EXELIXIS, INC.
Form 424B5
January 22, 2014
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PROSPECTUS SUPPLEMENT (Subject to Completion) **Dated January 22, 2014**
(To Prospectus dated June 8, 2012)

10,000,000 Shares

Common Stock

We are offering 10,000,000 shares of our common stock. Our common stock is quoted on The NASDAQ Global Select Market under the symbol EXEL. On January 21, 2014, the last reported sale price of our common stock was $8.24 per share.

Our business and an investment in our common stock involve significant risks. These risks are described under the caption Risk Factors beginning on page S-13 of this prospectus supplement.

Neither the Securities and Exchange Commission nor any state securities commission 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*
Public offering price	**$**	**$**
Underwriting discount	**$**	**$**
Proceeds, before expenses, to Exelixis	**$**	**$**

The underwriter may also purchase up to an additional 1,500,000 shares from us at the public offering price, less the underwriting discount, within 30 days from the date of this prospectus supplement to cover overallotments.

The underwriter expects to deliver the shares against payment in New York, New York on January , 2014.

Cowen and Company

January , 2014

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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. an 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.

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PROSPECTUS SUPPLEMENT SUMMARY

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

Exelixis, Inc.

We are a biotechnology company committed to developing small molecule therapies for the treatment of cancer. Our two most advanced assets, COMETRIQ® (cabozantinib), our wholly-owned inhibitor of multiple receptor tyrosine kinases, and cobimetinib (GDC-0973/XL518), a potent, highly selective inhibitor of MEK, which we out-licensed to Genentech, Inc. (a wholly-owned member of the Roche Group), or Genentech, are currently the subject of six ongoing phase 3 pivotal trials. Top-line results from four of these pivotal trials are expected in 2014.

We are focusing our proprietary resources and development and commercialization efforts primarily on COMETRIQ® (cabozantinib), which was approved on November 29, 2012, by the U.S. Food and Drug Administration, or FDA, for the treatment of progressive, metastatic medullary thyroid cancer, or MTC, in the United States, where it became commercially available in late January 2013. In December 2013, the European Committee for Medicinal Products for Human Use, or CHMP, issued a positive opinion on the Marketing Authorization Application, or MAA, submitted to the European Medicines Agency, or EMA, for COMETRIQ for the proposed indication of progressive, unresectable, locally advanced, or metastatic MTC. The CHMP s positive opinion will be reviewed by the European Commission, which has the authority to approve medicines for the European Union.

Cabozantinib is being evaluated in a broad development program, including two ongoing phase 3 pivotal trials in metastatic castration-resistant prostate cancer, or CRPC, an ongoing phase 3 pivotal trial in metastatic renal cell cancer, or RCC, and an ongoing phase 3 pivotal trial in advanced hepatocellular cancer, or HCC. We believe cabozantinib has the potential to be a high-quality, broadly-active and differentiated anti-cancer agent that can make a meaningful difference in the lives of patients. Our objective is to develop cabozantinib into a major oncology franchise, and we believe that the approval of COMETRIQ (cabozantinib) for the treatment of progressive, metastatic MTC provides us with the opportunity to establish a commercial presence in furtherance of this objective. We currently expect top-line data from our two phase 3 pivotal trials of cabozantinib in CRPC and the overall survival analysis of our phase 3 pivotal trial of cabozantinib in progressive, metastatic MTC in 2014.

Cobimetinib is also being evaluated in a broad development program, including a multicenter, randomized, double-blind, placebo-controlled phase 3 clinical trial evaluating the combination of vemurafenib with cobimetinib versus vemurafenib in previously untreated BRAFV600 mutation positive patients with unresectable locally advanced or metastatic melanoma that was initiated on November 1, 2012. Roche and Genentech have provided guidance that they expect top-line data from this trial in 2014.

Under the terms of our co-development agreement with Genentech for cobimetinib, we are entitled to an initial equal share of U.S. profits and losses for cobimetinib, which will decrease as sales increase, and will share equally in the U.S. marketing and commercialization costs. The profit share has multiple tiers we are entitled to 50% of profits from the first $200 million of U.S. actual sales, decreasing to 30% of profits from U.S. actual sales in excess of $400

million. We are entitled to low double-digit royalties on ex-U.S. net sales. In November

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2013, we exercised an option under the co-development agreement to co-promote in the United States. We will provide up to 25% of the total sales force for cobimetinib in the United States if commercialized, and will call on customers and otherwise engage in promotional activities using that sales force, consistent with the terms of the co-development agreement and a co-promotion agreement to be entered into by the parties.

Our Strategy

We believe that the available clinical data demonstrate that cabozantinib has the potential to be a broadly active anti-cancer agent, and our objective is to build cabozantinib into a major oncology franchise. The initial regulatory approval of COMETRIQ (cabozantinib) to treat progressive, metastatic MTC provides a niche market opportunity that allows us to gain commercialization experience while providing a solid foundation for potential expansion into larger cancer indications.

