment of all or any of the amounts advanced to us under the loan agreement may, at our election, be made in the form of our common stock at fair market value, subject to certain conditions, or cash. 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 to satisfy our repayment obligations. However, 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;

repayment of the notes under our note purchase agreement with Deerfield On June 2, 2010, we entered into a note purchase agreement with entities affiliated with Deerfield Management Company, L.P., or Deerfield, pursuant to which, on July 1, 2010, we sold to Deerfield an aggregate of $124.0 million initial principal amount of our secured convertible notes, due June 2015, for an aggregate purchase price of $80.0 million, less closing fees and expenses. The outstanding principal amount of the notes bears interest in the annual amount of $6.0 million, payable quarterly in arrears. We will be required to make mandatory prepayments on the notes on an annual basis in 2013, 2014 and 2015 equal to 15% of our collaborative arrangements received during the prior fiscal year, subject to a maximum annual prepayment amount of $27.5 million and, for payments due in January 2013 and 2014, a minimum prepayment amount of $10.0 million. We may also prepay all or a portion (not less than $5.0 million) of the principal amount of the notes at an optional prepayment price based on a discounted principal amount (during the first three years of the term, subject to a prepayment premium) determined as of the date of prepayment, plus accrued and unpaid interest, plus in the case of a prepayment of the full principal amount of the notes (other than prepayments upon the occurrence of specified transactions relating to a change of control or a substantial sale of assets), all accrued interest that would have accrued between the date of such prepayment and the next anniversary of the note purchase agreement. In lieu of making any optional or mandatory prepayment in cash, at any time after July 1, 2011, subject to certain limitations, we have the right to convert all or a portion of the principal amount of the notes into, or satisfy all or any portion of the optional prepayment amounts or mandatory prepayment amounts (other than the first $10.0 million of mandatory prepayments required in 2013 and 2014) with shares of our common stock. Additionally, in lieu of making any payment of accrued and unpaid interest in respect of the notes in cash, at any time after July 1, 2011, subject to certain limitations, we may elect to satisfy any such payment with shares of our common stock. The number of shares of our

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common stock issuable upon conversion or in settlement of principal and interest obligations will be based upon the discounted trading price of our common stock over a specified trading period. In the event the market price for our common stock is depressed, we may not be able to convert the principal amount of the notes or satisfy our payment obligations 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 convert the notes or satisfy our payment obligations may result in significant dilution to our stockholders. As a result, we may need to obtain additional funding to satisfy our repayment obligations. There can be no assurance that we will have sufficient funds to repay the notes or satisfy our payment obligations under the note purchase agreement when due or that we will comply with the conditions to our ability to convert the principal amount of the notes into or satisfy our payment obligations with shares of our common stock;

repayment of our loan from Silicon Valley Bank On June 2, 2010, we amended our loan and security agreement with Silicon Valley Bank to provide for a new seven-year term loan in an amount of $80.0 million. The principal amount outstanding under the term loan accrues interest at 1.0% per annum, which interest is due and payable monthly. We are required to repay the term loan in one balloon principal payment, representing 100% of the principal balance and accrued and unpaid interest, on May 31, 2017. We have the option to prepay all, but not less than all, of the amounts advanced under the term loan, provided that we pay all unpaid accrued interest thereon that is due through the date of such prepayment and the interest on the entire principal balance of the term loan that would otherwise have been paid after such prepayment date until the maturity date of the term loan. In accordance with the terms of the loan and security agreement, we are also required to maintain on deposit an amount equal to at least 100% of the outstanding principal balance of the term loan at all times as support for our obligations under the loan and security agreement. As a result, although the proceeds of the new term loan improve our ability to comply with minimum working capital and cash covenants imposed by our debt instruments with GlaxoSmithKline and Deerfield and thus provide us with more flexibility to use our other cash resources, the proceeds of the term loan cannot directly be used to satisfied our other obligations without causing a default under our loan and security agreement with Silicon Valley Bank;

the level of payments received under existing collaboration agreements, licensing agreements and other arrangements;

the degree to which we conduct funded development activity on behalf of partners to whom we have out-licensed compounds;

whether we enter into new collaboration agreements, licensing agreements or other arrangements (including, in particular, with respect to cabozantinib) that provide additional capital;

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;

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;

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the effect of competing technological and market developments;

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

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

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 additional strategic partnerships or collaborative arrangements 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 may need to obtain additional funding in order to stay in compliance with financial covenants contained in agreements with third parties. The terms of our debt owed to GlaxoSmithKline, Deerfield and Silicon Valley Bank each contain covenants requiring us to maintain specified cash balances or working capital. The failure to comply with these covenants could result in an acceleration of the underlying debt obligations. If we cannot raise additional capital in order to remain in compliance with such 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 $92.3 million for the year ended December 31, 2010. As of that date, we had an accumulated deficit of $1,182.1 million. We expect to continue to incur net losses and anticipate negative operating cash flow for the foreseeable future. We have not yet completed the development, including obtaining regulatory approval, of cabozantinib or any other product candidates and, consequently, have not generated revenues from the sale of pharmaceutical 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, research funding, the achievement of milestones and royalties we earn from any future products developed from the collaborative research. If research funding we receive from collaborators decreases, 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. 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 the development of cabozantinib. 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.

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***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, on December 1, 2010 we implemented a restructuring that will result in a reduction of our workforce by approximately 65% over a two-year period. We anticipate that we will incur restructuring charges through the end of 2017 as we implement this restructuring.

We are still assessing our ability to sublease certain of our facilities in light of the workforce reduction as well as the potential for sublease income. Estimates for sublease income would require significant assumptions regarding the time required to contract with subtenants, the amount of idle space we would be able to sublease and potential future sublease rates. If we are able to vacate certain of our facilities, we would need to continue to update our estimate of the lease exit costs in our financial statements until we were able to negotiate an exit to the lease or negotiate a sublease for the remaining term of the lease.

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 strategic objectives and could adversely impact our results of operations and financial condition.

***We are exposed to risks related to foreign currency exchange rates.***

Most of our foreign expenses incurred are associated with establishing and conducting clinical trials for cabozantinib. The amount of expenses incurred will be impacted by fluctuations in the currencies of those countries in which we conduct clinical trials. Our agreements with the foreign sites that conduct such clinical trials generally provide that payments for the services provided will be calculated in the currency of that country, and converted into U.S. dollars using various exchange rates based upon when services are rendered or the timing of invoices. When the U.S. dollar weakens against foreign currencies, the U.S. dollar value of the foreign-currency denominated expense increases, and when the U.S. dollar strengthens against these currencies, the U.S. dollar value of the foreign-currency denominated expense decreases. Consequently, changes in exchange rates may affect our results of operations.

***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 supplement 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 December 31, 2010, no assurance can be given that a 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.

**Risks Related to Development of Cabozantinib**

***We are dependent on the successful development and commercialization of cabozantinib.***

The success of our business is dependent upon the successful development and commercialization of cabozantinib. As part of our strategy, we intend to dedicate all of our proprietary resources to advance cabozantinib as aggressively as feasible. Our ability to realize the value of our

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investment is contingent on, among other things, successful clinical development, regulatory approval and market acceptance of cabozantinib. If we encounter difficulties in the development of cabozantinib due to any of the factors discussed in this Risk Factors section or otherwise, or we do not receive regulatory approval and are unable to commercialize cabozantinib, we will not have the resources necessary to continue our business in its current form.

***Clinical testing of cabozantinib and other 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 of cabozantinib 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 cabozantinib, including:

- cabozantinib may not prove to be efficacious or may cause, or potentially 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;
- our competitors may discover other compounds or therapies that show significantly improved safety or efficacy compared to cabozantinib;
- 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 withhold authorization of, or 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 we were to have significant delays in or termination of our clinical testing of cabozantinib as a result of any of the events described above or otherwise, our expenses could increase or our ability to generate revenues from cabozantinib 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 cabozantinib or meet current or future requirements of the FDA, including those identified based on our discussions with the FDA. Our planned clinical trials may not begin on time, or at all, may not be completed on schedule, or at all, may not be sufficient for registration of cabozantinib or may not result in an approvable product.

