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Subject to Completion. Dated August 6, 2012.

Prospectus Supplement to Prospectus dated June 8, 2012.

20,000,000 Shares



Common Stock

Exelixis, Inc. is offering 20,000,000 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 August 3, 2012, was \$5.58 per share.

Concurrently with this offering of common stock, we are offering \$225.0 million aggregate principal amount of convertible senior subordinated notes due 2019 (the "notes") (or a total of \$258.8 million aggregate principal amount if the underwriters for the concurrent notes offering exercise in full their option to purchase additional notes) pursuant to a separate prospectus supplement.

See "[Risk Factors](#)" beginning on page S-10 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 20,000,000 shares of common stock, the underwriters have the option to purchase up to an additional 3,000,000 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 August , 2012.

Joint Book-Running Managers

Goldman, Sachs & Co.

Cowen and Company

Co-Managers

Piper Jaffray

Stifel Nicolaus Weisel

William Blair

Prospectus Supplement dated August , 2012.

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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 June 8, 2012, 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 term “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.

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 proprietary resources and development efforts exclusively on cabozantinib, formerly known as XL184, our most advanced 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, many of which are being advanced by partners as part of collaborations.

Cabozantinib

Cabozantinib inhibits MET, VEGFR2 and RET, proteins that are key drivers of tumor growth, vascularization, and/or metastasis. Cabozantinib has shown novel and differentiated activity in multiple cancer indications. The current clinical program for cabozantinib is focused on the treatment of metastatic castration-resistant prostate cancer, or CRPC, and medullary thyroid cancer but also includes the evaluation of other tumor types.

Exelixis has implemented a strategy to investigate cabozantinib in a comprehensive development program for CRPC to potentially generate a product that could effectively compete in the CRPC marketplace. Two phase 3 pivotal trials, COMET-1 (Cabozantinib MET Inhibition CRPC Efficacy Trial-1, formerly known as XL184-307) and COMET-2 (Cabozantinib MET Inhibition CRPC Efficacy Trial-2, formerly known as XL184-306), were designed to provide an opportunity to commercially differentiate cabozantinib as an oncology agent with a potentially beneficial impact on overall survival, pain palliation and narcotic usage. We initiated the COMET-2 trial with a pain palliation endpoint in December 2011 and the COMET-1 trial with an overall survival endpoint in May 2012.

In May 2012, we completed the submission of our rolling new drug application, or NDA, with the United States Food and Drug Administration, or FDA, for cabozantinib as a treatment for medullary thyroid cancer. On July 30, 2012, we announced that the FDA has accepted our NDA for filing and granted a Priority Review designation with a stated action date of November 29, 2012. The NDA submission was based on the data from our phase 3 clinical trial of cabozantinib as a potential treatment for medullary thyroid cancer, known as the EXAM trial (Efficacy of XL184 (Cabozantinib) in Advanced Medullary Thyroid Cancer), with progression-free survival, or PFS, as the trial's primary endpoint. The EXAM trial has been conducted under a special protocol assessment, or SPA, with the FDA, which allows for full approval on the basis of PFS if the data are supportive. We announced in October 2011 that the primary endpoint of the EXAM trial had been met. Data from the EXAM trial was

reported at the American Society of Clinical Oncology Annual Meeting, or ASCO, in June 2012. Assuming approval of our NDA by the FDA, we currently anticipate a potential commercial launch of cabozantinib for the treatment of medullary thyroid cancer in late 2012 or early 2013.

We expect to expand the cabozantinib development program to other solid tumor indications, based on encouraging interim data that have emerged from the randomized discontinuation trial, or RDT, investigating cabozantinib in 9 distinct tumor types, as well as other clinical trials. Objective tumor responses have been observed in patients treated with cabozantinib in 12 of 13 individual tumor types investigated to date, reflecting the broad potential clinical activity and commercial opportunity of this new product candidate. Interim data suggest that cabozantinib has shown novel activity against bone and soft tissue lesions in patients with CRPC. We have also observed resolution of metastatic bone lesions on bone scan in patients with metastatic breast cancer, renal cell carcinoma, thyroid cancer, and melanoma.

Interim data from the CRPC cohort of the RDT reported at ASCO in June 2011 demonstrated that in addition to improvement of bone lesions on bone scan observed in the majority (75%) of patients, 67% of patients with bone metastases and bone pain at baseline also experienced alleviation of pain. This observation has been corroborated in a non-randomized expansion cohort, or NRE, of CRPC patients in the RDT, which collected prospectively defined patient reported outcomes on pain and narcotic use. Interim data reported at ASCO in June 2012 demonstrated that 64% of CRPC patients with moderate to severe pain in the NRE experienced durable pain reduction greater than or equal to 30%. The median best pain reduction was 46%. In addition, these interim data indicated that 56% of CRPC patients in the NRE with moderate to severe bone pain and on narcotics at baseline were able to reduce or discontinue narcotic medication. These interim data also indicated that 92% of evaluable CRPC patients in the NRE experienced a reduction greater than or equal to 30% in their circulating tumor cell, or CTC, count.

Lower starting doses of cabozantinib are being evaluated through a dose-ranging study in CRPC patients conducted through an investigator-sponsored trial, or IST. Interim data from this dose-ranging IST reported at ASCO in June 2012 demonstrated that a daily dose of 40 mg resulted in a rate of bone scan responses similar to that of a 100 mg daily dose used in the RDT, and was associated with improved tolerability compared with the higher dose. The interim data from the IST reported at ASCO in June 2012 also indicated that 92% of evaluable CRPC patients in the 40 mg dose cohort of the IST experienced a reduction greater than or equal to 30% in their CTC count. Interim data from a cohort of CRPC patients in the NRE treated at a daily dose of 40 mg has demonstrated pain palliation responses consistent with observations at the 100 mg daily dose.

We believe that cabozantinib's clinical profile is compelling and will allow commercial differentiation, assuming regulatory approval. Accordingly, it is a priority for us to generate additional data from the RDT as well as other ongoing exploratory clinical trials for cabozantinib in a broad range of tumor types, including ovarian cancer, melanoma, breast cancer, non-small cell lung cancer, hepatocellular cancer, renal cell carcinoma, and differentiated thyroid cancer, to support further prioritization of our clinical and commercial options. We have launched two initiatives to expand the cabozantinib development program beyond our internal development efforts: our IST program and our Cooperative Research and Development Agreement, or CRADA, with the National Cancer Institute's Cancer Therapy Evaluation Program, or NCI-CTEP.

We launched the IST program in 2011, and it has already provided important interim data through the dose-ranging study in CRPC patients described above. These data were important for dose selection in the COMET pivotal trial program, and we believe they will guide dose selection for a

potential future trial to evaluate the ability of cabozantinib to prevent bone metastases in men with prostate cancer. Other recently initiated ISTs include:

- Phase 2 clinical trial of cabozantinib in women with hormone receptor-positive metastatic breast cancer and bone metastases.
- Phase 1b clinical trial evaluating cabozantinib in combination with abiraterone in CRPC patients.
- Phase 2 clinical trial of cabozantinib in chemotherapy naïve CRPC patients with bone metastases.
- Phase 1b clinical trial evaluating cabozantinib in combination with androgen ablation in patients with androgen-dependent metastatic prostate cancer.
- Phase 2 clinical trial using magnetic resonance imaging to measure the effect of cabozantinib on bone metastases in patients with CRPC.
- Phase 1 clinical trial of cabozantinib in patients with relapsed or refractory multiple myeloma with bone disease.
- Phase 2 clinical trial evaluating cabozantinib in patients with advanced pancreatic neuroendocrine and carcinoid tumors.
- Phase 2 clinical trial of cabozantinib in patients with KIF5B/RET-positive advanced non-small cell lung cancer.
- Phase 2 clinical trial evaluating cabozantinib in patients with advanced solid malignancies and bone metastases.

We plan to further expand the IST program with new trials this year.

We entered into our CRADA with NCI-CTEP in November 2011, under which thirteen proposed clinical trials have been approved to date, as follows:

- Phase 2 clinical trials in disease settings where there is substantial unmet medical need and in which cabozantinib has previously demonstrated clinical activity, consisting of randomized phase 2 clinical trials in first line renal cell carcinoma, second line hepatocellular carcinoma, platinum-resistant or refractory ovarian cancer, ocular melanoma, second line non-small cell lung cancer, and second line/third line non-small cell lung cancer. We believe that data from these phase 2 clinical trials will help prioritize future phase 3 pivotal trials of cabozantinib.
- Additional phase 2 clinical trials to explore cabozantinib's potential utility in other tumor types, consisting of trials in endometrial cancer, bladder cancer, sarcoma and second line differentiated thyroid cancer. Positive results in these indications could lead to further study in randomized phase 2 or phase 3 clinical trials.
- Additional phase 1 clinical trials, consisting of a trial evaluating cabozantinib in combination with docetaxel in CRPC patients, a trial exploring the utility of combining cabozantinib with vemurafenib, a BRAF inhibitor, in patients with BRAF-mutated melanoma, and a trial to evaluate the safety and pharmacokinetics of cabozantinib in pediatric malignancies.

Commencement of each of the proposed trials approved under the CRADA is subject to protocol development and satisfaction of certain other conditions. The proposed trials approved under the CRADA will be conducted under an investigational new drug application held by NCI-CTEP. We believe our CRADA reflects a major commitment by NCI-CTEP to support the broad exploration of

cabozantinib's potential in a wide variety of cancers that have substantial unmet medical needs. Since NCI-CTEP provides funding for as many as 20 active clinical trials each year for a five year period, we believe the agreement will enable us to broadly expand the cabozantinib development program in a cost-efficient manner.

Collaborations

We have established collaborations with leading pharmaceutical and biotechnology companies, including Bristol-Myers Squibb Company, or Bristol-Myers Squibb, Sanofi, Genentech, Inc. (a wholly- owned member of the Roche Group), GlaxoSmithKline, Merck (known as MSD outside of the United States and Canada) and Daiichi Sankyo Company Limited, or Daiichi Sankyo, for various 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. Several of the out-licensed compounds are in multiple phase 2 studies and could potentially be of significant value to us if their development progresses successfully. With respect to our partnered compounds, we are eligible to receive potential milestone payments under our collaborations totaling approximately \$3.1 billion in the aggregate on a non-risk adjusted basis, of which 10% are related to clinical development milestones, 44% are related to regulatory milestones and 46% are related to commercial milestones.

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 210 East Grand Ave., South San Francisco, California 94080. 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.

The Offering

Common stock offered by Exelixis 20,000,000 shares
Underwriters' option to purchase additional shares

3,000,000 shares

Common stock to be outstanding after the offering

168,794,245 shares

Use of proceeds

We currently expect to use the net proceeds from this offering and the offering of our convertible senior subordinated notes (referenced below) for general corporate purposes, including for clinical trials, research and development, capital expenditures and working capital. In addition, we have agreed to place approximately \$ million (or approximately \$ million if the underwriters exercise their option to purchase additional notes in full) of the proceeds of the concurrent notes offering in an escrow account with the trustee under the indenture pursuant to which the notes are issued. See "Use of Proceeds" in this prospectus supplement.

Concurrent notes offering

Concurrently with this offering of common stock, we are offering \$225.0 million aggregate principal amount of notes (or a total of \$258.8 million aggregate principal amount if the underwriters for the concurrent notes offering exercise in full their option to purchase additional notes) pursuant to a separate prospectus supplement. See "Concurrent Convertible Notes Offering" in this prospectus supplement. We expect to raise approximately \$217.9 million in net proceeds from the concurrent notes offering (approximately \$250.6 million if the underwriters for the concurrent notes offering exercise in full their option to purchase additional notes), after deducting the estimated underwriting discounts and estimated offering expenses payable by us. See "Use of Proceeds" in this prospectus supplement.

This prospectus supplement shall not be deemed an offer to sell or a solicitation of an offer to buy any of the notes offered in the concurrent notes offering. The common stock offering is not contingent upon the concurrent notes offering, and the concurrent notes offering is not contingent upon this common stock offering. We cannot assure you that either or both of the offerings will be completed.

Unless we specifically state otherwise, the information in this prospectus supplement assumes the completion of the concurrent notes offering, and that the underwriters for the concurrent notes offering do not exercise their option to purchase additional notes in that offering.

Risk factors

See "Risk Factors" beginning on page S-10 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 June 30, 2012. As of that date, we had 148,794,245 shares of common stock outstanding, excluding:

- 16,345,993 shares of common stock underlying options outstanding as of June 30, 2012, at a weighted average exercise price of \$7.06 per share;
- 1,441,215 shares of common stock underlying warrants outstanding as of June 30, 2012, at a weighted average exercise price of \$6.99 per share;
- 907,697 shares reserved for future issuance pursuant to unvested restricted stock units as of June 30, 2012;
- 10,508,305 shares available for future grant under our 2011 Equity Incentive Plan, 2,481,973 shares available for future grant under our 2000 Employee Stock Purchase Plan, 987,656 shares available for future grant under our 2000 Non-Employee Directors' Stock Option Plan, and 568,062 shares available for future grant under our 401(k) Retirement Plan, all as of June 30, 2012; and
- shares of common stock reserved for issuance upon conversion of the convertible notes being offered by us in connection with our concurrent notes offering.

Unless we specifically state otherwise, the information in this prospectus supplement assumes that the underwriters in this offering and in the concurrent notes offering do not exercise their option to purchase up to 3,000,000 additional shares of our common stock in this offering or \$33.8 million aggregate principal amount of the notes in the concurrent notes offering, respectively, within 30 days after the date of this prospectus supplement.

Summary Consolidated Financial Data

We derived the information presented below as of December 31, 2011, and for each of the three years ended December 31, 2009, 2010 and 2011, from our audited consolidated financial statements. We derived the information presented below as of June 30, 2012, and for each of the six months ended June 30, 2011 and 2012, from our unaudited condensed consolidated financial statements. In the opinion of management, all adjustments, consisting of only normal recurring adjustments, necessary for a fair presentation of the unaudited financial data as of June 30, 2012, and for each of the six months ended June 30, 2011 and 2012, have been reflected therein. Operating results for the six months ended June 30, 2012, are not necessarily indicative of the results that may be expected for the full year. 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 from our Annual Report on Form 10-K for the fiscal year ended December 31, 2011, and our Quarterly Report on Form 10-Q for the fiscal quarter ended June 30, 2012.

The as adjusted balance sheet data as of June 30, 2012, reflects receipt of the estimated net proceeds of \$105.6 million from the sale of the common stock in this offering (assuming no exercise of the underwriters' option to purchase additional shares) at an assumed public offering price of \$5.58 per share, the closing price of our common stock on August 3, 2012, and the estimated net proceeds of \$217.9 million from the issuance of \$225.0 million principal amount of the notes (assuming no exercise of the underwriters' option to purchase additional notes) in our concurrent notes offering, in each case, after deducting the estimated underwriting discounts and estimated offering expenses payable by us as described under "Use of Proceeds."