We are focusing our internal efforts on cancers for which we believe cabozantinib has significant therapeutic and commercial potential in the near term, while utilizing our Cooperative Research and Development Agreement, or CRADA, with the National Cancer Institute s Cancer Therapy Evaluation Program, or NCI-CTEP, and investigator sponsored trials, or ISTs, to generate additional data to allow us to prioritize future late stage trials in a cost-effective fashion. We believe that this staged approach to building value represents the most rational and effective use of our resources.

COMETRIQ® (cabozantinib)

COMETRIQ inhibits the activity of multiple tyrosine kinases, including RET, MET, and VEGFR2. These receptor tyrosine kinases are involved in both normal cellular function and in pathologic processes such as oncogenesis, metastasis, tumor angiogenesis and maintenance of the tumor microenvironment. On November 29, 2012, the FDA approved COMETRIQ for the treatment of progressive, metastatic MTC in the United States, and we commercially launched COMETRIQ in January 2013.

The recommended dose of COMETRIQ in progressive, metastatic MTC is 140 mg orally, once daily (one 80 mg capsule and three 20 mg capsules) administered without food, and this dose may be reduced stepwise to 100 or 60 mg once daily to appropriately adjust the dose to each individual patient s tolerability.

The COMETRIQ label has boxed warnings concerning risk of gastrointestinal perforations and fistulas and severe hemorrhage. Other warnings and precautions include thrombotic events, wound complications, hypertension, osteonecrosis of the jaw, palmar-plantar erythrodysesthesia, proteinuria, reversible posterior leukoencephalopathy syndrome, caution regarding the potential for drug interactions with strong CYP3A4 inducers or inhibitors, the recommendation against use in patients with moderate or severe hepatic impairment and the potential for embryo-fetal toxicity.

EXAM Pivotal Trial

COMETRIQ s safety and efficacy were assessed in an international, multi-center, randomized double-blinded controlled trial of 330 patients with progressive, metastatic MTC, known as EXAM (Efficacy of XL184 (Cabozantinib) in Advanced Medullary Thyroid Cancer). Patients were required to have evidence of actively progressive disease within 14 months prior to study entry. This assessment was performed by an Independent Radiology Review Committee, or IRRC, in 89% of patients and by the treating physicians in 11% of patients. Patients were randomized (2:1) to receive COMETRIQ 140 mg (n = 219) or placebo (n = 111) orally, once daily until disease progression determined by the treating physician or until intolerable toxicity. Randomization was stratified by age

(£65 years vs. > 65 years) and prior use of a tyrosine kinase inhibitor. No cross-over was allowed at the time of progression. The primary endpoint was to compare progression-free survival, or PFS, in patients receiving COMETRIQ versus patients receiving placebo. Secondary endpoints included objective response rate and overall survival. The main efficacy outcome measures of PFS, objective response and response duration were based on IRRC-confirmed events using modified Response Evaluation Criteria in Solid Tumors

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(RECIST), which is a widely used set of rules that define when cancer patients improve (respond), stay the same (stabilize) or worsen (progress) during treatments.

A statistically significant prolongation in PFS was demonstrated among COMETRIQ-treated patients compared to those receiving placebo [HR 0.28 (95% CI: 0.19, 0.40); p<0.0001], with median PFS of 11.2 months in the COMETRIQ arm and 4.0 months in the placebo arm. Partial responses were observed only among patients in the COMETRIQ arm (27% vs 0%; p<0.0001). The median duration of objective response was 14.7 months (95% CI: 11.1, 19.3) for patients treated with COMETRIQ. There was no statistically significant difference in overall survival between the treatment arms at the planned interim analysis.

Postmarketing Commitments

In connection with the approval of COMETRIQ for the treatment of progressive, metastatic MTC, we are required to provide the analysis of mature overall survival data from the EXAM trial when the required 217 events (deaths) have occurred. We currently expect the overall survival analysis of EXAM to occur in 2014.

We are also subject to the following postmarketing requirements:

A phase 2 study comparing a lower dose of COMETRIQ with the labeled dose of 140 mg. This study will evaluate safety and PFS in progressive, metastatic MTC patients.

Two clinical pharmacology studies assessing the pharmacokinetics of COMETRIQ. One will address the effect of administering COMETRIQ in conjunction with agents that increase gastric pH such as proton pump inhibitors, and the other study will assess the pharmacokinetics of COMETRIQ in patients with hepatic impairment.

Four non-clinical studies to further assess the carcinogenicity, mutagenicity and teratogenicity of COMETRIQ.

Commercialization

COMETRIQ became commercially available in the United States in January 2013 and is being marketed in the United States principally through a small, internal commercial team with relevant expertise in the promotion, distribution and reimbursement of oncology drugs. Effective October 29, 2013, the wholesale acquisition cost of COMETRIQ is $10,395 for a 28-day supply. COMETRIQ has been flat priced, meaning each dosage strength is priced the same. We currently estimate that there are between 500 and 700 first and second line metastatic MTC patients diagnosed in the United States each year who will be eligible for COMETRIQ.