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 cabozantinib as a product candidate. The duration and the cost of clinical trials may vary significantly over the life of a project as a result of factors relating to the clinical trial, including, among others:

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

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

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the number of clinical sites included in the trials; and

the length of time required to enroll suitable patient subjects.

Any delay 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. Our partners may experience similar risks with respect to the compounds we have outlicensed to them. If any of the events described above were to occur with such programs or compounds, the likelihood of receipt of milestones and royalties under such collaboration agreements could decrease.

***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 cabozantinib.***

We do not have the ability to independently conduct clinical trials for cabozantinib, and we 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 cabozantinib.

***We lack the capability to manufacture compounds for clinical trials and rely on third parties to manufacture cabozantinib, 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 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 cabozantinib for 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 cabozantinib 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 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 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 cabozantinib. 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 cabozantinib, 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.

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***Materials necessary to manufacture cabozantinib may not be available on commercially reasonable terms, or at all, which may delay its development and commercialization.***

Some of the materials necessary for the manufacture of cabozantinib 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 cabozantinib. Suppliers may not sell us these materials at the time we need them or on commercially reasonable terms. If we are unable to obtain the materials needed to conduct our clinical trials, product testing and potential regulatory approval could be delayed, adversely affecting our ability to develop cabozantinib. Similarly, if we are unable to obtain critical manufacturing materials after regulatory approval has been obtained, the commercial launch of cabozantinib could be delayed or there could be a shortage in supply, which could materially affect our ability to generate revenues from sales of cabozantinib. If suppliers increase the price of manufacturing materials, the price for cabozantinib may increase, which may make it 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 cabozantinib.

**Risks Related to Our Relationships with Third Parties**

***We are dependent upon our collaborations with major companies, which subjects us to a number of risks.***

We have established collaborations with leading pharmaceutical and biotechnology companies, including Bristol-Myers Squibb, sanofi-aventis, Genentech, Boehringer Ingelheim GmbH, GlaxoSmithKline and Daiichi Sankyo Company Limited, for the development and ultimate commercialization of a significant number of compounds generated from our research and development efforts. We continue to pursue collaborations for selected unpartnered preclinical and clinical programs and compounds. Our dependence on our relationships with existing collaborators for the development and commercialization of our compounds subjects us to, and our dependence on future collaborators for development and commercialization of additional compounds will subject us to, a number of risks, including:

- we are not able to control the amount and timing of resources that our collaborators will devote to the development or commercialization of drug candidates or to their marketing and distribution;
- we may not be able to control the amount and timing of resources that our potential future collaborators may devote to the development or commercialization of drug candidates or to their marketing and distribution;
- collaborators may delay clinical trials, provide insufficient funding for a clinical trial program, stop a clinical trial or abandon a drug candidate, repeat or conduct new clinical trials or require a new formulation of a drug candidate for clinical testing;
- disputes may arise between us and our collaborators that result in the delay or termination of the research, development or commercialization of our drug candidates or that result in costly litigation or arbitration that diverts management s attention and resources;
- collaborators may experience financial difficulties;
- collaborators may not be successful in their efforts to obtain regulatory approvals in a timely manner, or at all;
- collaborators may not properly maintain or defend our intellectual property rights or may use our proprietary information in such a way as to invite litigation that could jeopardize or invalidate our proprietary information or expose us to potential litigation;

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- business combinations or significant changes in a collaborator s business strategy may adversely affect a collaborator s willingness or ability to complete its obligations under any arrangement;

- a collaborator could independently move forward with a competing drug candidate developed either independently or in collaboration with others, including our competitors;

- we may be precluded from entering into additional collaboration arrangements with other parties in an area or field of exclusivity;

- future collaborators may require us to relinquish some important rights, such as marketing and distribution rights; and

- collaborations may be terminated (as occurred with respect to cabozantinib, that was previously subject to our 2008 collaboration with Bristol-Myers Squibb) or allowed to expire, which would delay the development and may increase the cost of developing our drug candidates.

If any of these risks materialize, our product development efforts could be delayed and otherwise adversely affected, which could adversely impact our business, operating results and financial condition.

***If we are unable to continue current collaborations and achieve milestones or royalties, our revenues would suffer.***

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 royalties, or our collaborators fail to develop successful products, we will not earn the revenues contemplated under such collaborative agreements.

If any of these agreements is terminated early (as occurred with respect to cabozantinib, which was previously subject to our 2008 collaboration with Bristol-Myers Squibb), whether unilaterally or by mutual agreement, our revenues could suffer. Most of our collaboration agreements 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 revenues from the termination or expiration of any of our existing or recently terminated arrangements.

***We may be unable to establish collaborations for selected preclinical and clinical compounds.***

Our strategy includes the pursuit of new collaborations with leading pharmaceutical and biotechnology companies for the development and ultimate commercialization of selected preclinical and clinical programs and compounds, particularly those drug candidates for which we believe that the capabilities and resources of a partner can accelerate development and help to fully realize their therapeutic and commercial potential. We face significant competition in seeking appropriate collaborators, and these collaborations are complex and time consuming to negotiate and document. We may not be able to negotiate additional collaborations on acceptable terms, or at all. We are unable to predict when, if ever, we will enter into any additional collaborations because of the numerous risks and uncertainties associated with establishing additional collaborations. If we are unable to negotiate

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additional collaborations, we may not be able to realize value from a particular drug candidate, particularly those drug candidates as to which we believe a broad development program is appropriate or for which we have determined not to continue to utilize our own resources to develop. As a result, our revenues, capital resources and product development efforts could be adversely affected.

**Risks Related to Regulatory Approval of Cabozantinib**

***Cabozantinib is 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 this product candidate.***

Cabozantinib, as well as the activities associated with the research, development and commercialization of the product candidate, 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 cabozantinib would prevent us from commercializing this product candidate. We have not received regulatory approval to market cabozantinib 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 an NDA can be submitted to the FDA, the product candidate must undergo extensive clinical trials, which can take many years and requires 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. The FDA has substantial discretion in the approval process and may refuse to approve any NDA or decide that our data is insufficient for approval and require additional preclinical, clinical or other studies. For example, varying interpretations of the data obtained from preclinical and clinical testing could delay, limit or prevent regulatory approval of cabozantinib.

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 cabozantinib may cause delays in the approval or rejection of an application.

Even if the FDA or a comparable authority in another country approves cabozantinib, the approval may impose significant restrictions on the indicated uses, conditions for use, labeling, distribution, advertising, promotion, marketing and/or production of cabozantinib 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 Cabozantinib**

***The commercial success of cabozantinib will depend upon the degree of market acceptance of the product candidate among physicians, patients, health care payors, private health insurers and the medical community.***

Our ability to commercialize cabozantinib will be highly dependent upon the extent to which the product candidate gains 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 cabozantinib does not achieve an adequate

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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 cabozantinib, if approved for commercial sale, will depend upon a number of factors, including:

- the effectiveness, or perceived effectiveness, of cabozantinib in comparison to competing products;
- the existence of any significant side effects of cabozantinib, as well as their severity in comparison to any competing products;
- potential advantages over alternative treatments;
- other indications for which cabozantinib is approved;
- the ability to offer cabozantinib 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 cabozantinib, 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 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 cabozantinib 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 cabozantinib, our revenues and prospects for profitability will suffer.***

Our ability to commercialize cabozantinib will be highly dependent on the extent to which coverage and reimbursement for the product candidate 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 cabozantinib 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 cabozantinib, our revenues and prospects for profitability will suffer. In addition, even if third-party payors provide some coverage or reimbursement for cabozantinib, 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.

Another factor that may affect the pricing of drugs is proposed congressional action regarding drug reimportation into the United States. For example, 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 cabozantinib, 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 cabozantinib to other available therapies. The conduct of such a clinical trial could be expensive and result in delays in the commercialization of cabozantinib. 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 cabozantinib. Cost-control initiatives could decrease the price we might establish for cabozantinib, which would result in lower product revenues to us.