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."

	Year Ended December 31,			Six Months Ended June 30,	
	2009	2010	2011	2011	2012
	(unaudited)				
	(in thousands, except per share data)				
Consolidated Statement of Operations Data					
Total revenues	\$ 151,759	\$ 185,045	\$ 289,636	\$ 68,056	\$ 26,323
Total operating expenses	\$ 273,666	\$ 276,442	\$ 200,101	\$ 109,794	\$ 81,342
Consolidated net (loss) income	\$(139,557)	\$(92,330)	\$ 75,697	\$(48,464)	\$(62,638)
Loss attributed to noncontrolling interest	\$ 4,337	\$ —	\$ —	\$ —	\$ —
Net (loss) income attributable to Exelixis, Inc.	\$(135,220)	\$(92,330)	\$ 75,697	\$(48,464)	\$(62,638)
Net (loss) income per share, basic attributable to Exelixis, Inc.	\$ (1.26)	\$ (0.85)	\$ 0.60	\$ (0.40)	\$ (0.43)
Net (loss) income per share, diluted attributable to Exelixis, Inc.	\$ (1.26)	\$ (0.85)	\$ 0.58	\$ (0.40)	\$ (0.43)
Shares used in computing basic net (loss) income per share	107,073	108,522	126,018	120,768	145,297
Shares used in computing diluted net (loss) income per share	107,073	108,522	130,479	120,768	145,297
	As of June 30, 2012				
	Actual		As Adjusted(2)		
	(unaudited)				
	(in thousands)				
Consolidated Balance Sheet Data					
Cash and cash equivalents, marketable securities, restricted cash and investments and long-term investments(1)(3)			\$ 294,786	\$	616,756
Working capital(1)(3)			\$ 123,676	\$	
Total assets(1)(3)			\$ 374,488	\$	705,108
% Convertible senior subordinated notes due 2019(2)			\$ —	\$	
Debt obligations under the loan and security agreement with SVB			\$ 86,836	\$	86,836
Debt obligations under the Deerfield Notes			\$ 95,862	\$	95,862
Additional paid-in-capital(2)			\$ 1,267,890	\$	
Total stockholders' equity(2)			\$ 99,049	\$	

- (1) Each \$1.00 increase or decrease in the assumed offering price per share would increase or decrease the as adjusted amount shown above for each of "cash and cash equivalents, marketable securities, restricted cash and investments and long-term investments," "working capital" and "total assets" by approximately \$19.0 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 discounts 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 amount above for each of "cash and cash equivalents, marketable securities, restricted cash and investments and long-term investments," "working capital" and "total assets" by approximately \$2.7 million, after deducting the estimated underwriting discounts and estimated offering expenses payable by us. The as adjusted amounts shown above do not reflect the placement of amounts in the interest escrow, as described under "Use of Proceeds." Such amounts will be classified as restricted cash.
- (2) Amounts shown reflect the application of Financial Accounting Standards Board Staff Position No. APB 14-1, as codified by Accounting Standards Codification 470-20, or ASC 470-20, which requires issuers to separately account for the liability and equity components of convertible debt instruments that may be settled entirely or partially in cash. The determination of the fair values of the debt and equity components has been estimated but is subject to change based upon the completion of our analysis of non-convertible debt interest rates. In accordance with ASC 470-20, we estimate that approximately \$ million of the aggregate principal amount of the notes offered in our concurrent notes offering will be recognized as the equity component. The determination of the fair values of the debt and equity components has been estimated but is subject to change based upon the completion of our analysis of non-convertible debt interest rates.
- (3) The as adjusted amounts reflect the cash payment of a \$1.5 million consent fee to entities affiliated with Deerfield Management Company L.P., or Deerfield.

Our Fiscal Year

We have adopted a 52- or 53-week fiscal year that ends on the Friday closest to December 31st. Fiscal year 2009, a 52-week year, ended on January 1, 2010, fiscal year 2010, a 52-week year, ended on December 31, 2010, fiscal year 2011, a 52-week year, ended on December 30, 2011, and fiscal year 2012, a 52-week year, will end on December 28, 2012. For convenience, references in this prospectus supplement as of and for the fiscal years ended January 1, 2010, December 31, 2010, and December 30, 2011, and as of and for the fiscal quarters ended July 1, 2011, and June 29, 2012, are indicated on a calendar year basis as ended December 31, 2009, 2010 and 2011, and June 30, 2011 and 2012, respectively.

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 June 30, 2012, we had \$294.8 million in cash and cash equivalents, marketable securities and long-term investments, which included restricted cash and investments of \$4.1 million and approximately \$83.7 million of cash and cash equivalents and marketable securities that we are required to maintain on deposit with Silicon Valley Bank, or SVB, or one of its affiliates pursuant to covenants in our loan and security agreement with SVB. 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 and our concurrent notes offering, will enable us to maintain our operations for a period of at least 12 months following the end of the second quarter of 2012. However, our future capital requirements will be substantial, and we will need to raise additional capital in the future. Our capital requirements will depend on many factors, and we may need to use available capital resources and raise additional capital significantly earlier than we currently anticipate. These factors include:

- the progress and scope of the cabozantinib development program: We are focusing our proprietary resources and development efforts on cabozantinib, our most advanced product candidate, which is being studied in a variety of tumor types, with the goal of rapidly commercializing the compound. Cabozantinib is being evaluated in a broad development program encompassing multiple cancer indications. The current clinical program for cabozantinib is focused on the treatment of CRPC and medullary thyroid cancer and will be expanded to other solid tumor indications, based on encouraging interim data that have emerged from the RDT investigating cabozantinib in nine distinct tumor types and other clinical trials. In October 2011, we announced that our EXAM phase 3 clinical trial of cabozantinib in medullary thyroid cancer met its primary endpoint and on July 30, 2012, we announced that the FDA has accepted our NDA, based on data from our EXAM trial, for filing and granted a Priority Review designation with a stated action date of November 29, 2012. Assuming approval of our NDA by the FDA, we currently anticipate a potential commercial launch of cabozantinib for the treatment of medullary thyroid cancer in late 2012 or early 2013. As part of our comprehensive development plan for cabozantinib in CRPC, in December 2011, we initiated our first phase 3 pivotal trial of cabozantinib in patients with CRPC using an endpoint of pain reduction (COMET-2) and in May 2012 we initiated a second phase 3 pivotal trial in patients with CRPC with

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an overall survival endpoint (COMET-1). We are also planning other potential pivotal trials in prostate cancer. Our development and commercialization plans for cabozantinib are 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 the trials that are currently planned or in process, to fund other clinical trials that we may desire to initiate in the future or to fund commercialization efforts. If adequate funds are not available, we may be required to delay, discontinue or elect not to pursue one or more trials or commercialization efforts for cabozantinib;

- repayment of our secured convertible notes we previously issued to Deerfield, which we refer to as the Deerfield Notes: On June 2, 2010, we entered into a note purchase agreement with Deerfield, pursuant to which, on July 1, 2010, we sold to Deerfield an aggregate of \$124.0 million initial principal amount of the Deerfield Notes, due June 2015, for an aggregate purchase price of \$80.0 million, less closing fees and expenses. The outstanding principal amount of the Deerfield 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 Deerfield Notes on an annual basis in 2013, 2014 and 2015 equal to 15% of specified payments from 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 Deerfield 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 Deerfield 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. Contingent upon the closing of the concurrent note offering, we have agreed with Deerfield to amend the terms of the senior secured convertible notes we previously issued to Deerfield to permit us to issue the notes in exchange for the payment of a consent fee of \$1.5 million and revised terms for voluntary prepayments of the Deerfield Notes prior to July 2, 2013. In lieu of making any optional or mandatory prepayment in cash, subject to specified limitations, we have the right to convert all or a portion of the principal amount of the Deerfield 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 Deerfield Notes in cash, subject to specified limitations, we may elect to satisfy any such payment with shares of our common stock. The number of shares of our 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 or we do not have a sufficient number of authorized but unissued shares, 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 Deerfield 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 Deerfield 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 Deerfield Notes into or satisfy our payment obligations with shares of our common stock;
- repayment of our loan from SVB: On May 22, 2002, we entered into a loan and security agreement with SVB for an equipment line of credit, on December 21, 2004, December 21, 2006

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and December 21, 2007, we amended the loan and security agreement to provide for additional equipment lines of credit and on June 2, 2010, we amended our loan and security agreement with SVB 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 are required to repay any advances under an equipment line of credit in 48 equal monthly payments of principal and interest. 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. We have the option to prepay without penalty any advance under an equipment line of credit other than advances under a single equipment line of credit, which has a 1.0% prepayment penalty, provided that we pay all unpaid accrued interest thereon that is due through the date of such prepayment. In accordance with the terms of the loan and security agreement, we are also required to maintain an amount equal to at least 100%, but not to exceed 107%, of the outstanding principal balance of the term loan and all equipment lines of credit under the loan and security agreement at all times in one or more accounts with SVB and certain other designated financial institutions as support for our obligations under the loan and security agreement. As a result, the proceeds of the term loan cannot be used to satisfy our other obligations without causing a default under our loan and security agreement with SVB;

- 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 or programs;
- 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;
- 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.

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, collaborative arrangements or other strategic transactions. It is unclear whether any such partnership, arrangement or transaction will occur, on satisfactory terms or at all, or what the timing and nature of such a partnership, arrangement or transaction may be. 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 Deerfield and SVB contain covenants or events of default requiring us to maintain specified cash balances. 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 through 2010. While we were in a net income position of \$75.7 million for the year ended December 31, 2011, primarily as a result of the acceleration of revenue recognized under our 2008 collaboration agreement with Bristol-Myers Squibb that terminated in October 2011 and under our 2009 discovery collaboration agreement with Sanofi that terminated in December 2011, we anticipate net losses and negative operating cash flow for the foreseeable future. For the six months ended June 30, 2012, we had a net loss of \$62.6 million; as of June 30, 2012, we had an accumulated deficit of \$1.2 billion. 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 we are unable to successfully achieve milestones, our collaborators fail to develop successful products or research funding we receive from collaborators decreases, 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 through 2010 and for the six months ended June 30, 2012, 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 future 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.

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, during 2010, we implemented two restructurings that resulted in an overall reduction in our workforce by 386 employees. As a consequence of our decision to focus our proprietary resources and development efforts on the late-stage development and commercialization of cabozantinib, we implemented additional restructurings in both March 2011 and May 2012, that resulted in further reductions to our workforce. The aggregate reduction in headcount from the 2010, 2011 and 2012 restructurings, or the Restructurings, is 422 employees. We have recorded aggregate restructuring

charges of \$43.9 million in connection with the Restructurings and anticipate that we will incur additional restructuring charges related to the exit of all or portions of three of our South San Francisco buildings. These charges will be recorded through the end of the building lease terms, the last of which ends in 2017.

As part of the Restructurings, in 2011 we entered into two sublease agreements for portions of one of our buildings in South San Francisco, California. We are still assessing our ability to sublease portions of our facilities in light of the workforce reductions 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 portions 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 financial position and results of operations.

Global credit and financial market conditions could negatively impact the value of our current portfolio of cash equivalents, short-term investments or long-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 June 30, 2012, 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 or commercialize 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. For example, as discussed in “—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,” we were not able to reach a timely agreement with the FDA under a Special Protocol Assessment, or SPA, on the proposed design and analyses of the COMET-2 trial.

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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;
- 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 under our collaboration agreements may experience similar risks with respect to the compounds we have out-licensed 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

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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.

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, Genentech, Inc. (a wholly-owned member of the Roche Group), GlaxoSmithKline, Merck (known as MSD outside of the United States and Canada) and Daiichi Sankyo Company Limited, or Daiichi Sankyo, 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;

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- 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;
- 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 and XL281, which were previously subject to our 2008 collaboration agreement with Bristol-Myers Squibb, and with respect to our 2009 discovery collaboration with Sanofi, which was terminated in December 2011) or allowed to expire, which would delay, and may increase the cost of development of, 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 and XL281, which were previously subject to our 2008 collaboration agreement with Bristol-Myers Squibb, and with respect to our 2009 discovery collaboration with Sanofi, which was terminated in December 2011), 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 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 require substantial expenditures.

Our EXAM phase 3 trial of cabozantinib as a potential treatment for medullary thyroid cancer has been conducted under a SPA with the FDA. A SPA is designed to facilitate the FDA's review and provide feedback on the proposed design and size of clinical trials that are intended to form the primary basis for determining a product candidate's efficacy. If agreement is reached with the FDA, a SPA agreement documents the terms and conditions under which the design of the subject trial will be adequate for submission of the efficacy and human safety portion of an NDA. However, there are circumstances under which we may not receive the benefits of a SPA, notably if the FDA subsequently identifies a substantial scientific issue essential to determining the product candidate's safety or efficacy, and we may be required to conduct significant additional development in order to obtain regulatory approval notwithstanding the SPA. We completed the submission of our rolling NDA based on the data from our EXAM trial with the FDA in May 2012. On July 30, 2012, we announced that the FDA has accepted our NDA for filing and granted a Priority Review designation with a stated action date of November 29, 2012. However, our NDA may be subject to delay or lack of approval, including delay or lack of approval based on potential feedback from an FDA Advisory Committee.

In December 2011, we initiated COMET-2, our first phase 3 pivotal trial of cabozantinib in patients with metastatic castration-resistant prostate cancer, with pain response as the primary efficacy endpoint for the trial. We were not able to reach a timely agreement with the FDA for a SPA on the proposed design and analysis of the COMET-2 trial. We originally submitted the proposed protocol for this trial using primary endpoints of pain reduction and bone scan response to the FDA in June 2011 with a request for a SPA. The FDA's final response prior to our discontinuation of the SPA process, which we received in October 2011, raised the following concerns regarding the COMET-2 trial design in the context of its consideration of a SPA for the trial, among other comments:

• A concern about the ability to maintain blinding of the trial due to differences in toxicity profiles between cabozantinib and mitoxantrone.

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- A view that the assumed magnitude of pain improvement is modest and could represent a placebo effect or be attained with less toxicity by opioid therapy.
- A view that symptomatic improvement should be supported by evidence of anti-tumor activity, an acceptable safety profile and lack of survival decrement. The FDA also expressed the view that if the effect that we believe cabozantinib will have on pain is mediated by anti-tumor activity, that anti-tumor activity should translate into an improvement in overall survival.
- A recommendation that if we use pain response as a primary efficacy endpoint, that we conduct two adequate and well-controlled trials to demonstrate effectiveness as, according to the FDA, a conclusion based on two persuasive studies will always be more secure. The FDA advised that for a single randomized trial to support a new drug application, the trial must be well designed, well conducted, internally consistent and provide statistically persuasive efficacy findings so that a second trial would be ethically or practically impossible to perform.

In the context of its consideration of a SPA for the COMET-2 trial, the FDA also recommended that overall survival be the primary efficacy endpoint. The final FDA response prior to our discontinuation of the SPA process stated that we could choose to conduct the trial in the absence of a SPA agreement. We elected to proceed with initiation of the COMET-2 trial and the COMET-1 trial, and to discontinue further attempts to secure a SPA agreement with respect to the COMET-2 trial. We initiated the COMET-2 trial with a pain palliation endpoint in December 2011 and the COMET-1 trial with an overall survival endpoint in May 2012.

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 (regardless of prior receipt of a SPA) 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, and the medical community.*

Our ability to commercialize cabozantinib, if it is approved for commercial sale, 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; and the medical community.

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If cabozantinib does not achieve an adequate level of acceptance, we may not generate adequate product revenues, if at all, and we may not become profitable. The degree of market acceptance of 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 those of any competing products;
- potential advantages or disadvantages in relation to alternative treatments;
- the timing of market entry relative to competitive treatments;
- 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 and distribution of pharmaceutical products and do not have a sales organization. Developing a sales force could be expensive and time-consuming, could delay any product launch, including our potential launch of cabozantinib for the treatment of medullary thyroid cancer, 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 may 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. 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. The United States Supreme Court heard a constitutional challenge to the PPACA and in June 2012 held that the PPACA is constitutional. However, states are allowed to opt out of the expansion of eligibility criteria for Medicaid under the PPACA. 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. Insurers 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.

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 use tiered reimbursement and may adversely affect demand for our products by placing them in an expensive tier. 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. Some of our competitors are further along in the development of their products than we are. In addition, 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 than we do. 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 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 RET, VEGFR and EGFR inhibitor, vandetanib, Algeta's development-stage alpha-pharmaceutical Alparadin (Radium-223), other VEGF pathway inhibitors, including Genentech's bevacizumab, and other MET inhibitors, including Pfizer's crizotinib, ArQule's tivantinib (ARQ197), GlaxoSmithKline's foretinib (XL880), and Genentech's onartuzumab.

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

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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.

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 Restructurings 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 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.

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 progress and scope of our research and development activities;
- recognition of up-front licensing or other fees or revenues;
- payments of non-refundable up-front 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 out-licensed 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 of 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 our restructurings; 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 we fail to achieve anticipated levels of revenues, whether due to the

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expiration or termination of existing contracts, our failure to obtain new contracts, our inability to meet milestones or for other reasons, we may not be able to correspondingly reduce our operating expenses, which could 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 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 out-licensed 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, economic and political conditions and other factors, including factors unrelated to our operating performance or the operating performance of our competitors.

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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 and our issuance of convertible notes, which may result in future issuances of our common stock, or the perception that such sales may occur, 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, upon vesting of restricted stock units, under our employee stock purchase plan or upon conversion of the notes or the Deerfield Notes) in the public market, or if we issue additional shares of common stock, or securities convertible into or exchangeable or exercisable for common stock, 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.

Concurrently with this common stock offering, pursuant to a separate prospectus supplement, we are offering \$225.0 million aggregate principal amount of the notes (or a total of \$258.8 million aggregate principal amount if the underwriters in that offering exercise their option to purchase additional notes in full). A substantial number of shares of common stock is reserved for issuance upon conversion of the notes and the Deerfield Notes, upon the exercise of stock options, upon the vesting of restricted stock unit awards and upon the purchase of shares of common stock under our employee stock purchase program. The issuance and sale of substantial amounts of common stock, convertible notes, which may result in future issuances of our common stock, or the perception that such issuances and sales may occur, could adversely affect the market price of our common stock and impair our ability to raise capital through the sale of additional equity securities. Any market that develops for our notes is likely to influence the market for our common stock. For example, the price of our common stock could be affected by possible sales of common stock by investors who view the notes as a more attractive means of equity participation in our company and by hedging or arbitrage trading activity that we expect to occur involving our common stock.

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, which could cause the market price of our common stock to decline.

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;

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- 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. If you purchase shares of our common stock in this offering at the assumed public offering price of \$5.58 per share, you will experience immediate dilution of \$4.74 per share, representing the difference between the assumed public offering price and our as adjusted net tangible book value per share as of June 30, 2012, after giving effect to this offering. 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, may 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 the concurrent notes offering and may not use them effectively.

We will have broad discretion in the application of the net proceeds from this offering and the concurrent notes 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 and the concurrent notes offering, our actual uses of the proceeds of this offering and the concurrent notes 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.

Conversion of the notes offered and sold pursuant to the concurrent notes offering will dilute the ownership interests of existing stockholders.

If and to the extent that we deliver shares of our common stock in settlement of our conversion obligation with respect to any of the notes sold in the concurrent notes offering, the ownership interests of our existing stockholders will be diluted. Any sales in the public market of our common stock

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issuable upon such conversion could adversely affect prevailing market prices of our common stock. In addition, the existence of the notes may encourage short-selling by holders of the notes engaged in hedging or arbitrage, and by other market participants.

Our significant level of indebtedness, which will increase as a result of the concurrent notes offering, could limit cash flow available for our operations, expose us to risks that could adversely affect our business, financial condition and results of operations and impair our ability to satisfy our obligations under the notes.

Following the consummation of the concurrent notes offering, we will have a significant amount of indebtedness and substantial debt service requirements. As of June 30, 2012, after giving effect to the issuance of the notes (assuming no exercise of the underwriters' option to purchase additional notes) and the use of net proceeds therefrom, our total consolidated indebtedness would have been \$407.7 million (excluding trade payables). We may also incur additional indebtedness to meet future financing needs. Our indebtedness could have significant negative consequences for our business, results of operations and financial condition, including:

- making it more difficult for us to meet our payment and other obligations under the notes and our other indebtedness;
- resulting in an event of default if we fail to comply with the financial and other restrictive covenants contained in our debt agreements, which event of default could result in all of our debt becoming immediately due and payable;
- increasing our vulnerability to adverse economic and industry conditions;
- subjecting us to the risk of increased sensitivity to interest rate increases on our indebtedness with variable interest rates, including borrowings under our credit facility;
- limiting our ability to obtain additional financing;
- requiring the dedication of a substantial portion of our cash flow from operations to service our indebtedness, thereby reducing the amount of our cash flow available for other purposes, including working capital, capital expenditures, acquisitions and other general corporate purposes;
- limiting our flexibility in planning for, or reacting to, changes in our business;
- preventing us from raising funds necessary to purchase the notes following a fundamental change or settle conversions of the notes in cash;
- dilution experienced by our existing stockholders as a result of the conversion of the notes into shares of common stock; and
- placing us at a possible competitive disadvantage with less leveraged competitors and competitors that may have better access to capital resources.

As of June 30, 2012, our annual debt service obligation on our outstanding indebtedness was approximately \$9.2 million. If we complete the concurrent notes offering, our annual debt service obligation will increase substantially. If we are unable to generate sufficient cash flow or otherwise obtain funds necessary to make required payments, or if we fail to comply with the various requirements of the Deerfield Notes and our loan and security agreement with SVB, the notes to be offered and sold in the concurrent notes offering, or any indebtedness which we have incurred or may incur in the future, we would be in default, which would permit the holders of the affected notes or other indebtedness to accelerate the maturity of such notes or other indebtedness and could cause defaults under the Deerfield Notes, our loan and security agreement with SVB or our other indebtedness. Any default under the notes, the Deerfield Notes, our loan and security agreement with SVB, or any indebtedness that we have incurred or may incur in the future could have a material adverse effect on our business, results of operations and financial condition.

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 include statements related to the continued development and clinical, therapeutic and commercial potential of, and opportunities for, cabozantinib, the expected timing of various trials, regulatory review and approval events and the timing thereof and the potential of other of our compounds. 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," "objective," "will," "may," "should," "would," "could," "estimate," "predict," "potential," "continue," "encouraging," or the negative of such terms or other similar expressions, identify 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-10 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.

USE OF PROCEEDS

Based upon an assumed public offering price of \$5.58, we estimate that the net proceeds from the sale of the 20,000,000 shares of common stock we are offering will be approximately \$105.6 million, after deducting the estimated underwriting discounts and 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 \$121.5 million. We estimate that the net proceeds from our concurrent notes offering will be approximately \$217.9 million, or \$250.6 million if the underwriters exercise in full their option to purchase additional notes, after deducting the estimated underwriting discounts and estimated offering expenses payable by us. This offering is not contingent upon the completion of the concurrent notes offering, and the concurrent notes offering is not contingent upon the completion of this offering. We cannot assure you that either or both of the offerings will be completed.

We will retain broad discretion over the use of the net proceeds from this offering and the concurrent notes offering. We currently expect to use the net proceeds from this offering and the concurrent notes offering for general corporate purposes, including for clinical trials, research and development, capital expenditures and working capital. In addition, we have agreed to place approximately \$ million (or approximately \$ million if the underwriters exercise their option to purchase additional notes in full) of the proceeds of the concurrent notes offering in an escrow account with the trustee under the indenture pursuant to which the notes are issued. The escrow account will contain an amount of government securities and/or money market securities sufficient to fund, when due, the total aggregate amount of the first six scheduled semi-annual interest payments on the notes, excluding additional interest, if any, and our obligations under the notes will be secured in part until August 15, 2015, by a pledge of the assets in the escrow account.

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

The description and the other information in this prospectus supplement regarding the concurrent notes offering is included in this prospectus supplement solely for informational purposes. Nothing in this prospectus supplement should be construed as an offer to sell, or the solicitation of an offer to buy, our notes.

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 December 31, 2010		
Quarter ended April 2, 2010	\$ 7.53	\$5.77
Quarter ended July 2, 2010	\$ 7.00	\$3.11
Quarter ended October 1, 2010	\$ 4.29	\$2.86
Quarter ended December 31, 2010	\$ 9.20	\$3.84
Year Ended December 30, 2011		
Quarter ended April 1, 2011	\$12.82	\$7.10
Quarter ended July 1, 2011	\$12.61	\$8.03
Quarter ended September 30, 2011	\$ 9.24	\$5.45
Quarter ended December 30, 2011	\$ 8.25	\$3.94
Year Ended December 28, 2012		
Quarter ended March 30, 2012	\$ 6.57	\$4.47
Quarter ended June 29, 2012	\$ 5.59	\$4.37
Quarter ending September 28, 2012 (through August 3, 2012)	\$ 6.95	\$5.51

The reported last sale price of our common stock on the NASDAQ Global Select Market on August 3, 2012, was \$5.58 per share. As of August 2, 2012, there were approximately 542 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. Our loan and security agreement with SVB restricts our ability to pay dividends and make distributions. In addition, our note purchase agreement with Deerfield restricts our ability to make distributions.

DILUTION

Our net tangible book value on June 30, 2012, was approximately \$35.4 million, or approximately \$0.24 per share. Net tangible book value per share is equal to the amount of our total tangible assets, less total liabilities, divided by the aggregate number of shares of common stock outstanding as of June 30, 2012. Dilution in net tangible book value per share represents the difference between the amount per share paid by purchasers of shares of common stock in this offering and the net tangible book value per share of our common stock immediately after this offering. After giving effect to the purchase from us of 20,000,000 shares of common stock in this offering at an assumed public offering price of \$5.58 per share (which was the last reported sale price of our common stock on August 3, 2012), and after deducting the estimated underwriting discounts and estimated offering expenses payable by us, our net tangible book value on June 30, 2012, would have been approximately \$141.0 million, or approximately \$0.84 per share. This represents an immediate dilution of \$4.74 per share to investors purchasing shares of common stock in this offering. The following table illustrates this dilution:

Assumed public offering price per share		\$ 5.58
Net tangible book value as of June 30, 2012	\$0.24	
Increase per share attributable to new investors	<u>0.60</u>	
Net tangible book value per share as of June 30, 2011, after giving effect to this offering		<u>0.84</u>
Dilution per share to investors in this offering		<u>\$ 4.74</u>

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 3,000,000 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 3,000,000 additional shares, our net tangible book value on June 30, 2012, would have been approximately \$156.9 million, or approximately \$0.91 per share, representing an immediate dilution of \$4.67 per share to new investors purchasing shares of common stock in this offering.

Each \$0.50 increase (decrease) in the assumed public offering price of \$5.58 per share would increase (decrease) our as adjusted net tangible book value by \$9.5 million, or \$0.06 per share, and the dilution per share to investors in this offering by \$0.44 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 discounts 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 20.5 million shares, together with a concomitant \$0.50 increase in the assumed public offering price of \$5.58 per share, would increase our as adjusted net tangible book value by \$12.4 million, or \$0.07 per share, and the dilution per share to investors in this offering by \$0.43 per share. Similarly, a decrease of 500,000 shares in the number of shares offered by us, to a total of 19.5 million shares, together with a concomitant \$0.50 decrease in the assumed public offering price of \$5.58 per share, would decrease our as adjusted net tangible book value by \$11.9 million, or \$0.07 per share, and the dilution per share to investors in this offering by \$0.43 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.

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The foregoing discussion and table are based on 148,794,245 shares of common stock issued and outstanding as of June 30, 2012, and exclude:

- 16,345,993 shares of common stock underlying options outstanding as of June 30, 2012, at a weighted average exercise price of \$7.06 per share;
- 1,441,215 shares of common stock underlying warrants outstanding as of June 30, 2012, at a weighted average exercise price of \$6.99 per share;
- 907,697 unvested restricted stock units as of June 30, 2012; and
- 10,508,305 shares available for future grant under our 2011 Equity Incentive Plan, 2,481,973 shares available for future grant under our 2000 Employee Stock Purchase Plan, 987,656 shares available for future grant under our 2000 Non-Employee Directors' Stock Option Plan, and 568,062 shares available for future grant under our 401(k) Retirement Plan, all as of June 30, 2012.

To the extent that any of the notes sold in the concurrent notes offering or the Deerfield Notes are converted into shares of our common stock, options are exercised or restricted stock unit awards vest, you may experience further dilution. In addition, we may choose to raise additional capital due to market conditions or strategic considerations even if we believe that we have sufficient funds for our current or future operating plans. To the extent that additional capital is raised through the sale of equity or convertible debt securities, the issuance of these securities could result in further dilution to our stockholders.

CAPITALIZATION

The following table sets forth our capitalization as of June 30, 2012:

• on an actual basis; and

• on an as adjusted basis to give effect to the receipt of the estimated net proceeds of \$105.6 million from the sale of the common stock in this offering (assuming no exercise of the underwriters' option to purchase additional shares) at an assumed public offering price of \$5.58 per share and the estimated net proceeds of \$217.9 million from the concurrent issuance of \$225.0 million aggregate principal amount of the notes in our concurrent notes offering (assuming no exercise by the underwriters of the concurrent notes offering of their option to purchase additional notes), in each case, after deducting the estimated underwriting discounts and estimated offering expenses payable by us as described under "Use of Proceeds."