***Current healthcare laws and regulations and future legislative or regulatory reforms to the healthcare system may affect our ability to sell cabozantinib profitably.***

The U.S. and some foreign jurisdictions are considering or have enacted a number of legislative and regulatory proposals to change the healthcare system in ways that could affect our ability to sell our products profitably. Among policy makers and payors in the U.S. and elsewhere, there is significant interest in promoting changes in healthcare systems with the stated goals of containing healthcare costs, improving quality and/or expanding access. In the U.S., the pharmaceutical industry has been a particular focus of these efforts and has been significantly affected by major legislative initiatives.

In March 2010, the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Affordability Reconciliation Act, or collectively, PPACA, became law in the U.S. PPACA substantially changes the way healthcare is financed by both governmental and private insurers and significantly affects the pharmaceutical industry. Among the provisions of PPACA of greatest importance to the pharmaceutical industry are the following:

- an annual, nondeductible fee on any entity that manufactures or imports certain branded prescription drugs and biologic agents, apportioned among these entities according to their market share in certain government healthcare programs, beginning in 2011;

- an increase in the rebates a manufacturer must pay under the Medicaid Drug Rebate Program, retroactive to January 1, 2010, to 23.1% and 13% of the average manufacturer price for branded and generic drugs, respectively;

- a new Medicare Part D coverage gap discount program, in which manufacturers must agree to offer 50% point-of-sale discounts off negotiated prices of applicable brand drugs to eligible beneficiaries during their coverage gap period, as a condition for the manufacturer s outpatient drugs to be covered under Medicare Part D, beginning in 2011;

- extension of manufacturers Medicaid rebate liability to covered drugs dispensed to individuals who are enrolled in Medicaid managed care organizations, effective March 23, 2010;

- expansion of eligibility criteria for Medicaid programs by, among other things, allowing states to offer Medicaid coverage to additional individuals beginning in April 2010 and by adding new mandatory eligibility categories for certain individuals with income at or below 133% of the Federal Poverty Level beginning in 2014, thereby potentially increasing manufacturers Medicaid rebate liability;

- expansion of the entities eligible for discounts under the Public Health Service pharmaceutical pricing program, effective in January 2010;

- new requirements to report certain financial arrangements with physicians, including reporting any transfer of value made or distributed to prescribers and other healthcare providers, effective March 31, 2013, and reporting any investment interests held by

physicians and their immediate family members during the preceding calendar year;

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- a new requirement to annually report drug samples that manufacturers and distributors provide to physicians, effective April 1, 2012;

- a licensure framework for follow-on biologic products; and

- a new Patient-Centered Outcomes Research Institute to oversee, identify priorities in, and conduct comparative clinical effectiveness research, along with funding for such research.

We anticipate that the PPACA, as well as other healthcare reform measures that may be adopted in the future, may result in more rigorous coverage criteria and an additional downward pressure on the price that we receive for any approved product, and could seriously harm our business. Any reduction in reimbursement from Medicare or other government programs may result in a similar reduction in payments from private payors.

We also cannot be certain that cabozantinib will successfully be placed on the list of drugs covered by particular health plan formularies, nor can we predict the negotiated price for cabozantinib, which will be determined by market factors. Many states have also created preferred drug lists and include drugs on those lists only when the manufacturers agree to pay a supplemental rebate. If cabozantinib is not included on these preferred drug lists, physicians may not be inclined to prescribe it to their Medicaid patients, thereby diminishing the potential market for cabozantinib.

As a result of the PPACA and the trend towards cost-effectiveness criteria and managed healthcare in the United States, third-party payors are increasingly attempting to contain healthcare costs by limiting both coverage and the level of reimbursement of new drugs. They may also refuse to provide any coverage of uses of approved products for medical indications other than those for which the FDA has granted market approvals. As a result, significant uncertainty exists as to whether and how much third-party payors will reimburse for newly-approved drugs, which in turn will put pressure on the pricing of drugs. Further, we do not have experience in ensuring approval by applicable third-party payors outside of the United States for coverage and reimbursement of cabozantinib. We also anticipate pricing pressures in connection with the sale of our products due to the trend toward managed healthcare, the increasing influence of health maintenance organizations and additional legislative proposals.

***Our competitors may develop products and technologies that make cabozantinib 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 cabozantinib could allow our competitors to bring products to market before us, which would impair our ability to commercialize cabozantinib. 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. There may also be drug candidates of which we are not aware at an earlier stage of development that may compete with cabozantinib. In addition, if cabozantinib is successfully developed, it may compete

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with existing therapies that have long histories of use, such as chemotherapy and radiation treatments in cancer indications. Examples of potential competition for cabozantinib include AstraZeneca s development-stage RET, VEGFR and EGFR inhibitor, vandetanib, other VEGF pathway inhibitors, including Genentech s bevacizumab, and other MET inhibitors, including Pfizer s crizotinib, ArQule s ARQ197, GlaxoSmithKline s foretinib (XL880) and Genentech s Met MAb.

***We may not be able to manufacture cabozantinib in commercial quantities, which would prevent us from commercializing the product candidate.***

To date, cabozantinib has been manufactured in small quantities for preclinical and clinical trials. If cabozantinib is approved by the FDA or other regulatory agencies for commercial sale, we will need to manufacture it 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 cabozantinib 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 cabozantinib, the regulatory approval or commercial launch of the product candidate may be delayed or there may be a shortage in supply. Cabozantinib requires 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 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 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.

***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.

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**Risks Related to Employees 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 may not have sufficient personnel to 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. The restructuring that we implemented on December 1, 2010 could have an adverse impact on our ability to retain and recruit qualified personnel. 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.

***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 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

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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 insurance coverage at a reasonable cost or in sufficient amounts to protect us against losses due to liability. If we obtain marketing approval for cabozantinib, 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.

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**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 to volatility, including:

- the scope of our research and development activities;
- recognition of upfront licensing or other fees or revenues;
- 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 efforts leading to milestone payments and royalties;
- the introduction of new technologies or products by our competitors;
- the timing and willingness of collaborators to further develop or, if approved, commercialize our product outlicensed to them;
- 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 cabozantinib;
- adjustments to expenses accrued in prior periods based on management s estimates after the actual level of activity relating to such expenses becomes more certain;
- the impairment of acquired goodwill and other assets;
- the impact of the restructuring of the company implemented on December 1, 2010; 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.

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.

***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 our or our collaborators clinical trials;

announcement of FDA approval or non-approval, or delays in the FDA review process, of cabozantinib or our collaborators product candidates or those of our competitors or actions

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taken by regulatory agencies with respect to our, our collaborators or our competitors clinical trials;

the timing of achievement of our clinical, regulatory, partnering and other milestones, such as the commencement of clinical development, the completion of a clinical trial, the filing for regulatory approval or the establishment of collaborative arrangements for one or more of our outlicensed programs and compounds;

actions taken by regulatory agencies with respect to cabozantinib or our clinical trials for cabozantinib;

the announcement of new products by our competitors;

quarterly variations in our or our competitors results of operations;

developments in our relationships with our collaborators, including the termination or modification of our agreements;

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;

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. Excessive volatility may continue for an extended period of time following the date of this prospectus supplement.

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.

***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 or upon vesting of restricted stock units 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.

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

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

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

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

- a classified Board of Directors;
- a prohibition on actions by our stockholders by written consent;
- the inability of our stockholders to call special meetings of stockholders;
- the ability of our Board of Directors to issue preferred stock without stockholder approval, which could be used to institute a poison pill that would work to dilute the stock ownership of a potential hostile acquirer, effectively preventing acquisitions that have not been approved by our Board of Directors;
- limitations on the removal of directors; and
- advance notice requirements for director nominations and stockholder proposals.

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

**Risks Related to this Offering**

***If you purchase shares of common stock in this offering, you will experience immediate dilution in your investment. You will experience further dilution if we issue additional equity securities in future fundraising transactions.***

Purchasers of common stock in this offering will pay a price per share in this offering that exceeds the net tangible book value per share of our common stock. Assuming that we sell 12,500,000 shares of our common stock in this offering at an assumed public offering price of $11.75 per share (which was the last reported sale price of our common stock as reported on the NASDAQ Global Select Market on March 4, 2011), and after deducting the estimated underwriting discount and estimated offering expenses payable by us, you will experience immediate dilution of $13.01 per share, representing the difference between our as adjusted net tangible book value per share as of

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December 31, 2010 after giving effect to this offering and the assumed public offering price. See the section entitled Dilution below for a more detailed illustration of the dilution you would incur if you purchase common stock in this offering.