You should read the data set forth in the table below in conjunction with (i) our consolidated financial statements, including the related notes, and "Management's Discussion and Analysis of Financial Condition and Results of Operations" from our Annual Report on Form 10-K for the fiscal year ended December 31, 2011, and (ii) our condensed consolidated financial statements, including the related notes, and "Management's Discussion and Analysis of Financial Condition and Results of Operations" from our Quarterly Report on Form 10-Q for the quarterly period ended June 30, 2012, which are incorporated by reference into this prospectus supplement.

(In thousands, except share and per share amounts)	As of June 30, 2012	
	Actual	As Adjusted
Current portion of debt obligations under the loan and security agreement with SVB	\$ 3,158	\$ 3,158
Current portion of debt obligations under the Deerfield Notes	10,000	10,000
Long-term debt, less current portion:		
% Convertible senior subordinated notes due 2019(1)	—	
Long-term portion of debt obligations under the loan and security agreement with SVB	83,678	83,678
Long-term portion of debt obligations under the Deerfield Notes	85,862	85,862
Total long-term debt	<u>\$ 169,540</u>	<u>\$</u>
Stockholders' equity:		
Preferred stock, par value of \$0.001 per share, 10,000,000 shares authorized; no shares issued and outstanding, actual and as adjusted	—	—
Common stock, par value of \$0.001 per share, 400,000,000 shares authorized; 148,794,245 shares issued and outstanding, actual, 168,794,245 shares issued and outstanding as adjusted(2)	149	169
Additional paid-in capital(1)	1,267,890	
Accumulated other comprehensive income	5	5
Accumulated deficit	<u>(1,168,995)</u>	<u>(1,168,995)</u>
Total stockholders' equity(1)	99,049	
Total capitalization	<u>\$ 268,589</u>	<u>\$</u>

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- (1) Amounts shown reflect the application of ASC 470-20, which requires issuers to separately account for the liability and equity components of convertible debt instruments that may be settled entirely or partially in cash. In accordance with ASC 470-20, we estimate that the \$225.0 million aggregate principal amount of the notes will be recognized (and, to the extent applicable, reflected in the table above) as follows (in thousands):

Equity Component	\$
Liability Component	\$
Principal	\$ 225,000
Less: debt discount	\$
Net carrying amount	\$

The determination of the fair values of the debt and equity components has been estimated but is subject to change based upon the completion of our analysis of non-convertible debt interest rates.

- (2) The common stock shown as issued and outstanding in the table above is based on 148,794,245 shares of common stock outstanding as of June 30, 2012, and excludes the shares of common stock reserved for issuance upon conversion of the notes, and also excludes, as of June 30, 2012: (i) 16,345,993 shares of common stock issuable upon the exercise of outstanding stock options, having a weighted average exercise price of \$7.06 per share; (ii) 1,441,215 shares of common stock issuable upon the exercise of outstanding warrants, having a weighted average exercise price of \$6.99 per share; (iii) 907,697 shares of common stock issuable upon the vesting of outstanding restricted stock units, stock appreciation rights and performance share awards; and (iv) an aggregate of up to 14,545,996 shares of common stock reserved for future issuance under our equity incentive plans and our 401(k) retirement plan.

CONCURRENT CONVERTIBLE NOTES OFFERING

Concurrently with this offering of common stock, we are offering \$225.0 million aggregate principal amount of % Convertible Senior Subordinated Notes due 2019, or the notes (or a total of \$258.8 million aggregate principal amount of the notes if the underwriters for the concurrent convertible notes offering exercise in full their option to purchase additional notes), pursuant to a separate prospectus supplement. The notes will pay interest semi-annually in arrears at a rate of % per year.

The notes will be convertible by the holders beginning on May 15, 2019, or earlier upon the occurrence of certain events. The notes will be convertible at an initial conversion rate of shares per \$1,000 principal amount of notes. The conversion rate will be subject to adjustment upon certain events, but will not be adjusted for accrued and unpaid interest. Upon conversion, the notes may be settled, at our election, in cash, shares of our common stock, or a combination of cash and shares of our common stock. We may redeem some or all of the notes for cash under certain circumstances on or after August 15, 2016. If we undergo a “fundamental change”, holders may require us to purchase the notes in whole or in part for cash at a purchase price equal to 100% of the principal amount plus accrued and unpaid interest.

Our obligations under the notes will be secured in part by a pledge of a portion of the proceeds from the sale of the notes. We have agreed to place approximately \$ million (or approximately \$ million if the underwriters exercise their option to purchase additional notes in full) of the proceeds of the concurrent notes offering in an escrow account with the trustee under the indenture pursuant to which the notes are issued. The escrow account will contain an amount of government securities and/or money market securities sufficient to fund, when due, the total aggregate amount of the first six scheduled semi-annual interest payments on the notes, excluding additional interest, if any, and our obligations under the notes will be secured in part until August 15, 2015, by a pledge of the assets in the escrow account.

The notes will be our general unsecured senior subordinated obligations (other than the interest escrow described above), will rank senior in right of payment to any existing or future subordinated indebtedness; equal in right of payment to our existing and future unsecured senior indebtedness; subordinate in right of payment to the Deerfield Notes (other than to the extent of the interest escrow); effectively subordinate (other than to the extent of the interest escrow) to any of our existing and future secured indebtedness, to the extent of the value of the assets securing such indebtedness, including amounts outstanding under our loan and security agreement with SVB; and structurally subordinate to all existing and future indebtedness (including trade payables) of our subsidiaries, as well as to any of our existing or future indebtedness that may be guaranteed by any of our subsidiaries (to the extent of any such guarantee).

We expect to raise approximately \$217.9 million in net proceeds from the concurrent notes offering, after deducting the estimated underwriting discounts and estimated offering expenses payable by us. If the underwriters of the concurrent notes offering exercise in full their option to purchase additional notes, we estimate that the net proceeds to us will be approximately \$250.6 million, after deducting the estimated underwriting discounts and estimated offering expenses payable by us. See “Use of Proceeds” in this prospectus supplement. The concurrent notes offering is not contingent upon the common stock offering, and the common stock offering is not contingent upon the concurrent notes offering. We cannot assure you that either or both of these offerings will be completed.

This description and the other information in this prospectus supplement regarding the concurrent notes offering is included in this prospectus supplement for informational purposes only. This prospectus supplement shall not be deemed an offer to sell or a solicitation of an offer to buy any of the notes offered in the concurrent notes offering.

MATERIAL U.S. FEDERAL INCOME TAX CONSIDERATIONS FOR NON-U.S. HOLDERS

The following discussion is a summary of the material U.S. federal income tax consequences relevant to the purchase, ownership and disposition of the common stock by a Non-U.S. Holder. For these purposes, a "Non-U.S. Holder" is a beneficial owner of common stock that is for U.S. federal income tax purposes:

- an individual who is classified as a nonresident alien;
- a foreign corporation; or
- a foreign estate or trust.

"Non-U.S. Holder" does not include a holder who is an individual present in the United States for 183 days or more in the taxable year of disposition of the common stock, or a holder that owns, or is deemed to beneficially own, more than 5% of our common stock. Such a holder is urged to consult his or her own tax advisor regarding the U.S. federal income tax consequences of the sale, exchange or other disposition of common stock.

This summary is based on the Internal Revenue Code of 1986, as amended to the date hereof (the "Code"), administrative pronouncements, judicial decisions and final, temporary and proposed Treasury regulations, changes to any of which subsequent to the date of this prospectus supplement may affect the tax consequences described herein (possibly with retroactive effect). The summary does not address U.S. federal tax consequences other than income tax consequences or any state, local or foreign tax consequences. In addition, special rules may apply to certain Non-U.S. Holders that are subject to special treatment under the Code, such as financial institutions, insurance companies, tax-exempt organizations, broker-dealers and traders in securities, U.S. expatriates, "controlled foreign corporations," "passive foreign investment companies," corporations that accumulate earnings to avoid U.S. federal income tax, persons that hold our common stock as part of a "straddle," "hedge," "conversion transaction," "synthetic security" or integrated investment, partnerships and other pass-through entities, and investors in such pass-through entities. Persons considering the purchase of common stock are urged to consult their tax advisors with regard to the application of the U.S. federal income tax laws to their particular situations as well as any tax consequences arising under the laws of any state, local or foreign taxing jurisdiction.

If a partnership or other entity classified as a partnership for U.S. federal income tax purposes holds common stock, the tax treatment of a partner will generally depend upon the status of the partner and the activities of the partnership. If you are a partner of a partnership holding common stock, you should consult your tax advisor.

Prospective investors should consult their own independent tax advisors with regard to the application of the tax consequences discussed below to their particular situations as well as the application of any state, local, foreign or other tax laws, including gift and estate tax laws and any applicable tax treaty.

Dividends

Dividends paid to a Non-U.S. Holder of common stock generally will be subject to withholding tax at a 30% rate or a reduced rate specified by an applicable income tax treaty. In order to obtain a reduced rate of withholding, a Non-U.S. Holder will be required to provide an IRS Form W-8BEN certifying its entitlement to benefits under a treaty.

The withholding tax does not apply to dividends paid to a Non-U.S. Holder who provides a Form W-8ECI, certifying that the dividends are effectively connected with the Non-U.S. Holder's conduct of a trade or business within the United States. Instead, the effectively connected dividends will be subject

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to regular U.S. income tax as if the Non-U.S. Holder were a U.S. resident (unless an applicable income tax treaty provides otherwise). A non-U.S. corporation receiving effectively connected dividends may also be subject to an additional "branch profits tax" imposed at a rate of 30% (or a reduced treaty rate).

Sale, Exchange or Other Disposition of the Shares of Common Stock

Subject to the discussion of backup withholding below and the discussion of withholding on foreign accounts below, any gain realized by a Non-U.S. Holder on the sale, exchange or other disposition of shares of our common stock generally will not be subject to U.S. federal income tax, unless:

- such gain is effectively connected with the conduct by such Non-U.S. Holder of a trade or business within the United States, subject to an applicable income tax treaty providing otherwise; or
- we are or have been a U.S. real property holding corporation as defined below, at any time within the five-year period preceding the disposition or the Non-U.S. Holder's holding period, whichever period is shorter, and the common stock has ceased to be traded on an established securities market prior to the beginning of the calendar year in which the sale or disposition occurs.

We believe that we are not, and do not anticipate becoming, a U.S. real property holding corporation. Generally, a corporation is a U.S. real property holding corporation if the fair market value of its U.S. real property interests, as defined in the Code and applicable regulations, equals or exceeds 50% of the aggregate fair market value of its worldwide real property interests and its other assets used or held for use in a trade or business.

Except to the extent that an applicable income tax treaty provides otherwise, a Non-U.S. Holder whose gain with respect to common stock is effectively connected with the conduct of a trade or business in the United States by such holder will be subject to U.S. federal income tax on a net income basis at the rate applicable to U.S. persons generally (and, with respect to corporate holders, may also be subject to a branch profits tax at 30% or a reduced treaty rate).

Information Reporting and Backup Withholding

Information returns will be furnished to Non-U.S. Holders and filed with the IRS in connection with payments on the common stock and the amount of tax, if any, withheld with respect to those payments. Copies of the information returns reporting such dividend payments and any withholding may also be made available to the tax authorities in the country in which the Non-U.S. Holder resides under the provisions of an applicable income tax treaty. Unless the Non-U.S. Holder complies with certification procedures to establish that it is not a United States person, information returns may be filed with the IRS in connection with the proceeds from a sale or other disposition of common stock, and the Non-U.S. Holder may be subject to backup withholding on payments on the common stock or on the proceeds from a sale or other disposition of the common stock. The amount of any backup withholding from a payment to a Non-U.S. Holder will be allowed as a credit against the Non-U.S. Holder's U.S. federal income tax liability and may entitle the Non-U.S. Holder to a refund, provided that the required information is timely furnished to the IRS.

Withholding on Foreign Accounts

Legislation enacted in 2010 may impose withholding taxes on certain types of payments made to "foreign financial institutions" (as specifically defined in this legislation) and certain other non-U.S. entities (including financial intermediaries). Under this legislation, failure to comply with additional

certification, information reporting and other specified requirements could result in withholding tax being imposed on payments of dividends and sales proceeds of any property of a type which can produce U.S. source dividends to foreign intermediaries and certain Non-U.S. Holders. The legislation imposes a 30% withholding tax on dividends, or gross proceeds from the sale or other disposition of common stock paid to a foreign financial institution or to a foreign non-financial entity, unless (i) the foreign financial institution undertakes certain diligence and reporting obligations or (ii) the foreign non-financial entity either certifies it does not have any substantial United States owners or furnishes identifying information regarding each substantial United States owner. If the payee is a foreign financial institution, it must enter into an agreement with the United States Treasury requiring, among other things, that it undertake to identify accounts held by certain United States persons or United States-owned foreign entities, annually report certain information about such accounts, and withhold 30% on payments to account holders whose actions prevent it from complying with these reporting and other requirements. Under certain transition rules, any obligation to withhold under the legislation with respect to payments of dividends on common stock will not begin until January 1, 2014, and with respect to the gross proceeds of a sale or other disposition of the common stock will not begin until January 1, 2015. Prospective investors should consult their tax advisors regarding this legislation.

New Tax on Net Investment Income

For taxable years beginning after December 31, 2012, certain Non-U.S. Holders who are estates or trusts may be subject to a 3.8% tax on all or a portion of their "net investment income", which may include all or a portion of their dividends on shares of our common stock and net gains from the disposition of shares of our common stock. Such Non-U.S. Holders should consult their tax advisors regarding the applicability of this additional tax to any of their income or gains in respect of shares of our common stock.

UNDERWRITING

We 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.

<u>Underwriters</u>	<u>Number of Shares</u>
Goldman, Sachs & Co.	
Cowen and Company, LLC	
Piper Jaffray & Co.	
Stifel, Nicolaus & Company, Incorporated	
William Blair & Company, L.L.C.	
Total	<u>20,000,000</u>

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 3,000,000 shares from us. 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 3,000,000 additional shares.

	<u>No Exercise</u>	<u>Full Exercise</u>
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.

We and our 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 (including withholding by, or transfer to, us of shares vested in respect of previously granted restricted stock unit awards required to cover applicable withholding tax obligations and, in the case of one director, transfers pursuant to a plan under Rule 10b5-1 under the Exchange Act that is in effect on the date of the lock-up agreement), except with the prior written consent of Goldman, Sachs & Co. However, the agreement with us does not prohibit the issuance of shares of common stock or any securities convertible into or exchangeable for shares of common stock by us pursuant to its existing equity incentive plans or 401(k) plan or any future equity incentive plans approved by our stockholders, or the issuance by us following the date 45 days after the date of this prospectus supplement of shares of common stock or any securities convertible into or exchangeable

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for shares of common stock in an amount up to an aggregate of 10% of our 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 us; provided that in the case of any issuances in 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 they are 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(1) of the FSMA does not apply to us; and
- (b) it has complied and will comply with all applicable provisions of the FSMA with respect to anything done by it in relation to the shares in, from or otherwise involving the United Kingdom.