If we issue additional common stock, or securities convertible into or exchangeable or exercisable for common stock, our stockholders, including investors who purchase shares of common stock in this offering, will experience additional dilution, and any such issuances may result in downward pressure on the price of our common stock. We also cannot assure you that we will be able to sell shares or other securities in any other offering at a price per share that is equal to or greater than the price per share paid by investors in this offering, and investors purchasing shares or other securities in the future could have rights superior to existing stockholders.

***We have broad discretion in the use of the net proceeds from this offering and may not use them effectively.***

We will have broad discretion in the application of the net proceeds from this offering. Stockholders may not deem such uses desirable, and our use of the proceeds may not yield a significant return or any return for our stockholders. Because the number and variability of factors that determine our use of the proceeds from this offering, our actual uses of the proceeds of this offering may vary substantially from our current planned uses. Our failure to apply the proceeds effectively could have a material adverse effect on our business, delay the development of cabozantinib and cause the price of our common stock to decline.

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## FORWARD-LOOKING STATEMENTS

Some of the statements in this prospectus supplement, the accompanying prospectus, the documents incorporated by reference and any free writing prospectus that we have authorized for use in connection with this offering are forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, as amended, and Section 21E of the Securities Exchange Act of 1934, as amended. These statements are based on our current expectations, assumptions, estimates and projections about our business and our industry and involve known and unknown risks, uncertainties and other factors that may cause our company s or our industry s results, levels of activity, performance or achievements to be materially different from any future results, levels of activity, performance or achievements expressed or implied in, or contemplated by, the forward-looking statements. Words such as believe, anticipate, expect, intend, plan, focus, assume, goal, obj may should, would, could, estimate, predict, potential, continue, encouraging, or the negative of such terms or other similar expr forward-looking statements, but the absence of these words does not necessarily mean that a statement is not forward-looking. In addition, any statements that refer to expectations, projections or other characterizations of future events or circumstances are forward-looking statements. Our actual results and the timing of events may differ significantly from the results discussed in the forward-looking statements. Factors that might cause such a difference include those discussed under the caption Risk Factors beginning on page S-8 of this prospectus supplement, in the documents incorporated by reference, in any free writing prospectus that we have authorized for use in connection with this offering or as a result of other circumstances beyond our control. The forward-looking statements made in this prospectus supplement, the accompanying prospectus and any free writing prospectus that we have authorized for use in connection with this offering speak only as of the date on which the statements are made.

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## USE OF PROCEEDS

Based upon an assumed public offering price of $11.75, we estimate that the net proceeds from the sale of the 12,500,000 shares of common stock we are offering will be approximately $138.8 million, after deducting the estimated underwriting discount and the estimated offering expenses payable by us. If the underwriters exercise in full their option to purchase additional shares, we estimate that the net proceeds to us will be approximately $159.7 million.

We will retain broad discretion over the use of the net proceeds from this public offering. We currently expect to use the net proceeds from this offering for general corporate purposes, including for research and development, capital expenditures and working capital. We may also use a portion of the net proceeds to acquire or invest in businesses, products and technologies that are complementary to our own, although we are not currently planning or negotiating any such transactions.

Pending the use of the net proceeds, we may invest the net proceeds in investment grade, interest-bearing securities.

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## PRICE RANGE OF OUR COMMON STOCK

Our common stock has traded on the NASDAQ Global Select Market (formerly the NASDAQ National Market) under the symbol EXEL since April 11, 2000. The following table sets forth, for the periods indicated, the high and low intraday sales prices for our common stock as reported by the NASDAQ Global Select Market:

| | Common Stock Price | |
|---|---|---|
| | High | Low |
| **Year Ended January 2, 2009** | | |
| Quarter ended January 2, 2009 | $ 6.30 | $ 2.11 |
| Quarter ended September 26, 2008 | $ 7.35 | $ 4.64 |
| Quarter ended June 27, 2008 | $ 8.15 | $ 5.00 |
| Quarter ended March 28, 2008 | $ 8.95 | $ 4.81 |
| **Year Ended January 1, 2010** | | |
| Quarter ended January 1, 2010 | $ 8.00 | $ 5.30 |
| Quarter ended October 2, 2009 | $ 7.25 | $ 4.25 |
| Quarter ended July 3, 2009 | $ 6.10 | $ 4.09 |
| Quarter ended April 3, 2009 | $ 6.11 | $ 4.18 |
| **Year Ended December 31, 2010** | | |
| Quarter ended December 31, 2010 | $ 9.20 | $ 3.84 |
| Quarter ended October 1, 2010 | $ 4.29 | $ 2.86 |
| Quarter ended July 2, 2010 | $ 7.00 | $ 3.11 |
| Quarter ended April 2, 2010 | $ 7.53 | $ 5.77 |
| **Year Ended December 30, 2011** | | |
| Quarter ended April 1, 2011 (through March 4, 2011) | $ 12.82 | $ 7.10 |

The reported last sale price of our common stock on the Nasdaq Global Select Market on March 4, 2011 was $11.75 per share. As of February 15, 2011, there were approximately 589 stockholders of record of our common stock.

## DIVIDEND POLICY

Since inception, we have not paid dividends on our common stock. We currently intend to retain all future earnings, if any, for use in our business and currently do not plan to pay any cash dividends in the foreseeable future. Any future determination to pay dividends will be at the discretion of our Board of Directors.

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## DILUTION

Our net tangible book value (deficit) on December 31, 2010 was approximately $(292.0 million), or approximately $(2.67) per share. Net tangible book value (deficit) per share is equal to the amount of our total tangible assets, less total liabilities, divided by the aggregate number of shares of common stock outstanding as of December 31, 2010. Dilution in net tangible book value (deficit) per share represents the difference between the amount per share paid by purchasers of shares of common stock in this offering and the net tangible book value (deficit) per share of our common stock immediately after this offering. After giving effect to the purchase from us of 12,500,000 shares of common stock in this offering at an assumed public offering price of $11.75 per share (which was the last reported sale price of our common stock on March 4, 2011), and after deducting the estimated underwriting discount and estimated offering expenses payable by us, our net tangible book value (deficit) on December 31, 2010 would have been approximately $(153.2 million), or approximately $(1.26) per share. This represents an immediate dilution of $13.01 per share to investors purchasing shares of common stock in this offering. The following table illustrates this dilution:

| | | |
|---|---|---|
| Assumed public offering price per share | | $ 11.75 |
| Net tangible book value (deficit) as of December 31, 2010 | $ (2.67) | |
| Increase per share attributable to new investors | 1.41 | |
| Net tangible book value (deficit) per share as of December 31, 2010 after giving effect to this offering | | (1.26) |
| Dilution per share to investors in this offering | | $ 13.01 |

The foregoing discussion and table do not take into account further dilution to new investors that could occur upon the exercise of the underwriters option to purchase up to an additional 1,875,000 shares within 30 days of the date of this prospectus supplement or the exercise of other outstanding options and warrants having a per share exercise price less than the assumed public offering price per share in this offering. If the underwriters exercise in full their option to purchase 1,875,000 additional shares, our net tangible book value (deficit) on December 31, 2010 would have been approximately $(132.3 million), or approximately $(1.07) per share, representing an immediate dilution of $12.82 per share to new investors purchasing shares of common stock in this offering.

Each $1.00 increase (decrease) in the assumed public offering price of $11.75 per share would increase (decrease) our as adjusted net tangible book value by $11.8 million, or $0.10 per share, and the dilution per share to investors in this offering by $0.90 per share, assuming that the number of shares offered by us, as set forth on the cover page of this prospectus supplement, remains the same and after deducting the estimated underwriting discount and estimated offering expenses payable by us. We may also increase or decrease the number of shares we are offering. An increase of 500,000 shares in the number of shares offered by us, to a total of 13.0 million shares, together with a concomitant $1.00 increase in the assumed public offering price of $11.75 per share, would increase our as adjusted net tangible book value by $17.9 million, or $0.15 per share, and the dilution per share to investors in this offering by $0.85 per share. Similarly, a decrease of 500,000 shares in the number of shares offered by us, to a total of 12.0 million shares, together with a concomitant $1.00 decrease in the assumed public offering price of $11.75 per share, would decrease our as adjusted net tangible book value by $16.9 million, or $0.14 per share, and the dilution per share to investors in this offering by $0.86 per share. The as adjusted information discussed above is illustrative only and will be adjusted based on the actual public offering price and other terms of this offering determined at pricing.

The foregoing discussion and table are based on 109,287,160 shares of common stock issued and outstanding as of December 31, 2010 and exclude:

- 19,630,030 shares of common stock underlying options outstanding as of December 31, 2010 at a weighted average exercise price of $7.52 per share;

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2,250,000 shares of common stock underlying warrants outstanding as of December 31, 2010 at a weighted average exercise price of $7.60 per share;

2,172,431 unvested restricted stock units as of December 31, 2010; and

3,060,505 shares available for future grant under our 2000 Employee Stock Purchase Plan, 2,727,656 shares available for future grant under our 2000 Non-Employee Directors Stock Option Plan, 861,050 shares available for future grant under our 2010 Inducement Award Plan and 755,781 shares available for future grant under our 401(k) Retirement Plan, all as of December 31, 2010.

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## UNDERWRITING

The company and the underwriters have entered into an underwriting agreement with respect to the shares being offered. Subject to certain conditions, each underwriter has severally agreed to purchase the number of shares indicated in the following table. Goldman, Sachs & Co. and Cowen and Company, LLC are the representatives of the underwriters.

| Underwriters | Number of Shares |
|---|---|
| Goldman, Sachs & Co. | |
| Cowen and Company, LLC | |
| Citigroup Global Markets Inc | |
| Lazard Capital Markets LLC | |
| Total | |

The underwriters are committed to take and pay for all of the shares being offered, if any are taken, other than the shares covered by the option described below unless and until this option is exercised.

If the underwriters sell more shares than the total number set forth in the table above, the underwriters have an option to buy up to an additional 1,875,000 shares from the company. They may exercise that option for 30 days after the date of this prospectus supplement. If any shares are purchased pursuant to this option, the underwriters will severally purchase shares in approximately the same proportion as set forth in the table above.

The following table shows the per share and total underwriting discounts and commissions to be paid to the underwriters by the company. Such amounts are shown assuming both no exercise and full exercise of the underwriters option to purchase 1,875,000 additional shares.

| | No Exercise | Full Exercise |
|---|---|---|
| Per Share | $ | $ |
| Total | $ | $ |

Shares sold by the underwriters to the public will initially be offered at the initial public offering price set forth on the cover of this prospectus supplement. Any shares sold by the underwriters to securities dealers may be sold at a discount of up to $ per share from the initial public offering price. If all the shares are not sold at the initial public offering price, the representatives may change the offering price and the other selling terms. The offering of the shares by the underwriters is subject to receipt and acceptance and subject to the underwriters right to reject any order in whole or in part.

Exelixis and its directors and executive officers have agreed not to dispose of or hedge any shares of the common stock or any securities convertible into or exchangeable for shares of the common stock during the period ending 90 days after the date of this prospectus supplement, subject to certain permitted exceptions, except with the prior written consent of Goldman, Sachs & Co. However, these agreements do not prohibit the issuance of shares of common stock or any securities convertible into or exchangeable for shares of common stock by Exelixis pursuant to its existing equity incentive plans or 401(k) plan or any future equity incentive plans approved by Exelixis s stockholders, or the issuance by Exelixis following the date 45 days after the date of this prospectus supplement of shares of common stock or any securities convertible into or exchangeable for shares of common stock in an amount up to an aggregate of 10% of Exelixis s outstanding shares of common stock after giving effect to this offering if such shares are issued for cash in connection with a strategic transaction that includes a commercial relationship involving Exelixis; provided that in the case of any issuances in

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connection with a strategic transaction, the recipients of these shares agree to be bound by the lock-up agreement described above. Goldman, Sachs & Co., in its sole discretion, may release any of the securities subject to these lock-up agreements at any time without notice.

In connection with the offering, the underwriters may purchase and sell shares of common stock in the open market. These transactions may include short sales, stabilizing transactions and purchases to cover positions created by short sales. Short sales involve the sale by the underwriters of a greater number of shares than it is required to purchase in the offering. Covered short sales are sales made in an amount not greater than the underwriters option to purchase additional shares from the company in the offering. The underwriters may close out any covered short position by either exercising their option to purchase additional shares or purchasing shares in the open market. In determining the source of shares to close out the covered short position, the underwriters will consider, among other things, the price of shares available for purchase in the open market as compared to the price at which they may purchase additional shares pursuant to the option granted to them. Naked short sales are any sales in excess of such option. The underwriters must close out any naked short position by purchasing shares in the open market. A naked short position is more likely to be created if the underwriters are concerned that there may be downward pressure on the price of the common stock in the open market after pricing that could adversely affect investors who purchase in the offering. Stabilizing transactions consist of various bids for or purchases of common stock made by the underwriters in the open market prior to the completion of the offering.

The underwriters may also impose a penalty bid. This occurs when a particular underwriter repays to the underwriters a portion of the underwriting discount received by it because the representatives have repurchased shares sold by or for the account of such underwriter in stabilizing or short covering transactions.

Purchases to cover a short position and stabilizing transactions, as well as other purchases by the underwriters for their own accounts, may have the effect of preventing or retarding a decline in the market price of the company s stock, and, together with the penalty bid, may stabilize, maintain or otherwise affect the market price of the common stock. As a result, the price of the common stock may be higher than the price that otherwise might exist in the open market. If these activities are commenced, they may be discontinued at any time. These transactions may be effected on NASDAQ, in the over-the-counter market or otherwise.

Each underwriter has represented and agreed that:

(a) it has only communicated or caused to be communicated and will only communicate or cause to be communicated an invitation or inducement to engage in investment activity (within the meaning of section 21 of the Financial Service and Markets Act 2000, or the FSMA) received by it in connection with the issue or sale of the shares in circumstances in which section 21 of FSMA does not apply to the company; and

(b) it has complied with, and will comply with all applicable provisions of FSMA with respect to anything done by it in relation to the shares in, from or otherwise involving the United Kingdom.

In relation to each Member State of the European Economic Area which has implemented the Prospectus Directive (each, a Relevant Member State), each underwriter has represented and agreed that with effect from and including the date on which the Prospectus Directive is implemented in that Relevant Member State (the Relevant Implementation Date) it has not made and will not make an offer of shares to the public in that Relevant Member State prior to the publication of a prospectus in relation to the shares which has been approved by the competent authority in that Relevant Member State or, where appropriate, approved in another Relevant Member State and notified to the competent authority

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in that Relevant Member State, all in accordance with the Prospectus Directive, except that it may, with effect from and including the Relevant Implementation Date, make an offer of shares to the public in that Relevant Member State at any time:

(a) to legal entities which are authorised or regulated to operate in the financial markets or, if not so authorised or regulated, whose corporate purpose is solely to invest in securities;

(b) to any legal entity which has two or more of (1) an average of at least 250 employees during the last financial year; (2) a total balance sheet of more than 43,000,000 and (3) an annual net turnover of more than 50,000,000, as shown in its last annual or consolidated accounts;

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

(d) in any other circumstances which do not require the publication by the Company of a prospectus pursuant to Article 3 of the Prospectus Directive.

For the purposes of this provision, the expression an offer of shares to the public in relation to any shares in any Relevant Member State means the communication in any form and by any means of sufficient information on the terms of the offer and the shares to be offered so as to enable an investor to decide to purchase or subscribe the shares, as the same may be varied in that Relevant Member State by any measure implementing the Prospectus Directive in that Relevant Member State and the expression Prospectus Directive means Directive 2003/71/EC and includes any relevant implementing measure in each Relevant Member State.