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

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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 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 authorized or regulated to operate in the financial markets or, if not so authorized 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 us 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

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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.

We estimate that our share of the total expenses of the offering, excluding underwriting discounts and commissions, will be approximately \$400,000.

We have agreed to indemnify the several underwriters and their controlling persons against certain liabilities, including liabilities under the Securities Act of 1933, as amended.

The underwriters and their respective affiliates are full service financial institutions engaged in various activities, which may include sales and trading, commercial and investment banking, advisory, investment management, investment research, principal investment, hedging, market making, brokerage and other financial and non-financial activities and services. Certain of the underwriters and their respective affiliates have provided, and may in the future provide, a variety of these services to us and to persons and entities with relationships with us, for which they received or will receive customary fees and expenses.

In the ordinary course of their various business activities, the underwriters and their respective affiliates, officers, directors and employees may purchase, sell or hold a broad array of investments and actively trade securities, derivatives, loans, commodities, currencies, credit default swaps and other financial instruments for their own account and for the accounts of their customers, and such investment and trading activities may involve or relate to assets, securities and/or instruments of ours (directly, as collateral securing other obligations or otherwise) and/or persons and entities with relationships with us. The underwriters and their respective affiliates may also communicate independent investment recommendations, market color or trading ideas and/or publish or express independent research views in respect of such assets, securities or instruments and may at any time hold, or recommend to clients that they should acquire, long and/or short positions in such assets, securities and instruments.

VALIDITY OF COMMON STOCK

The validity of the common stock offered hereby will be passed upon for us by Cooley LLP, San Francisco, 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, 2011, and the effectiveness of our internal control over financial reporting as of December 31, 2011, as set forth in their reports, which are 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 reports, given on their authority as experts in accounting and auditing.

Prospectus



**Common Stock
Preferred Stock
Debt Securities
Warrants**

From time to time, we may offer and sell any combination of the securities described in this prospectus, either individually or in combination. We may also offer common stock or preferred stock upon conversion of debt securities, common stock upon conversion of preferred stock, or common stock, preferred stock or debt securities upon the exercise of warrants.

We will provide the specific terms of these offerings and securities in one or more supplements 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. You should carefully read this prospectus, the applicable prospectus supplement and any related free writing prospectus, as well as any documents incorporated by reference, before buying any of the securities being offered.

Our common stock is listed on The NASDAQ Global Select Market under the trading symbol "EXEL." On June 6, 2012, the last reported sale price of our common stock was \$4.86 per share. The applicable prospectus supplement will contain information, where applicable, as to other listings, if any, on The NASDAQ Global Select Market or other securities 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 in any free writing prospectuses we have authorized for use in connection with a specific offering, and under similar headings in the other documents that are incorporated by reference into this prospectus.

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

The securities may be sold directly by us to investors, through agents designated from time to time or to or through underwriters or dealers, on a continuous or delayed basis. The supplements to this prospectus will provide the specific terms of the plan of distribution. If any agents or underwriters are involved in the sale of any securities with respect to which this prospectus is being delivered, the names of such agents or underwriters and any applicable fees, commissions, discounts and over-allotment options will be set forth in a prospectus supplement. The price to the public of such securities and the net proceeds that 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 June 8, 2012.

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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 SEC, utilizing a “shelf” registration process. Under this shelf registration process, we may offer and sell, either individually or in combination, in one or more offerings, any combination of the securities described in this prospectus. This prospectus provides you with a general description of the securities we may offer.

Each time we offer securities under this prospectus, we will provide a prospectus supplement that will contain more 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 these 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 any of the information contained in this prospectus or in the documents that we have incorporated by reference into this prospectus. We urge you to read carefully this prospectus, any applicable prospectus supplement and any free writing prospectuses we have authorized for use in connection with a specific offering, together with the information incorporated herein by reference as described under the heading “Incorporation of Certain Information by Reference,” before buying any of the securities being offered.

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 contained in, or incorporated by reference into, this prospectus and any applicable prospectus supplement, along with the information contained in any free writing prospectuses we have authorized for use in connection with a specific offering. We have not authorized anyone to provide you with different or additional information. 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.

The information appearing 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 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. Our business, financial condition, results of operations and prospects may have changed since those dates.

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 section entitled “Where You Can Find More Information.”

This prospectus contains and incorporates by reference market data and industry statistics and forecasts that are based on independent industry publications and other publicly available information. Although we believe these sources are reliable, we do not guarantee the accuracy or completeness of this information and we have not independently verified this information. Although we are not aware of any misstatements regarding the market and industry data presented in this prospectus and the documents incorporated herein by reference, these estimates involve risks and uncertainties and are subject to change based on various factors, including those discussed 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. Accordingly, investors should not place undue reliance on this information.

This prospectus and the information incorporated herein by reference include trademarks, service marks and trade names owned by us or other companies. 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.

PROSPECTUS SUMMARY

This summary highlights selected information contained elsewhere in this prospectus 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 the entire prospectus, the applicable prospectus supplement and any related free writing prospectus, including the risks of investing in our securities discussed 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. You should also carefully read the information incorporated by reference into this prospectus, including our financial statements, and the exhibits to the registration statement of which this prospectus is a part.

References in this prospectus to “Exelixis”, “the Company,” “we”, “us” and “our” refer to Exelixis, Inc., a Delaware corporation, and its consolidated subsidiaries, if any, unless otherwise specified.

Exelixis, Inc.

Overview

We are a biotechnology company committed to developing small molecule therapies for the treatment of cancer. We are focusing our proprietary resources and development efforts exclusively on cabozantinib, or XL184, our most advanced 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, many of which are being advanced by partners as part of collaborations.

Company 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 corporate address is 210 East Grand Avenue, South San Francisco, CA 94080, and our telephone number is (650) 837-7000. Our website address is www.exelixis.com. Information found on, or accessible through, our website is not a part of, and is not incorporated into, this prospectus, and you should not consider it part of this prospectus or part of any prospectus supplement or free writing prospectus. Our website address is included in this document as an inactive textual reference only.

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 combination, from time to time under this prospectus, together with the applicable prospectus supplement and any related free writing prospectus, at prices and on terms to be determined by market conditions at the time of any offering. We may also offer common stock, preferred stock and/or debt securities upon the exercise of warrants. 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 date, 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
- material or special U.S. federal income tax considerations, if any.

The applicable prospectus supplement and any related free writing prospectus that we may authorize to be provided to you may also add, update or change any of the information contained in this prospectus or in the 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 to or 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.

THIS PROSPECTUS MAY NOT BE USED TO CONSUMMATE A SALE OF SECURITIES UNLESS IT IS ACCOMPANIED BY A PROSPECTUS SUPPLEMENT.

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 stockholders. Subject to preferences that may be applicable to any outstanding shares of preferred stock, the holders of common stock are entitled to receive ratably such dividends as may be declared by our board of directors out of legally available funds. Upon our liquidation, dissolution or winding up, holders of our common stock are entitled to share ratably in all assets remaining after payment of liabilities and the liquidation preferences of any outstanding shares of preferred stock. Holders of 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. 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 applicable prospectus supplement (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 designations, voting powers, preferences and rights of the preferred stock, as well as the qualifications, limitations or restrictions thereof, including dividend rights, conversion rights,

preemptive rights, terms of redemption or repurchase, liquidation preferences, sinking fund terms and the number of shares constituting any series or the designation of any series. Convertible preferred stock will be convertible into our common stock or exchangeable for other securities. Conversion may be mandatory or at your option and would be at prescribed conversion rates.

If we sell any series of preferred stock under this prospectus, we will fix the designations, voting powers, preferences and rights of the preferred stock of each series we issue under this prospectus, as well as the qualifications, limitations or restrictions thereof, 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 reports that we file with the SEC, the form of any certificate of designation that contains the terms of the series of preferred stock we are offering. 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 applicable prospectus supplement (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 unsecured and unsubordinated debt. 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 of our senior indebtedness. Convertible debt securities will be convertible into or exchangeable for our common stock or other securities. Conversion may be mandatory or at your option and would be at prescribed conversion rates.

Any debt securities issued under this prospectus will be issued under one or more documents called indentures, which are contracts between us and a national banking association or other eligible party, as trustee. 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 applicable prospectus supplement (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 debt securities. We have filed the form of indenture as an exhibit to the registration statement of which this prospectus is a part, and supplemental indentures and forms of debt securities containing the terms of the 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 reports that we file with the SEC.

Warrants. We may issue warrants for the purchase of common stock, preferred stock and/or debt securities in one or more series. We may issue warrants independently or in combination with common stock, preferred stock and/or debt securities. In this prospectus, we have summarized certain general features of the warrants under “Description of Warrants.” We urge you, however, to read the applicable prospectus supplement (and any related free writing prospectus that we may authorize to be provided to you) related to the particular series of warrants being offered, as well as any warrant agreements and warrant certificates that contain the terms of the warrants. We have filed forms of the warrant agreements and forms of warrant certificates containing the terms of the warrants that may be offered as exhibits to the registration statement of which this prospectus is a part. We will file as exhibits to the registration statement of which this prospectus is a part, or will incorporate by reference from reports that we file with the SEC, the form of warrant and/or the warrant agreement and warrant certificate, as applicable, that contain the terms of the particular series of warrants we are offering, and any supplemental agreements, before the issuance of such warrants.

Any warrants issued under this prospectus may be evidenced by warrant certificates. Warrants also may be issued under an applicable warrant agreement that we enter into with a warrant agent. We will indicate the name and address of the warrant agent, if applicable, in the prospectus supplement relating to the particular series of warrants being offered.

Use of Proceeds

Except as described in any applicable prospectus supplement or in any free writing prospectuses we have authorized for use in connection with a specific offering, we currently intend to use the net proceeds from the sale of the securities offered by us hereunder, if any, for working capital and general corporate purposes, including research and development expenses and capital expenditures. See “Use of Proceeds” in this prospectus.

The NASDAQ Global Select Market Listing

Our common stock is listed on The NASDAQ Global Select Market under the symbol “EXEL.” The applicable prospectus supplement will contain information, where applicable, as to other listings, if any, on The NASDAQ Global Select Market or any other securities market or other exchange of the securities covered by the applicable prospectus supplement.

RISK FACTORS

Investing in our securities involves a high degree of risk. Before deciding whether to invest in our securities, you should consider carefully the risks and uncertainties described under the heading “Risk Factors” contained in the applicable prospectus supplement and any related free writing prospectus, and discussed under the section entitled “Risk Factors” contained 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, which are incorporated by reference into this prospectus in their entirety, together with other information in this prospectus, the documents incorporated by reference and any free writing prospectus that we may authorize for use in connection with this offering. The risks described in these documents are not the only ones we face, but those that we consider to be material. There may be other unknown or unpredictable economic, business, competitive, regulatory or other factors that could have material adverse effects on our future results. Past financial performance may not be a reliable indicator of future performance, and historical trends should not be used to anticipate results or trends in future periods. If any of these risks actually occurs, our business, financial condition, results of operations or cash flow could be seriously harmed. This could cause the trading price of our common stock to decline, resulting in a loss of all or part of your investment. Please also read carefully the section below entitled “Special Note Regarding Forward-Looking Statements.”

SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

This prospectus and the documents we have filed with the SEC that are incorporated by reference contain “forward-looking statements” within the meaning of Section 27A of the Securities Act of 1933, as amended, or the Securities Act, and Section 21E of the Securities Exchange Act of 1934, as amended, or the Exchange Act. These statements relate to future events or to our future operating or financial performance and involve known and unknown risks, uncertainties and other factors which may cause our actual results, performance or achievements to be materially different from any future results, performances or achievements expressed or implied by the forward-looking statements. 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 cabozantinib and any other 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,” “expect,” “plan,” “anticipate,” “believe,” “estimate,” “project,” “predict,” “potential” and similar expressions intended to identify forward-looking statements. These statements reflect our current views with respect to future events and are based on assumptions and are subject to risks and uncertainties. Given these uncertainties, you should not place undue reliance on these forward-looking statements. We discuss in greater detail many of these risks under the heading “Risk Factors” contained in the applicable prospectus supplement, in any free writing prospectuses we may authorize for use in connection with a specific offering, 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, which are incorporated by reference into this prospectus in their entirety. Also, these forward-looking statements represent our estimates and assumptions only as of the date of the document containing the applicable statement. Unless required by law, we undertake no obligation to update or revise any forward-looking statements to reflect new information or future events or developments. Thus, you should not assume that our silence over time means that actual events are bearing out as

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expressed or implied in such forward-looking statements. You should read this prospectus, any applicable prospectus supplement, together with the documents we have filed with the SEC that are incorporated by reference and any free writing prospectus that we may authorize for use in connection with this offering completely and with the understanding that our actual future results may be materially different from what we expect. We qualify all of the forward-looking statements in the foregoing documents by these cautionary statements.

USE OF PROCEEDS

Except as described in any applicable prospectus supplement or in any free writing prospectuses we have authorized for use in connection with a specific offering, we currently intend to use the net proceeds from the sale of the securities offered by us hereunder, if any, for working capital and general corporate purposes, including research and development expenses and capital expenditures.

The amounts and timing of our use of the net proceeds from this offering will depend on a number of factors, such as the timing and progress of our research and development efforts, the timing and progress of any partnering and commercialization efforts, technological advances and the competitive environment for our products. As of the date of this prospectus, we cannot specify with certainty all of the particular uses for the net proceeds to us from the sale of the securities offered by us hereunder. Accordingly, our management will have broad discretion in the timing and application of these proceeds. Pending application of the net proceeds as described above, we intend to temporarily invest the proceeds in short-term, interest-bearing instruments.

RATIO OF EARNINGS TO FIXED CHARGES

The following table sets forth, for each of the periods presented, our ratio of earnings to fixed charges or our deficiency of earnings to cover fixed charges. For the quarter ended March 31, 2012 and the fiscal years ended December 31, 2010, 2009, 2008 and 2007 ratio information is not applicable due to the deficiency of earnings. This table is qualified by the more detailed information appearing in the computation table found in Exhibit 12.1 to the registration statement of which this prospectus is a part.

	Three Months Ended March 31, 2012	Year Ended December 31,				
		2011	2010	2009	2008	2007
Ratio of earnings to fixed charges	—	5.57	—	—	—	—
Deficiency of earnings available to cover fixed charges (in thousands)	<u>\$ (26,140)</u>	<u>—</u>	<u>\$ (92,402)</u>	<u>\$ (140,843)</u>	<u>\$ (175,570)</u>	<u>\$ (111,022)</u>

For purposes of computing the ratio above, earnings consist of income before income taxes plus fixed charges. Fixed charges include interest expense and the portion of operating lease expense that represents interest.

DESCRIPTION OF CAPITAL STOCK

Our authorized capital stock consists of 400,000,000 shares of common stock, \$0.001 par value, and 10,000,000 shares of preferred stock, \$0.001 par value. A description of material terms and provisions of our certificate of incorporation and bylaws affecting the rights of holders of our capital stock is set forth below. The description is intended as a summary, and is qualified in its entirety by reference to our certificate of incorporation and the bylaws.