The shares may not be offered or sold by means of any document other than (i) in circumstances which do not constitute an offer to the public within the meaning of the Companies Ordinance (Cap.32, Laws of Hong Kong), or (ii) to professional investors within the meaning of the Securities and Futures Ordinance (Cap.571, Laws of Hong Kong) and any rules made thereunder, or (iii) in other circumstances which do not result in the document being a prospectus within the meaning of the Companies Ordinance (Cap.32, Laws of Hong Kong), and no advertisement, invitation or document relating to the shares may be issued or may be in the possession of any person for the purpose of issue (in each case whether in Hong Kong or elsewhere), which is directed at, or the contents of which are likely to be accessed or read by, the public in Hong Kong (except if permitted to do so under the laws of Hong Kong) other than with respect to shares which are or are intended to be disposed of only to persons outside Hong Kong or only to professional investors within the meaning of the Securities and Futures Ordinance (Cap. 571, Laws of Hong Kong) and any rules made thereunder.

This prospectus supplement has not been registered as a prospectus with the Monetary Authority of Singapore. Accordingly, this prospectus supplement and any other document or material in connection with the offer or sale, or invitation for subscription or purchase, of the shares may not be circulated or distributed, nor may the shares be offered or sold, or be made the subject of an invitation for subscription or purchase, whether directly or indirectly, to persons in Singapore other than (i) to an institutional investor under Section 274 of the Securities and Futures Act, Chapter 289 of Singapore (the SFA ), (ii) to a relevant person, or any person pursuant to Section 275(1A), and in accordance with the conditions, specified in Section 275 of the SFA or (iii) otherwise pursuant to, and in accordance with the conditions of, any other applicable provision of the SFA.

Where the shares are subscribed or purchased under Section 275 by a relevant person which is: (a) a corporation (which is not an accredited investor) the sole business of which is to hold investments and the entire share capital of which is owned by one or more individuals, each of whom is an accredited investor; or (b) a trust (where the trustee is not an accredited investor) whose sole purpose

is to hold investments and each beneficiary is an accredited investor, shares, debentures and units of shares and debentures of that corporation or the beneficiaries rights and interest in that trust shall not be transferable for 6 months after that corporation or that trust has acquired the shares under Section 275 except: (1) to an institutional investor under Section 274 of the SFA or to a relevant person, or any person pursuant to Section 275(1A), and in accordance with the conditions, specified in Section 275 of the SFA; (2) where no consideration is given for the transfer; or (3) by operation of law.

The shares have not been and will not be registered under the Securities and Exchange Law of Japan (the Financial Instruments and Exchange Law) and each underwriter has agreed that it will not offer or sell any securities, directly or indirectly, in Japan or to, or for the benefit of, any resident of Japan (which term as used herein means any person resident in Japan, including any corporation or other entity organized under the laws of Japan), or to others for re-offering or resale, directly or indirectly, in Japan or to a resident of Japan, except pursuant to an exemption from the registration requirements of, and otherwise in compliance with, the Securities and Exchange Law and any other applicable laws, regulations and ministerial guidelines of Japan.

The company estimates that its share of the total expenses of the offering, excluding underwriting discounts, will be approximately $350,000.

The company has agreed to indemnify the several underwriters and their controlling persons against certain liabilities, including liabilities under the Securities Act of 1933.

The underwriters and their respective affiliates are full service financial institutions engaged in various activities, which may include securities trading, commercial and investment banking, financial advisory, investment management, investment research, principal investment, hedging, financing and brokerage activities. Certain of the underwriters and their respective affiliates have, from time to time, performed, and may in the future perform, various financial advisory and investment banking services for the company, for which they received or will receive customary fees and expenses.

Lazard Frères & Co. LLC referred this transaction to Lazard Capital Markets LLC and will receive a referral fee from Lazard Capital Markets LLC in connection therewith.

In the ordinary course of their various business activities, the underwriters and their respective affiliates may make or hold a broad array of investments and actively trade debt and equity securities (or related derivative securities) and financial instruments (including bank loans) for their own account and for the accounts of their customers, and such investment and securities activities may involve securities and/or instruments of the issuer. The underwriters and their respective affiliates may also make investment recommendations and/or publish or express independent research views in respect of such securities or instruments and may at any time hold, or recommend to clients that they acquire, long and/or short positions in such securities and instruments.

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## VALIDITY OF COMMON STOCK

The validity of the common stock offered hereby will be passed upon for us by Cooley LLP, Palo Alto, California, and for the underwriters by Sullivan & Cromwell LLP, Palo Alto, California.

## EXPERTS

Ernst & Young LLP, 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 December 31, 2010, and the effectiveness of our internal control over financial reporting as of December 31, 2010, as set forth in their report, which is incorporated by reference in this prospectus supplement and accompanying prospectus and elsewhere in the registration statement. Our financial statements are incorporated by reference in reliance on Ernst & Young LLP s report, given on their authority as experts in accounting and auditing.

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**PROSPECTUS**

**$250,000,000**

**Common Stock**

**Preferred Stock**

**Debt Securities**

**Warrants**

**Units**

From time to time, we may offer up to $250,000,000 of any combination of the securities described in this prospectus, either individually or in units. We may also offer common stock or preferred stock issuable upon conversion of debt securities, common stock issuable upon conversion of preferred stock, or common stock, preferred stock or debt securities issuable upon the exercise of warrants.

This prospectus provides a general description of the securities that we may offer. Each time we sell securities, we will provide specific terms of the securities offered in a supplement to this prospectus. We may also authorize one or more free writing prospectuses to be provided to you in connection with these offerings. The prospectus supplement and any related free writing prospectus may also add, update or change information contained in this prospectus or in the documents incorporated by reference into this prospectus. You should carefully read this prospectus, the applicable prospectus supplement and any related free writing prospectus, as well as any documents incorporated by reference in this prospectus and any prospectus supplement, carefully before investing in any of the securities being offered. This prospectus may not be used to consummate a sale of securities unless accompanied by the applicable prospectus supplement.

Our common stock is traded on The NASDAQ Global Select Market under the symbol EXEL. On May 7, 2009, the last reported sales price of our common stock was $4.59 per share. The applicable prospectus supplement will contain information, where applicable, as to any other listing, if any, on The NASDAQ Global Select Market or any securities market or other exchange of the securities covered by the prospectus supplement.

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

We will sell these securities directly to investors, through agents designated from time to time or to or through underwriters or dealers, on a continuous or delayed basis. For additional information on the methods of sale, you should refer to the section entitled Plan of Distribution in this prospectus. If any underwriters are involved in the sale of any securities with respect to which this prospectus is being delivered, the names of such underwriters and any applicable commissions or discounts will be set forth in a prospectus supplement. The price to the public of such securities and the net proceeds we expect to receive from such sale will also be set forth in a prospectus supplement.

**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 May 8, 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, or the SEC, using the shelf registration process. By using a shelf registration statement, we may offer and sell from time to time in one or more offerings the common stock, preferred stock, debt securities, warrants, and units described in this prospectus or a combination of the foregoing up to a total dollar amount of $250,000,000.

This prospectus provides you with a general description of the securities we may offer. Each time we sell securities under this prospectus, we will provide a prospectus supplement that will contain specific information about the terms of that offering. We may also authorize one or more free writing prospectuses to be provided to you that may contain material information relating to the offerings. The prospectus supplement and any related free writing prospectus that we may authorize to be provided to you may also add, update or change the information set forth in this prospectus or in any documents that we have incorporated by reference into this prospectus. **This prospectus may not be used to consummate a sale of securities unless it is accompanied by a prospectus supplement.**

You should rely only on the information that we have provided or incorporated by reference in this prospectus, any applicable prospectus supplement and any related free writing prospectus that we may authorize to be delivered to you. We have not authorized anyone to provide you with different information. No dealer, salesperson or other person is authorized to give any information or to represent anything not contained in this prospectus, any applicable prospectus supplement or any related free writing prospectus that we may authorize to be delivered to you. You must not rely on any unauthorized information or representation. This prospectus is an offer to sell only the securities offered hereby, but only under circumstances and in jurisdictions where it is lawful to do so. You should assume that the information in this prospectus, any applicable prospectus supplement or any related free writing prospectus is accurate only as of the date on the front of the document and that any information we have incorporated by reference is accurate only as of the date of the document incorporated by reference, regardless of the time of delivery of this prospectus, any applicable prospectus supplement or any related free writing prospectus, or any sale of a security.