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Common stock

Dividend rights. Subject to preferences that may apply to shares of preferred stock outstanding at the time, the holders of outstanding shares of our common stock are entitled to receive dividends out of funds legally available if our board of directors, in its discretion, determines to issue dividends and then only at the times and in the amounts that our board of directors may determine.

Voting rights. Each holder of common stock is entitled to one vote for each share of common stock held on all matters submitted to a vote of stockholders. Our certificate of incorporation does not provide for the right of stockholders to cumulate votes for the election of directors. Our certificate of incorporation establishes a classified board of directors, divided into three classes with staggered three-year terms. Only one class of directors is elected at each annual meeting of our stockholders, with the other classes continuing for the remainder of their respective three-year terms.

No preemptive or similar rights. Our common stock is not entitled to preemptive rights and is not subject to conversion, redemption or sinking fund provisions. The rights, preferences and privileges of the holders of our common stock are subject to, and may be adversely affected by, the rights of the holders of any series of our preferred stock that we may designate and issue in the future.

Right to receive liquidation distributions. Upon our dissolution, liquidation or winding-up, the assets legally available for distribution to holders of our common stock are distributable ratably among the holders of our common stock, subject to prior satisfaction of all outstanding debt and liabilities and the preferential rights and payment of liquidation preferences, if any, on any outstanding shares of our preferred stock.

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

Our board of directors is authorized, subject to limitations prescribed by Delaware law, to issue preferred stock in one or more series, to establish from time to time the number of shares to be included in each series and to fix the designation, powers, preferences and rights of the shares of each series and any of its qualifications, limitations or restrictions. Our board of directors can also increase or decrease the number of shares of any series, but not below the number of shares of that series then outstanding, without any further vote or action by our stockholders. Our board of directors may authorize the issuance of preferred stock with voting or conversion rights that could adversely affect the voting power or other rights of the holders of the common stock. The issuance of preferred stock, while providing flexibility in connection with financings, possible acquisitions and other corporate purposes, could, among other things, have the effect of delaying, deferring, discouraging or preventing a change in control of our company, may adversely affect the market price of our common stock and the voting and other rights of the holders of common stock, and may reduce the likelihood that common stockholders will receive dividend payments and payments upon liquidation.

We will fix the designations, voting powers, preferences and rights of the preferred stock of each series we issue under this prospectus, as well as the qualifications, limitations or restrictions thereof, 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 reports that we file with the SEC, the form of any certificate of designation that contains the terms of the series of preferred stock we are offering. We will describe in the applicable prospectus supplement the terms of the series of preferred stock being offered, including, to the extent applicable:

- the title and stated value;
- the number of shares we are offering;
- the liquidation preference per share;

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- 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 applicable;
- the provisions for a sinking fund, if applicable;
- 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 of the preferred stock;
- preemptive rights, if any;
- restrictions on transfer, sale or other assignment;
- whether interests in the preferred stock will be represented by depositary shares;
- a discussion of material United States federal income tax considerations applicable to the preferred stock;
- the relative ranking and preferences of the preferred stock as to dividend rights and rights if we liquidate, dissolve or wind up our affairs;
- any limitations on the issuance of any class or series of preferred stock ranking senior to or on a parity with the series of preferred stock as to dividend rights and rights if we liquidate, dissolve or wind up our affairs; and
- any other specific terms, preferences, rights or limitations of, or restrictions on, the preferred stock.

Outstanding warrants

As of March 31, 2012, we had warrants outstanding to purchase an aggregate of 1,000,000 shares of common stock with an exercise price of \$7.40 per share expiring on June 4, 2014, and 441,215 shares of common stock with an exercise price of \$6.05 per share expiring on June 10, 2014.

Anti-takeover effects of provisions of our certificate of incorporation and bylaws and Delaware law

Certificate of incorporation and bylaws. Our certificate of incorporation provides that our board of directors is divided into three classes with staggered three-year terms. Only one class of directors is elected at each annual meeting of our stockholders, with the other classes continuing for the remainder of their respective three-year terms. Because holders of our common stock do not have cumulative voting rights in the election of directors, stockholders holding a majority of the shares of common stock outstanding are able to elect all of the directors to be elected at each annual meeting of our stockholders. Our board of directors is able to elect a director to fill a vacancy created by the expansion of the board of directors or due to the resignation or departure of an existing board member. Our certificate of incorporation and bylaws also provide that all stockholder actions must be effected at a duly called meeting of stockholders and not by a consent in writing, and that only the board of directors pursuant to a resolution adopted by a majority of the total number of authorized directors may call a special meeting of stockholders. In addition, our bylaws include a requirement for the advance notice of

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nominations for election to the board of directors or for proposing matters that can be acted upon at a stockholders' meeting. Our certificate of incorporation provides for the ability of the board of directors to issue, without stockholder approval, up to 10,000,000 shares of preferred stock with terms set by the board of directors, which rights could be senior to those of our common stock. Our certificate of incorporation and bylaws also provides that approval of at least 66 2/3% of the shares entitled to vote at an election of directors will be required to adopt, amend or repeal our bylaws, or repeal the provisions of our certificate of incorporation regarding the election of directors and the inability of stockholders to take action by written consent in lieu of a meeting.

The foregoing provisions make it difficult for holders of our common stock to replace our board of directors. In addition, the authorization of undesignated preferred stock makes it possible for our board of directors to issue preferred stock with voting or other rights or preferences that could impede the success of any attempt to change control of our company.

Section 203 of the Delaware General Corporation Law

We are subject to the provisions of Section 203 of the Delaware General Corporation Law regulating corporate takeovers. This section prevents some Delaware corporations from engaging, under some circumstances, in a business combination, which includes a merger or sale of at least 10% of the corporation's assets with any interested stockholder, meaning a stockholder who, together with affiliates and associates, owns or, within three years prior to the determination of interested stockholder status, did own 15% or more of the corporation's outstanding voting stock, unless:

- the transaction is approved by the board of directors prior to the time that the interested stockholder became an interested stockholder;
- upon consummation of the transaction which resulted in the stockholder's becoming an interested stockholder, the interested stockholder owned at least 85% of the voting stock of the corporation outstanding at the time the transaction commenced; or
- at or subsequent to such time that the stockholder became an interested stockholder the business combination is approved by the board of directors and authorized at an annual or special meeting of stockholders by at least two-thirds of the outstanding voting stock which is not owned by the interested stockholder.

A Delaware corporation may "opt out" of these provisions with an express provision in its original certificate of incorporation or an express provision in its certificate of incorporation or bylaws resulting from a stockholders' amendment approved by a majority of the outstanding voting shares. We have not "opted out" of these provisions and do not plan to do so. The statute could prohibit or delay mergers or other takeover or change in control attempts and, accordingly, may discourage attempts to acquire us.

Transfer Agent and Registrar

The transfer agent and registrar for our common stock is Computershare Shareowner Services LLC: 1-877-813-9419.

Listing on The NASDAQ Global Select Market

Our common stock is listed on The NASDAQ Global Select Market under the symbol "EXEL". 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 preferred stock covered by such prospectus supplement.

DESCRIPTION OF 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. While the terms we have summarized below will apply generally to any debt securities that we may offer under this prospectus, we will describe the particular terms of any debt securities that we may offer in more detail in the applicable prospectus supplement. The terms of any debt securities offered under a prospectus supplement may differ from the terms described below. Unless the context requires otherwise, whenever we refer to the indenture, we also are referring to any supplemental indentures that specify the terms of a particular series of debt securities.

We will issue the debt securities under the indenture that we will enter into with trustee named in the indenture. The indenture will be qualified under the Trust Indenture Act of 1939, as amended, or the Trust Indenture Act. We have filed the form of indenture as an exhibit to the registration statement of which this prospectus is a part, and supplemental indentures and forms of debt securities containing the terms of the 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 reports that we file with the SEC.

The following summary of material provisions of the debt securities and the indenture is subject to, and qualified in its entirety by reference to, all of the provisions of the indenture applicable to a particular series of debt securities. We urge you to read the applicable prospectus supplements and any related free writing prospectuses related to the debt securities that we may offer under this prospectus, as well as the complete indenture that contains the terms of the debt securities.

General

The indenture does not limit the amount of debt securities that we may issue. It provides that we may issue debt securities up to the principal amount that we may authorize and may be in any currency or currency unit that we may designate. Except for the limitations on consolidation, merger and sale of all or substantially all of our assets contained in the indenture, the terms of the indenture do not contain any covenants or other provisions designed to give holders of any debt securities protection against changes in our operations, financial condition or transactions involving us.

We may issue the debt securities under the indenture as “discount securities,” which means they may be sold at a discount below their stated principal amount. These debt securities, as well as other debt securities that are not issued at a discount, may be issued with “original issue discount,” or OID, for U.S. federal income tax purposes because of interest payment and other characteristics or terms of the debt securities. Material U.S. federal income tax considerations applicable to debt securities issued with OID will be described in more detail in any applicable prospectus supplement.

We will describe in the applicable prospectus supplement the terms of the series of debt securities being offered, including:

- the title of the series of debt securities;
- any limit upon the aggregate principal amount that may be issued;
- the maturity date or dates;
- the form of the debt securities of the series;
- the applicability of any guarantees;
- whether or not the debt securities will be secured or unsecured, and the terms of any secured debt;
- whether the debt securities rank as senior debt, senior subordinated debt, subordinated debt or any combination thereof, and the terms of any subordination;

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- if the price (expressed as a percentage of the aggregate principal amount thereof) at which such debt securities will be issued is a price other than the principal amount thereof, the portion of the principal amount thereof payable upon declaration of acceleration of the maturity thereof, or if applicable, the portion of the principal amount of such debt securities that is convertible into another security or the method by which any such portion shall be determined;
- the interest rate or rates, which may be fixed or variable, or the method for determining the rate and the date interest will begin to accrue, the dates interest will be payable and the regular record dates for interest payment dates or the method for determining such dates;
- our right, if any, to defer payment of interest and the maximum length of any such deferral period;
- if applicable, the date or dates after which, or the period or periods during which, and the price or prices at which, we may, at our option, redeem the series of debt securities pursuant to any optional or provisional redemption provisions and the terms of those redemption provisions;
- the date or dates, if any, on which, and the price or prices at which we are obligated, pursuant to any mandatory sinking fund or analogous fund provisions or otherwise, to redeem, or at the holder's option to purchase, the series of debt securities and the currency or currency unit in which the debt securities are payable;
- the denominations in which we will issue the series of debt securities, if other than denominations of \$1,000 and any integral multiple thereof;
- any and all terms, if applicable, relating to any auction or remarketing of the debt securities of that series and any security for our obligations with respect to such debt securities and any other terms which may be advisable in connection with the marketing of debt securities of that series;
- whether the debt securities of the series shall be issued in whole or in part in the form of a global security or securities; the terms and conditions, if any, upon which such global security or securities may be exchanged in whole or in part for other individual securities; and the depository for such global security or securities;
- if applicable, the provisions relating to conversion or exchange of any debt securities of the series and the terms and conditions upon which such debt securities will be so convertible or exchangeable, including the conversion or exchange price, as applicable, or how it will be calculated and may be adjusted, any mandatory or optional (at our option or the holders' option) conversion or exchange features, the applicable conversion or exchange period and the manner of settlement for any conversion or exchange;
- if other than the full principal amount thereof, the portion of the principal amount of debt securities of the series which shall be payable upon declaration of acceleration of the maturity thereof;
- additions to or changes in the covenants applicable to the particular debt securities being issued, including, among others, the consolidation, merger or sale covenant;
- additions to or changes in the Events of Default with respect to the securities and any change in the right of the trustee or the holders to declare the principal, premium, if any, and interest, if any, with respect to such securities to be due and payable;
- additions to or changes in or deletions of the provisions relating to covenant defeasance and legal defeasance;
- additions to or changes in the provisions relating to satisfaction and discharge of the indenture;
- additions to or changes in the provisions relating to the modification of the indenture both with and without the consent of holders of debt securities issued under the indenture;
- the currency of payment of debt securities if other than U.S. dollars and the manner of determining the equivalent amount in U.S. dollars;

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- whether interest will be payable in cash or additional debt securities at our or the holders' option and the terms and conditions upon which the election may be made;
- the terms and conditions, if any, upon which we will pay amounts in addition to the stated interest, premium, if any and principal amounts of the debt securities of the series to any holder that is not a "United States person" for federal tax purposes;
- any restrictions on transfer, sale or assignment of the debt securities of the series; and
- any other specific terms, preferences, rights or limitations of, or restrictions on, the debt securities, any other additions or changes in the provisions of the indenture, and any terms that may be required by us or advisable under applicable laws or regulations.

Conversion or Exchange Rights

We will set forth in the prospectus supplement the terms on which a series of debt securities may be convertible into or exchangeable for our common stock or our other securities or other property or assets. We will include provisions as to settlement upon conversion or exchange and whether conversion or exchange is mandatory, at the option of the holder or at our option. We may include provisions pursuant to which the number of shares of our common stock or our other securities or units of other property or assets that the holders of the series of debt securities receive would be subject to adjustment.

Consolidation, Merger or Sale

Unless we provide otherwise in the prospectus supplement applicable to a particular series of debt securities, the indenture will not contain any covenant that restricts our ability to merge or consolidate, or sell, convey, transfer or otherwise dispose of all or substantially all of our assets. However, any successor to or acquirer of such assets must assume all of our obligations under the indenture or the debt securities, as appropriate.

Events of Default Under the Indenture

Unless we provide otherwise in the prospectus supplement applicable to a particular series of debt securities, the following are events of default under the indenture with respect to any series of debt securities that we may issue:

- if we fail to pay any installment of interest on any series of debt securities, as and when the same shall become due and payable, and such default continues for a period of 90 days; provided, however, that a valid extension of an interest payment period by us in accordance with the terms of any indenture supplemental thereto shall not constitute a default in the payment of interest for this purpose;
- if we fail to pay the principal of, or premium, if any, on any series of debt securities as and when the same shall become due and payable whether at maturity, upon redemption, by declaration or otherwise, or in any payment required by any sinking or analogous fund established with respect to such series; provided, however, that a valid extension of the maturity of such debt securities in accordance with the terms of any indenture supplemental thereto shall not constitute a default in the payment of principal or premium, if any;
- if we fail to observe or perform any other covenant or agreement contained in the debt securities or the indenture, other than a covenant specifically relating to another series of debt securities, and our failure continues for 90 days after we receive written notice of such failure, requiring the same to be remedied and stating that such is a notice of default thereunder, from the trustee or holders of at least 25% in aggregate principal amount of the outstanding debt securities of the applicable series; and
- if specified events of bankruptcy, insolvency or reorganization occur.