This prospectus contains summaries of certain provisions contained in some of the documents described herein, but reference is made to the actual documents for complete information. All of the summaries are qualified in their entirety by the actual documents. Copies of some of the documents referred to herein have been filed, will be filed or will be incorporated by reference as exhibits to the registration statement of which this prospectus is a part, and you may obtain copies of those documents as described below under the heading Where You Can Find More Information.

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, any applicable prospectus supplement or any related free writing prospectus are the property of their respective owners.

We urge you to read carefully this prospectus, any applicable prospectus supplement and any related free writing prospectus that we may authorize to be delivered to you, 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.

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## SUMMARY

This summary highlights selected information appearing elsewhere or incorporated by reference in this prospectus and does not contain all of the information that you need to consider in making your investment decision. You should carefully read this prospectus and the applicable prospectus supplement, including the information incorporated by reference and any free writing prospectuses we have authorized for use in connection with any offering, as well as the exhibits to the registration statement of which this prospectus is a part, in their entirety. Investors should also carefully consider the information set forth under Risk Factors contained in the applicable prospectus supplement and any related free writing prospectus and under similar headings in the other documents that are incorporated by reference in this prospectus.

References in this prospectus to Exelixis , the Company, we , us and our refer to Exelixis, Inc., a Delaware corporation.

**Our Company**

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.

We were incorporated in Delaware in November 1994 as Exelixis Pharmaceuticals, Inc., and we changed our name to Exelixis, Inc. in February 2000. Our principal executive offices are located at 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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**The Securities We May Offer**

We may offer shares of our common stock and preferred stock, various series of debt securities and/or warrants to purchase any of such securities, either individually or in units, with a total value of up to $250,000,000 from time to time under this prospectus, together with any applicable prospectus supplement and related free writing prospectus, at prices and on terms to be determined by market conditions at the time of offering. This prospectus provides you with a general description of the securities we may offer. Each time we offer a type or series of securities under this prospectus, we will provide a prospectus supplement that will describe the specific amounts, prices and other important terms of the securities, including, to the extent applicable:

- designation or classification;
- aggregate principal amount or aggregate offering price;
- maturity, if applicable;
- original issue discount, if any;
- rates and times of payment of interest or dividends, if any;
- redemption, conversion, exercise exchange or sinking fund terms, if any;
- conversion or exchange prices or rates, if any, and, if applicable, any provisions for changes to or adjustments in the conversion or exchange prices or rates and in the securities or other property receivable upon conversion or exchange;
- ranking;
- restrictive covenants, if any;
- voting or other rights, if any; and
- important United States federal income tax considerations.

A prospectus supplement and any related free writing prospectus that we may authorize to be provided to you may also add, update or change information contained in this prospectus or in documents we have incorporated by reference. However, no prospectus supplement or free writing prospectus will offer a security that is not registered and described in this prospectus at the time of the effectiveness of the registration statement of which this prospectus is a part.

We may sell the securities directly to investors or to or through agents, underwriters or dealers. We, and our agents or underwriters, reserve the right to accept or reject all or part of any proposed purchase of securities. If we do offer securities through agents or underwriters, we will include in the applicable prospectus supplement:

the names of those agents or underwriters;

applicable fees, discounts and commissions to be paid to them;

details regarding over-allotment options, if any; and

the net proceeds to us.

***Common Stock.*** We may issue shares of our common stock from time to time. The holders of our common stock are entitled to one vote for each share held of record on all matters submitted to a vote of the stockholders and do not have cumulative voting rights. Subject to preferences that may be applicable to any shares of our preferred stock that may become outstanding, the holders of outstanding shares of our common stock are entitled to receive ratably such dividends as may be declared by the board of directors out of funds legally available therefor. Upon the liquidation, dissolution or winding up of Exelixis, holders of our common stock are entitled to share ratably in all assets remaining after payment of liabilities and the liquidation preferences of any shares of

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our preferred stock then outstanding. In this prospectus, we have summarized certain general features of the common stock under Description of Capital Stock Common Stock. We urge you, however, to read the prospectus supplements and any related free writing prospectus that we may authorize to be provided to you related to any common stock being offered.

***Preferred Stock.*** We may issue shares of our preferred stock from time to time, in one or more series. Our board of directors will determine the rights, preferences, privileges and restrictions of the preferred stock, including dividend rights, conversion rights, voting rights, terms of redemption, liquidation preferences, sinking fund terms and the number of shares constituting any series or the designation of any series. Preferred stock offered under this prospectus may be convertible into our common stock or exchangeable for our other securities. If we sell any series of preferred stock under this prospectus and applicable prospectus supplements, we will fix the rights, preferences, privileges, qualifications and restrictions of the preferred stock of such series in the certificate of designation relating to that series. We will file as an exhibit to the registration statement of which this prospectus is a part, or will incorporate by reference from a current report on Form 8-K that we file with the SEC, the form of any certificate of designation that describes the terms of the series of preferred stock that we are offering before the issuance of the related series of preferred stock. In this prospectus, we have summarized certain general features of the preferred stock under Description of Capital Stock Preferred Stock. We urge you, however, to read the prospectus supplements and any related free writing prospectus that we may authorize to be provided to you related to the series of preferred stock being offered, as well as the complete certificate of designation that contains the terms of the applicable series of preferred stock.

***Debt Securities.*** We may issue debt securities from time to time, in one or more series, as either senior or subordinated debt or as senior or subordinated convertible debt. The senior debt securities will rank equally with any other unsubordinated debt that we may have and may be secured or unsecured. The subordinated debt securities will be subordinate and junior in right of payment, to the extent and in the manner described in the instrument governing the debt, to all or some portion of our indebtedness. Any convertible debt securities that we issue will be convertible into or exchangeable for our common stock or other securities of ours. Conversion may be mandatory or at the holder s option and would be at prescribed conversion rates. The debt securities will be issued under one or more documents called indentures, which are contracts between us and a trustee for the holders of the debt securities. Forms of indentures have been filed as exhibits to the registration statement of which this prospectus is a part, and supplemental indentures and forms of debt securities containing the terms of debt securities being offered will be filed as exhibits to the registration statement of which this prospectus is a part, or will be incorporated by reference from a current report on Form 8-K that we file with the SEC. In this prospectus, we have summarized certain general features of the debt securities under Description of Debt Securities. We urge you, however, to read the prospectus supplements and any free writing prospectus that we may authorize to be provided to you related to the series of debt securities being offered, as well as the complete indentures that contain the terms of the series of debt securities.

***Warrants.*** We may issue warrants for the purchase of our common stock, preferred stock and/or debt securities in one or more series, from time to time. We may issue warrants independently or together with common stock, preferred stock and/or debt securities, and the warrants may be attached to or separate from those securities. The warrants will be evidenced by warrant certificates that may be issued under one or more warrant agreements, which are contracts between us and an agent for the holders of the warrants. Forms of the warrant agreements and forms of warrant certificates containing the terms of the warrants being offered have been filed as exhibits to the registration statement of which this prospectus is a part, and supplemental agreements and forms of warrant certificates will be filed as exhibits to the registration statement of which this prospectus is a part, or will be incorporated by reference from a current report on Form 8-K that we file with the SEC. In this prospectus, we have summarized certain general features of the warrants under Description of Warrants. We urge you, however, to read the prospectus supplements and any free writing prospectus that we may authorize to be provided to you related to the series of warrants being offered, as well as the complete warrant agreements and warrant certificates that contain the terms of the warrants.