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If an event of default with respect to debt securities of any series occurs and is continuing, other than an event of default specified in the last bullet point above, the trustee or the holders of at least 25% in aggregate principal amount of the outstanding debt securities of that series, by notice to us in writing, and to the trustee if notice is given by such holders, may declare the unpaid principal of, premium, if any, and accrued interest, if any, due and payable immediately. If an event of default specified in the last bullet point above occurs with respect to us, the principal amount of and accrued interest, if any, of each issue of debt securities then outstanding shall be due and payable without any notice or other action on the part of the trustee or any holder.

The holders of a majority in principal amount of the outstanding debt securities of an affected series may waive any default or event of default with respect to the series and its consequences, except defaults or events of default regarding payment of principal, premium, if any, or interest, unless we have cured the default or event of default in accordance with the indenture. Any waiver shall cure the default or event of default.

Subject to the terms of the indenture, if an event of default under an indenture shall occur and be continuing, the trustee will be under no obligation to exercise any of its rights or powers under such indenture at the request or direction of any of the holders of the applicable series of debt securities, unless such holders have offered the trustee reasonable indemnity. The holders of a majority in principal amount of the outstanding debt securities of any series will have the right to direct the time, method and place of conducting any proceeding for any remedy available to the trustee, or exercising any trust or power conferred on the trustee, with respect to the debt securities of that series, provided that:

- the direction so given by the holder is not in conflict with any law or the applicable indenture; and
- subject to its duties under the Trust Indenture Act, the trustee need not take any action that might involve it in personal liability or might be unduly prejudicial to the holders not involved in the proceeding.

A holder of the debt securities of any series will have the right to institute a proceeding under the indenture or to appoint a receiver or trustee, or to seek other remedies only if:

- the holder has given written notice to the trustee of a continuing event of default with respect to that series;
- the holders of at least 25% in aggregate principal amount of the outstanding debt securities of that series have made written request, and such holders have offered reasonable indemnity to the trustee to institute the proceeding as trustee; and
- the trustee does not institute the proceeding, and does not receive from the holders of a majority in aggregate principal amount of the outstanding debt securities of that series other conflicting directions within 90 days after the notice, request and offer.

These limitations do not apply to a suit instituted by a holder of debt securities if we default in the payment of the principal, premium, if any, or interest on, the debt securities.

We will periodically file statements with the trustee regarding our compliance with specified covenants in the indenture.

Modification of Indenture; Waiver

We and the trustee may change an indenture without the consent of any holders with respect to specific matters:

- to cure any ambiguity, defect or inconsistency in the indenture or in the debt securities of any series;
- to comply with the provisions described above under “Description of Debt Securities — Consolidation, Merger or Sale;”

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- to provide for uncertificated debt securities in addition to or in place of certificated debt securities;
- to add to our covenants, restrictions, conditions or provisions such new covenants, restrictions, conditions or provisions for the benefit of the holders of all or any series of debt securities, to make the occurrence, or the occurrence and the continuance, of a default in any such additional covenants, restrictions, conditions or provisions an event of default or to surrender any right or power conferred upon us in the indenture;
- to add to, delete from or revise the conditions, limitations, and restrictions on the authorized amount, terms, or purposes of issue, authentication and delivery of debt securities, as set forth in the indenture;
- to make any change that does not adversely affect the interests of any holder of debt securities of any series in any material respect;
- to provide for the issuance of and establish the form and terms and conditions of the debt securities of any series as provided above under “Description of Debt Securities — General” to establish the form of any certifications required to be furnished pursuant to the terms of the indenture or any series of debt securities, or to add to the rights of the holders of any series of debt securities;
- to evidence and provide for the acceptance of appointment under any indenture by a successor trustee; or
- to comply with any requirements of the SEC in connection with the qualification of any indenture under the Trust Indenture Act.

In addition, under the indenture, the rights of holders of a series of debt securities may be changed by us and the trustee with the written consent of the holders of a majority in aggregate principal amount of the outstanding debt securities of each series that is affected. However, unless we provide otherwise in the prospectus supplement applicable to a particular series of debt securities, we and the trustee may make the following changes only with the consent of each holder of any outstanding debt securities affected:

- extending the fixed maturity of any debt securities of any series;
- reducing the principal amount, reducing the rate of or extending the time of payment of interest, or reducing any premium payable upon the redemption of any series of any debt securities; or
- reducing the percentage of debt securities, the holders of which are required to consent to any amendment, supplement, modification or waiver.

Discharge

Each indenture provides that we can elect to be discharged from our obligations with respect to one or more series of debt securities, except for specified obligations, including obligations to:

- provide for payment;
- register the transfer or exchange of debt securities of the series;
- replace stolen, lost or mutilated debt securities of the series;
- pay principal of and premium and interest on any debt securities of the series;
- maintain paying agencies;
- hold monies for payment in trust;
- recover excess money held by the trustee;
- compensate and indemnify the trustee; and
- appoint any successor trustee.

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In order to exercise our rights to be discharged, we must deposit with the trustee money or government obligations sufficient to pay all the principal of, any premium, if any, and interest on, the debt securities of the series on the dates payments are due.

Form, Exchange and Transfer

We will issue the debt securities of each series only in fully registered form without coupons and, unless we provide otherwise in the applicable prospectus supplement, in denominations of \$1,000 and any integral multiple thereof. The indenture provides that we may issue debt securities of a series in temporary or permanent global form and as book-entry securities that will be deposited with, or on behalf of, The Depository Trust Company, or DTC, or another depository named by us and identified in a prospectus supplement with respect to that series. To the extent the debt securities of a series are issued in global form and as book-entry, a description of terms relating will be set forth in the applicable prospectus supplement.

At the option of the holder, subject to the terms of the indenture and the limitations applicable to global securities described in the applicable prospectus supplement, the holder of the debt securities of any series can exchange the debt securities for other debt securities of the same series, in any authorized denomination and of like tenor and aggregate principal amount.

Subject to the terms of the indenture and the limitations applicable to global securities set forth in the applicable prospectus supplement, holders of the debt securities may present the debt securities for exchange or for registration of transfer, duly endorsed or with the form of transfer endorsed thereon duly executed if so required by us or the security registrar, at the office of the security registrar or at the office of any transfer agent designated by us for this purpose. Unless otherwise provided in the debt securities that the holder presents for transfer or exchange, we will impose no service charge for any registration of transfer or exchange, but we may require payment of any taxes or other governmental charges.

We will name in the applicable prospectus supplement the security registrar, and any transfer agent in addition to the security registrar, that we initially designate for any debt securities. We may at any time designate additional transfer agents or rescind the designation of any transfer agent or approve a change in the office through which any transfer agent acts, except that we will be required to maintain a transfer agent in each place of payment for the debt securities of each series.

If we elect to redeem the debt securities of any series, we will not be required to:

- issue, register the transfer of, or exchange any debt securities of that series during a period beginning at the opening of business 15 days before the day of mailing of a notice of redemption of any debt securities that may be selected for redemption and ending at the close of business on the day of the mailing; or
- register the transfer of or exchange any debt securities so selected for redemption, in whole or in part, except the unredeemed portion of any debt securities we are redeeming in part.

Information Concerning the Trustee

The trustee, other than during the occurrence and continuance of an event of default under an indenture, undertakes to perform only those duties as are specifically set forth in the applicable indenture. Upon an event of default under an indenture, the trustee must use the same degree of care as a prudent person would exercise or use in the conduct of his or her own affairs. Subject to this provision, the trustee is under no obligation to exercise any of the powers given it by the indenture at the request of any holder of debt securities unless it is offered reasonable security and indemnity against the costs, expenses and liabilities that it might incur.

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Payment and Paying Agents

Unless we otherwise indicate in the applicable prospectus supplement, we will make payment of the interest on any debt securities on any interest payment date to the person in whose name the debt securities, or one or more predecessor securities, are registered at the close of business on the regular record date for the interest.

We will pay principal of and any premium and interest on the debt securities of a particular series at the office of the paying agents designated by us, except that unless we otherwise indicate in the applicable prospectus supplement, we will make interest payments by check that we will mail to the holder or by wire transfer to certain holders. Unless we otherwise indicate in the applicable prospectus supplement, we will designate the corporate trust office of the trustee as our sole paying agent for payments with respect to debt securities of each series. We will name in the applicable prospectus supplement any other paying agents that we initially designate for the debt securities of a particular series. We will maintain a paying agent in each place of payment for the debt securities of a particular series.

All money we pay to a paying agent or the trustee for the payment of the principal of or any premium or interest on any debt securities that remains unclaimed at the end of two years after such principal, premium or interest has become due and payable will be repaid to us, and the holder of the debt security thereafter may look only to us for payment thereof.

Governing Law

The indenture and the debt securities will be governed by and construed in accordance with the laws of the State of New York, except to the extent that the Trust Indenture Act of 1939 is applicable.

DESCRIPTION OF WARRANTS

The following description, together with the additional information that we include in any applicable prospectus supplement and in any related free writing prospectus that we may authorize to be distributed to you, summarizes the material terms and provisions of the warrants that we may offer under this prospectus, which may be issued in one or more series. Warrants may be offered independently or in combination with other securities offered by any prospectus supplement. While the terms we have summarized below will apply generally to any warrants that we may offer under this prospectus, we will describe the particular terms of any series of warrants in more detail in the applicable prospectus supplement. The following description of warrants will apply to the warrants offered by this prospectus unless we provide otherwise in the applicable prospectus supplement. The applicable prospectus supplement for a particular series of warrants may specify different or additional terms.

We have filed forms of the warrant agreements and forms of warrant certificates containing the terms of the warrants that may be offered as exhibits to the registration statement of which this prospectus is a part. We will file as exhibits to the registration statement of which this prospectus is a part, or will incorporate by reference from reports that we file with the SEC, the form of warrant and/or the warrant agreement and warrant certificate, as applicable, that contain the terms of the particular series of warrants we are offering, and any supplemental agreements, before the issuance of such warrants. The following summaries of material terms and provisions of the warrants are subject to, and qualified in their entirety by reference to, all the provisions of the form of warrant and/or the warrant agreement and warrant certificate, as applicable, and any supplemental agreements applicable to a particular series of warrants that we may offer under this prospectus. We urge you to read the applicable prospectus supplement related to the particular series of warrants that we may offer under this prospectus, as well as any related free writing prospectuses, and the complete form of warrant and/or the warrant agreement and warrant certificate, as applicable, and any supplemental agreements, that contain the terms of the warrants.

General

We will describe in the applicable prospectus supplement the terms of the series of warrants being offered, including:

- the offering price and aggregate number of warrants offered;
- the currency for which the warrants may be purchased;
- if applicable, the designation and terms of the securities with which the warrants are issued and the number of warrants issued with each such security or each principal amount of such security;
- in the case of warrants to purchase debt securities, the principal amount of debt securities purchasable upon exercise of one warrant and the price at, and currency in which, this principal amount of debt securities may be purchased upon such exercise;
- in the case of warrants to purchase common stock or preferred stock, the number of shares of common stock or preferred stock, as the case may be, purchasable upon the exercise of one warrant and the price at which these shares may be purchased upon such exercise;
- the effect of any merger, consolidation, sale or other disposition of our business on the warrant agreements and the warrants;
- the terms of any rights to redeem or call the warrants;
- any provisions for changes to or adjustments in the exercise price or number of securities issuable upon exercise of the warrants;
- the dates on which the right to exercise the warrants will commence and expire;
- the manner in which the warrant agreements and warrants may be modified;

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- a discussion of any material or special U.S. federal income tax considerations of holding or exercising the warrants;
- the terms of the securities issuable upon exercise of the warrants; and
- any other specific terms, preferences, rights or limitations of or restrictions on the warrants.

Before exercising their warrants, holders of warrants will not have any of the rights of holders of the securities purchasable upon such exercise, including:

- in the case of warrants to purchase debt securities, the right to receive payments of principal of, or premium, if any, or interest on, the debt securities purchasable upon exercise or to enforce covenants in the applicable indenture; or
- in the case of warrants to purchase common stock or preferred stock, the right to receive dividends, if any, or, payments upon our liquidation, dissolution or winding up or to exercise voting rights, if any.

Exercise of Warrants

Each warrant will entitle the holder to purchase the securities that we specify in the applicable prospectus supplement at the exercise price that we describe in the applicable prospectus supplement. The warrants may be exercised as set forth in the prospectus supplement relating to the warrants offered. Unless we otherwise specify in the applicable prospectus supplement, warrants may be exercised at any time up to the close of business on the expiration date set forth in the prospectus supplement relating to the warrants offered thereby. After the close of business on the expiration date, unexercised warrants will become void.

Upon receipt of payment and the warrant or warrant certificate, as applicable, properly completed and duly executed at the corporate trust office of the warrant agent, if any, or any other office, including ours, indicated in the prospectus supplement, we will, as soon as practicable, issue and deliver the securities purchasable upon such exercise. If less than all of the warrants (or the warrants represented by such warrant certificate) are exercised, a new warrant or a new warrant certificate, as applicable, will be issued for the remaining warrants.

Governing Law

Unless we otherwise specify in the applicable prospectus supplement, the warrants and any warrant agreements will be governed by and construed in accordance with the laws of the State of New York.

Enforceability of Rights by Holders of Warrants

Each warrant agent, if any, will act solely as our agent under the applicable warrant agreement and will not assume any obligation or relationship of agency or trust with any holder of any warrant. A single bank or trust company may act as warrant agent for more than one issue of warrants. A warrant agent will have no duty or responsibility in case of any default by us under the applicable warrant agreement or warrant, including any duty or responsibility to initiate any proceedings at law or otherwise, or to make any demand upon us. Any holder of a warrant may, without the consent of the related warrant agent or the holder of any other warrant, enforce by appropriate legal action its right to exercise, and receive the securities purchasable upon exercise of, its warrants.

LEGAL OWNERSHIP OF SECURITIES

We can issue securities in registered form or in the form of one or more global securities. We describe global securities in greater detail below. We refer to those persons who have securities registered in their own names on the books that we or any applicable trustee, depository or warrant agent maintain for this purpose as the “holders” of those securities. These persons are the legal holders of the securities. We refer to those persons who,

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indirectly through others, own beneficial interests in securities that are not registered in their own names, as “indirect holders” of those securities. As we discuss below, indirect holders are not legal holders, and investors in securities issued in book-entry form or in street name will be indirect holders.

Book-Entry Holders

We may issue securities in book-entry form only, as we will specify in the applicable prospectus supplement. This means securities may be represented by one or more global securities registered in the name of a financial institution that holds them as depository on behalf of other financial institutions that participate in the depository’s book-entry system. These participating institutions, which are referred to as participants, in turn, hold beneficial interests in the securities on behalf of themselves or their customers.

Only the person in whose name a security is registered is recognized as the holder of that security. Securities issued in global form will be registered in the name of the depository or its participants. Consequently, for securities issued in global form, we will recognize only the depository as the holder of the securities, and we will make all payments on the securities to the depository. The depository passes along the payments it receives to its participants, which in turn pass the payments along to their customers who are the beneficial owners. The depository and its participants do so under agreements they have made with one another or with their customers; they are not obligated to do so under the terms of the securities.