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***Units.*** We may issue units consisting of common stock, preferred stock, debt securities and/or warrants to purchase any of such securities in one or more series. We will evidence each series of units by unit certificates that we may issue under a separate agreement with a unit agent. Any unit agent will be a bank or trust company that we select. We will indicate the name and address of any unit agent in the applicable prospectus supplement relating to a particular series of units. We will file as exhibits to the registration statement of which this prospectus is a part, or will incorporate by reference from a current report on Form 8-K that we file with the SEC, the form of unit agreement and any supplemental agreements that describe the terms of the series of units we are offering before the issuance of the related series of units. In this prospectus, we have summarized certain general features of the units under Description of Units. We urge you, however, to read the prospectus supplements and any free writing prospectus that we may authorize to be provided to you related to the series of units being offered, as well as the unit agreements that contain the terms of the units.

**This prospectus may not be used to consummate a sale of any securities unless it is accompanied by a prospectus supplement.**

## RISK FACTORS

Investing in our securities involves a high degree of risk. You should carefully review the risks and uncertainties described under the heading Risk Factors contained in the applicable prospectus supplement and any related free writing prospectus, and under similar headings in the other documents that are incorporated by reference into this prospectus, before deciding to invest in any of the securities offered pursuant to this prospectus. Each of the risk factors could adversely affect our business, operating results and financial condition, as well as adversely affect the value of an investment in our securities, and the occurrence of any of these risks might cause you to lose all or part of your investment. Additional risks not presently known to us or that we currently believe are immaterial may also significantly impair our business operations.

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## SPECIAL NOTE REGARDING 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 contained in the applicable prospectus supplement and any related free writing prospectus, and in our most recent annual report on Form 10-K and in our most recent quarterly report on Form 10-Q, as well as any amendments thereto reflected in subsequent filings with the SEC. Given these risks, uncertainties and other factors, you should not place undue reliance on these forward-looking statements. Also, these forward-looking statements represent our estimates and assumptions only as of the date such forward-looking statements are made. You should read carefully this prospectus, the applicable prospectus supplement and any related free writing 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 duty, obligation or undertaking 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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**RATIO OF EARNINGS TO FIXED CHARGES AND**

**COMBINED FIXED CHARGES AND PREFERRED STOCK DIVIDENDS**

Our earnings were insufficient to cover fixed charges and combined fixed charges and preferred stock dividends in each of the years in the years ended December 31, 2004, 2005, 2006, 2007 and 2008 and in the three months ended March 31, 2009. Accordingly, the following table sets forth the deficiency of earnings to cover fixed charges and the deficiency of earnings to cover combined fixed charges and preferred stock dividends for each of the foregoing periods. Because of the deficiency, ratio information is not applicable. Amounts shown are in thousands.

| | Three Months Ended March 31, | Year Ended December 31, | | | | |
|---|---|---|---|---|---|---|
| | 2009 | 2008 | 2007 | 2006 | 2005 | 2004 |
| Deficiency of earnings available to cover fixed charges | $(38,336) | $ (175,570) | $ (111,022) | $ (123,189) | $ (94,810) | $ (137,245) |
| Deficiency of earnings available to cover combined fixed charges and preferred stock dividends | $(38,366) | $ (175,570) | $ (111,022) | $ (123,189) | $ (94,810) | $ (137,245) |

For purposes of computing the deficiency of earnings to cover fixed charges and combined fixed charges and preferred stock dividends, earnings consist of loss from operations before income taxes and fixed charges. Fixed charges consist of interest expense and the portion of operating lease expense that represents interest.

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## USE OF PROCEEDS

Except as described in any applicable prospectus supplement and in any related free writing prospectus that we may authorize to be delivered to you in connection with a specific offering, we anticipate using the net proceeds to us from the sale of securities offered hereby for research and development and other general corporate purposes. We may also use a portion of the net proceeds to acquire or invest in businesses, products and technologies that we believe are complementary to our own, although we are not currently planning or negotiating any such transactions. Pending these uses, we intend to invest the net proceeds in investment-grade, interest-bearing securities.

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## DESCRIPTION OF CAPITAL STOCK

Our authorized capital stock consists of 200,000,000 shares of common stock, $0.001 par value, and 10,000,000 shares of preferred stock, $0.001 par value. As of March 31, 2009, there were 106,383,931 shares of our common stock outstanding and no shares of our preferred stock outstanding. We may issue shares of our common stock and/or our preferred stock from time to time in one or more offerings. We will set forth in the applicable prospectus supplement and/or in any related free writing prospectus that we may authorize to be delivered to you in connection with a specific offering, a description of the terms of the offering of common stock and/or preferred stock, including the offering price, the net proceeds to us and other material terms relating to such offering.

The following summary description of our capital stock is based on the provisions of our amended and restated certificate of incorporation and amended and restated bylaws, and the applicable provisions of the Delaware General Corporation Law. This information may not be complete in all respects and is qualified entirely by reference to the provisions of our amended and restated certificate of incorporation and amended and restated bylaws, and the Delaware General Corporation Law. For information on how to obtain copies of our amended and restated certificate of incorporation and amended and restated bylaws, which are exhibits to the registration statement of which this prospectus forms a part, see the section entitled Where You Can Find More Information.

### Common Stock

The holders of our common stock are entitled to one vote for each share held of record on all matters submitted to a vote of the stockholders and do not have cumulative voting rights. Accordingly, holders of a majority of the shares of our common stock entitled to vote in any election of directors may elect all of the directors standing for election. Subject to preferences that may be applicable to any shares of our preferred stock that may become outstanding, the holders of outstanding shares of our common stock are entitled to receive ratably such dividends as may be declared by the board of directors out of funds legally available therefor. Upon the liquidation, dissolution or winding up of Exelixis, holders of our common stock are entitled to share ratably in all assets remaining after payment of liabilities and the liquidation preferences of any shares of our preferred stock then outstanding. Holders of our common stock have no preemptive rights and no right to convert their common stock into any other securities. There are no redemption or sinking fund provisions applicable to our common stock. If we issue shares of common stock under this prospectus, the shares will be fully paid and non-assessable.

The rights of the holders of our common stock are subject to, and may be adversely affected by, the rights of holders of shares of any preferred stock that we may designate and issue in the future.

### Preferred Stock

Pursuant to our amended and restated certificate of incorporation, our board of directors has the authority, without further action by the stockholders (unless such stockholder action is required by applicable law or NASDAQ rules), to issue up to 10,000,000 shares of preferred stock, in one or more series. Our board of directors is authorized to fix or alter from time to time the designation, powers, preferences and rights of the shares of each series, including dividend rights, conversion rights, voting rights, terms of redemption, liquidation preferences and sinking fund terms, as well as the qualifications, limitations or restrictions of any unissued series of preferred stock. Our board of directors may also establish from time to time the number of shares constituting any series of preferred stock, and to increase or decrease the number of shares of any series subsequent to the issuance of shares of that series, but not below the number of shares of any series then outstanding.

We will fix the rights, preferences, privileges and restrictions of the preferred stock of each series in the certificate of designation relating to that series. We will incorporate by reference as an exhibit to the registration

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statement that includes this prospectus or as an exhibit to a current report on Form 8-K, the form of any certificate of designation that describes the terms of the series of preferred stock we are offering before the issuance of the related series of preferred stock. This description will include:

- the title and stated value;
- the number of shares we are offering;
- the liquidation preference per share;
- the purchase price;
- the dividend rate, period and payment date and method of calculation for dividends;
- whether dividends will be cumulative or non-cumulative and, if cumulative, the date from which dividends will accumulate;
- the procedures for any auction and remarketing, if any;
- the provisions for a sinking fund, if any;
- the provisions for redemption or repurchase, if applicable, and any restrictions on our ability to exercise those redemption and repurchase rights;
- any listing of the preferred stock on any securities exchange or market;
- whether the preferred stock will be convertible into our common stock, and, if applicable, the conversion price, or how it will be calculated, and the conversion period;
- whether the preferred stock will be exchangeable into debt securities, and, if applicable, the exchange price, or how it will be calculated, and the exchange period;
- voting rights, if any, of the preferred stock;
- preemption rights, if any;
- restrictions on transfer, sale or other assignment, if any;