As a result, investors in a book-entry security will not own securities directly. Instead, they will own beneficial interests in a global security, through a bank, broker or other financial institution that participates in the depository’s book-entry system or holds an interest through a participant. As long as the securities are issued in global form, investors will be indirect holders, and not holders, of the securities.

Street Name Holders

We may terminate a global security or issue securities in non-global form. In these cases, investors may choose to hold their securities in their own names or in “street name.” Securities held by an investor in street name would be registered in the name of a bank, broker or other financial institution that the investor chooses, and the investor would hold only a beneficial interest in those securities through an account he or she maintains at that institution.

For securities held in street name, we will recognize only the intermediary banks, brokers and other financial institutions in whose names the securities are registered as the holders of those securities, and we will make all payments on those securities to them. These institutions pass along the payments they receive to their customers who are the beneficial owners, but only because they agree to do so in their customer agreements or because they are legally required to do so. Investors who hold securities in street name will be indirect holders, not holders, of those securities.

Legal Holders

Our obligations, as well as the obligations of any applicable trustee and of any third parties employed by us or a trustee, run only to the legal holders of the securities. We do not have obligations to investors who hold beneficial interests in global securities, in street name or by any other indirect means. This will be the case whether an investor chooses to be an indirect holder of a security or has no choice because we are issuing the securities only in global form.

For example, once we make a payment or give a notice to the holder, we have no further responsibility for the payment or notice even if that holder is required, under agreements with depository participants or customers or by law, to pass it along to the indirect holders but does not do so. Similarly, we may want to obtain the approval of the holders to amend an indenture, to relieve us of the consequences of a default or of our obligation

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to comply with a particular provision of the indenture or for other purposes. In such an event, we would seek approval only from the holders, and not the indirect holders, of the securities. Whether and how the holders contact the indirect holders is up to the holders.

Special Considerations For Indirect Holders

If you hold securities through a bank, broker or other financial institution, either in book-entry form or in street name, you should check with your own institution to find out:

- the performance of third party service providers;
- how it handles securities payments and notices;
- whether it imposes fees or charges;
- how it would handle a request for the holders' consent, if ever required;
- whether and how you can instruct it to send you securities registered in your own name so you can be a holder, if that is permitted in the future;
- how it would exercise rights under the securities if there were a default or other event triggering the need for holders to act to protect their interests; and
- if the securities are in book-entry form, how the depository's rules and procedures will affect these matters.

Global Securities

A global security is a security that represents one or any other number of individual securities held by a depository. Generally, all securities represented by the same global securities will have the same terms.

Each security issued in book-entry form will be represented by a global security that we deposit with and register in the name of a financial institution or its nominee that we select. The financial institution that we select for this purpose is called the depository. Unless we specify otherwise in the applicable prospectus supplement, DTC will be the depository for all securities issued in book-entry form.

A global security may not be transferred to or registered in the name of anyone other than the depository, its nominee or a successor depository, unless special termination situations arise. We describe those situations below under the section entitled "Special Situations When a Global Security Will Be Terminated" in this prospectus. As a result of these arrangements, the depository, or its nominee, will be the sole registered owner and holder of all securities represented by a global security, and investors will be permitted to own only beneficial interests in a global security. Beneficial interests must be held by means of an account with a broker, bank or other financial institution that in turn has an account with the depository or with another institution that does. Thus, an investor whose security is represented by a global security will not be a holder of the security, but only an indirect holder of a beneficial interest in the global security.

If the prospectus supplement for a particular security indicates that the security will be issued in global form only, then the security will be represented by a global security at all times unless and until the global security is terminated. If termination occurs, we may issue the securities through another book-entry clearing system or decide that the securities may no longer be held through any book-entry clearing system.

Special Considerations For Global Securities

The rights of an indirect holder relating to a global security will be governed by the account rules of the investor's financial institution and of the depository, as well as general laws relating to securities transfers. We do not recognize an indirect holder as a holder of securities and instead deal only with the depository that holds the global security.

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If securities are issued only in the form of a global security, an investor should be aware of the following:

- an investor cannot cause the securities to be registered in his or her name, and cannot obtain non-global certificates for his or her interest in the securities, except in the special situations we describe below;
- an investor will be an indirect holder and must look to his or her own bank or broker for payments on the securities and protection of his or her legal rights relating to the securities, as we describe above;
- an investor may not be able to sell interests in the securities to some insurance companies and to other institutions that are required by law to own their securities in non-book-entry form;
- an investor may not be able to pledge his or her interest in a global security in circumstances where certificates representing the securities must be delivered to the lender or other beneficiary of the pledge in order for the pledge to be effective;
- the depositary's policies, which may change from time to time, will govern payments, transfers, exchanges and other matters relating to an investor's interest in a global security;
- we and any applicable trustee have no responsibility for any aspect of the depositary's actions or for its records of ownership interests in a global security, nor do we or any applicable trustee supervise the depositary in any way;
- the depositary may, and we understand that DTC will, require that those who purchase and sell interests in a global security within its book-entry system use immediately available funds, and your broker or bank may require you to do so as well; and
- financial institutions that participate in the depositary's book-entry system, and through which an investor holds its interest in a global security, may also have their own policies affecting payments, notices and other matters relating to the securities.

There may be more than one financial intermediary in the chain of ownership for an investor. We do not monitor and are not responsible for the actions of any of those intermediaries.

Special Situations When a Global Security Will Be Terminated

In a few special situations described below, the global security will terminate and interests in it will be exchanged for physical certificates representing those interests. After that exchange, the choice of whether to hold securities directly or in street name will be up to the investor. Investors must consult their own banks or brokers to find out how to have their interests in securities transferred to their own name, so that they will be direct holders. We have described the rights of holders and street name investors above.

Unless we provide otherwise in the applicable prospectus supplement, the global security will terminate when the following special situations occur:

- if the depositary notifies us that it is unwilling, unable or no longer qualified to continue as depositary for that global security and we do not appoint another institution to act as depositary within 90 days;
- if we notify any applicable trustee that we wish to terminate that global security; or
- if an event of default has occurred with regard to securities represented by that global security and has not been cured or waived.

The applicable prospectus supplement may also list additional situations for terminating a global security that would apply only to the particular series of securities covered by the applicable prospectus supplement. When a global security terminates, the depositary, and not we or any applicable trustee, is responsible for deciding the names of the institutions that will be the initial direct holders.

PLAN OF DISTRIBUTION

We may sell the securities from time to time pursuant to underwritten public offerings, direct sales to the public, negotiated transactions, block trades or a combination of these methods. We may sell the securities to or through underwriters or dealers, through agents, or directly to one or more purchasers. We may distribute securities from time to time in one or more transactions:

- at a fixed price or prices, which may be changed;
- at market prices prevailing at the time of sale;
- at prices related to such prevailing market prices; or
- at negotiated prices.

A prospectus supplement or supplements (and any related free writing prospectus that we may authorize to be provided to you) will describe the terms of the offering of the securities, including, to the extent applicable:

- the name or names of the underwriters, if any;
- the purchase price of the securities or other consideration therefor, and the proceeds, if any, we will receive from the sale;
- any over-allotment options under which underwriters may purchase additional securities from us;
- any agency fees or underwriting discounts and other items constituting agents' or underwriters' compensation;
- any public offering price;
- any discounts or concessions allowed or reallocated or paid to dealers; and
- any securities exchange or market on which the securities may be listed.

Only underwriters named in the prospectus supplement will be underwriters of the securities offered by the prospectus supplement.

If underwriters are used in the sale, they will acquire the securities for their own account and may resell the securities from time to time in one or more transactions at a fixed public offering price or at varying prices determined at the time of sale. The obligations of the underwriters to purchase the securities will be subject to the conditions set forth in the applicable underwriting agreement. We may offer the securities to the public through underwriting syndicates represented by managing underwriters or by underwriters without a syndicate. Subject to certain conditions, the underwriters will be obligated to purchase all of the securities offered by the prospectus supplement, other than securities covered by any over-allotment option. Any public offering price and any discounts or concessions allowed or reallocated or paid to dealers may change from time to time. We may use underwriters with whom we have a material relationship. We will describe in the prospectus supplement, naming the underwriter, the nature of any such relationship.

We may sell securities directly or through agents we designate from time to time. We will name any agent involved in the offering and sale of securities and we will describe any commissions we will pay the agent in the prospectus supplement. Unless the prospectus supplement states otherwise, our agent will act on a best-efforts basis for the period of its appointment.

We may authorize agents or underwriters to solicit offers by certain types of institutional investors to purchase securities from us at the public offering price set forth in the prospectus supplement pursuant to delayed delivery contracts providing for payment and delivery on a specified date in the future. We will describe the conditions to these contracts and the commissions we must pay for solicitation of these contracts in the prospectus supplement.

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We may provide agents and underwriters with indemnification against civil liabilities, including liabilities under the Securities Act, or contribution with respect to payments that the agents or underwriters may make with respect to these liabilities. Agents and underwriters may engage in transactions with, or perform services for, us in the ordinary course of business.

All securities we may offer, other than common stock, will be new issues of securities with no established trading market. Any underwriters may make a market in these securities, but will not be obligated to do so and may discontinue any market making at any time without notice. We cannot guarantee the liquidity of the trading markets for any securities.

Any underwriter may engage in over-allotment, stabilizing transactions, short-covering transactions and penalty bids in accordance with Regulation M under the Exchange Act. Over-allotment involves sales in excess of the offering size, which create a short position. Stabilizing transactions permit bids to purchase the underlying security so long as the stabilizing bids do not exceed a specified maximum price. Syndicate-covering or other short-covering transactions involve purchases of the securities, either through exercise of the over-allotment option or in the open market after the distribution is completed, to cover short positions. Penalty bids permit the underwriters to reclaim a selling concession from a dealer when the securities originally sold by the dealer are purchased in a stabilizing or covering transaction to cover short positions. Those activities may cause the price of the securities to be higher than it would otherwise be. If commenced, the underwriters may discontinue any of the activities at any time.

Any underwriters or agents that are qualified market makers on The NASDAQ Global Select Market may engage in passive market making transactions in the common stock on The NASDAQ Global Select Market in accordance with Regulation M under the Exchange Act, during the business day prior to the pricing of the offering, before the commencement of offers or sales of the common stock. Passive market makers must comply with applicable volume and price limitations and must be identified as passive market makers. In general, a passive market maker must display its bid at a price not in excess of the highest independent bid for such security; if all independent bids are lowered below the passive market maker's bid, however, the passive market maker's bid must then be lowered when certain purchase limits are exceeded. Passive market making may stabilize the market price of the securities at a level above that which might otherwise prevail in the open market and, if commenced, may be discontinued at any time.

In compliance with guidelines of the Financial Industry Regulatory Authority, or FINRA, the maximum consideration or discount to be received by any FINRA member or independent broker dealer may not exceed 8% of the aggregate amount of the securities offered pursuant to this prospectus and any applicable prospectus supplement.

LEGAL MATTERS

Unless otherwise indicated in the applicable prospectus supplement, the validity of the securities offered by this prospectus, and any supplement thereto, will be passed upon for us by Cooley LLP, San Francisco, 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 30, 2011, and the effectiveness of our internal control over financial reporting as of December 30, 2011, as set forth in their reports thereon which are incorporated by reference in this prospectus and elsewhere in the registration statement. Our financial statements are incorporated by reference in reliance on Ernst & Young LLP's reports, given on their authority as experts in accounting and auditing.

WHERE YOU CAN FIND MORE INFORMATION

This prospectus is part of the registration statement on Form S-3 we filed with the SEC under the Securities Act and does not contain all the information set forth in the registration statement. Whenever a reference is made in this prospectus to any of our contracts, agreements or other documents, the reference may not be complete and you should refer to the exhibits that are a part of the registration statement or the exhibits to the reports or other documents incorporated by reference into this prospectus for a copy of such contract, agreement or other document. Because we are subject to the information and reporting requirements of the Exchange Act, we file annual, quarterly and current reports, proxy statements and other information with the SEC. Our SEC filings are available to the public over the Internet at the SEC's website at <http://www.sec.gov>. You may also read and copy any document we file at the SEC's Public Reference Room at 100 F Street, N.E., Washington, D.C. 20549. Please call the SEC at 1-800-SEC-0330 for further information on the operation of the Public Reference Room.

INCORPORATION OF CERTAIN INFORMATION BY REFERENCE

The SEC allows us to “incorporate by reference” information from other documents that we file with it, which means that we can disclose important information to you by referring you to those documents. The information incorporated by reference is considered to be part of this prospectus. Information in this prospectus supersedes information incorporated by reference that we filed with the SEC prior to the date of this prospectus, while information that we file later with the SEC will automatically update and supersede the information in this prospectus. We incorporate by reference into this prospectus and the registration statement of which this prospectus is a part the information or documents listed below that we have filed with the SEC (Commission File No. 000-59687):

- our Annual Report on Form 10-K for the year ended December 30, 2011, which was filed on February 22, 2012;
- the information specifically incorporated by reference into the 2011 Form 10-K from our definitive proxy statement on Schedule 14A which was filed on April 20, 2012;
- our Quarterly Report on Form 10-Q which was filed on May 3, 2012;
- our Current Reports on Form 8-K filed on February 7, 2012, February 10, 2012, May 25, 2012, and June 8, 2012; and
- the description of our common stock in our registration statement on Form 8-A filed with the SEC on April 6, 2000, including any amendments thereto or reports filed for the purposes of updating this description.

We also incorporate by reference any future filings (other than current reports furnished under Item 2.02 or Item 7.01 of Form 8-K and exhibits filed on such form that are related to such items unless such Form 8-K expressly provides to the contrary) made with the SEC pursuant to Sections 13(a), 13(c), 14 or 15(d) of the Exchange Act, including those made after the date of the initial filing of the registration statement of which this prospectus is a part and prior to effectiveness of such registration statement, until we file a post-effective amendment that indicates the termination of the offering of the securities made by this prospectus and will become a part of this prospectus from the date that such documents are filed with the SEC. Information in such future filings updates and supplements the information provided in this prospectus. Any statements in any such future filings will automatically be deemed to modify and supersede any information in any document we previously filed with the SEC that is incorporated or deemed to be incorporated herein by reference to the extent that statements in the later filed document modify or replace such earlier statements.

You can request a copy of these filings, at no cost, by writing or telephoning us at the following address or telephone number:

Exelixis, Inc.
210 East Grand Avenue
South San Francisco, CA 94080
(650) 837-7000
Attn: Secretary

20,000,000 Shares

Exelixis, Inc.

Common Stock



Joint Book-Running Managers

Goldman, Sachs & Co.

Cowen and Company

Co-Managers

Piper Jaffray

Stifel Nicolaus Weisel

William Blair