We have scaled our commercial organization so that it is commensurate with the size of the market opportunity for progressive, metastatic MTC. We have also designed our commercial organization to maintain flexibility, and to enable us to quickly scale up if additional indications are approved in the future. We believe we have created an efficient commercial organization, taking advantage of outsourcing options where prudent to maximize the effectiveness of our commercial expenditures.

To help ensure that all eligible progressive, metastatic MTC patients have appropriate access to COMETRIQ, we have established a comprehensive reimbursement and support program called Exelixis Access Services. Through Exelixis

Access Services, we: provide co-pay assistance to qualified, commercially insured patients to help minimize out-of-pocket costs; provide free drug to uninsured patients who meet certain clinical and financial criteria; and make contributions to an independent co-pay assistance charity to help patients who don t qualify for our co-pay assistance program. In addition, Exelixis Access Services is designed to provide comprehensive reimbursement support services, such as prior authorization support, benefits investigation and, if needed, appeals support.

COMETRIQ is distributed in the United States exclusively through Diplomat Specialty Pharmacy, an independent specialty pharmacy that allows for efficient delivery of the medication by mail directly to patients.

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To further support appropriate utilization and future development of COMETRIQ, our Medical Affairs department is responsible for providing appropriate scientific and medical education and information to physicians, and preparing scientific presentations and publications, and overseeing the process for ISTs.

EMA Marketing Authorization Application for COMETRIQ

In December 2013, the CHMP issued a positive opinion on the MAA, submitted to the EMA, for COMETRIQ for the proposed indication of progressive, unresectable, locally advanced, or metastatic MTC. The CHMP s positive opinion will be reviewed by the European Commission, which has the authority to approve medicines for the European Union.

COMETRIQ received orphan drug designation in the European Union from the Committee for Orphan Medicinal Products for the treatment of MTC in February 2009.

During 2013, we entered into an agreement with a term ending on December 31, 2015, with Swedish Orphan Biovitrum, or Sobi, to support the distribution and commercialization of COMETRIQ for metastatic MTC primarily in the European Union and potentially other countries in the event that COMETRIQ is approved for commercial sale in such jurisdictions. No other indication is covered by this agreement, and we maintain full commercial rights with respect to COMETRIQ in MTC outside the covered territory and for all other indications on a global basis. Under the terms of the agreement, we will continue to be responsible for regulatory approvals in the covered territory. Our payments to Sobi include certain pre-determined fixed fees as well as potential performance-based milestones related to the commercialization of the product in the covered territory. We have the ability to terminate the agreement at will at any time upon payment of certain pre-determined fees.

Named Patient Use Program

Through our agreement with Sobi, we have established the infrastructure to make COMETRIQ available under a named patient use, or NPU, program in countries of the European Union and in other regions outside of the United States. An NPU program provides access to drugs unapproved in that country, but approved elsewhere, for a single patient or a group of patients in a particular country.

Cabozantinib Development Program

We believe that cabozantinib s broad clinical profile is attractive and will allow commercial differentiation, assuming regulatory approval. The most advanced clinical program for cabozantinib beyond progressive, metastatic MTC is focused on the treatment of metastatic CRPC. We expect to expand the cabozantinib development program to other solid tumor indications based on encouraging interim data that have emerged from our randomized discontinuation trial, or RDT, as well as other clinical trials. Objective tumor responses have been observed in patients treated with cabozantinib in 15 individual tumor types investigated to date, reflecting the broad potential clinical activity and commercial opportunity of this product candidate. In addition to 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 and melanoma in the RDT, in RCC and differentiated thyroid cancer in a phase 1 trial, and in bladder cancer in an NCI-CTEP-sponsored trial. It is a priority for us to generate additional data in a broad range of tumor types, including HCC, RCC, non-small cell lung cancer, ovarian cancer, melanoma, breast cancer and differentiated thyroid cancer, to support further prioritization of our clinical and commercial options. In addition, postmarketing requirements in connection with the approval of COMETRIQ in progressive, metastatic MTC dictate that we conduct additional studies related to dosing in progressive, metastatic MTC, pharmacokinetics, carcinogenicity, mutagenicity and teratogenicity of COMETRIQ as more fully described above under --Postmarketing Commitments.

CRPC

Exelixis has implemented a focused clinical strategy to investigate cabozantinib in a comprehensive development program for CRPC that could potentially lead to a product that can effectively compete in the

CRPC marketplace. Interim data from our RDT suggest that cabozantinib has novel activity against bone and soft tissue lesions in patients with CRPC. Updated interim data from docetaxel-pretreated patients with metastatic CRPC and bone metastases treated with cabozantinib in an ongoing non-randomized expansion, or NRE, cohort of the RDT, reported at the American Society of Clinical Oncology Annual Meeting, or ASCO, in June 2013, showed a median overall survival of 10.8 months. A retrospective analysis of the updated interim data also showed that early responses in bone scan, circulating tumor cell levels and pain were associated with longer median overall survival as compared to non-responders.

In addition, interim data demonstrated that CRPC patients with bone metastases and bone pain at baseline experienced alleviation of pain, were able to reduce or discontinue narcotic medication and experienced a reduction in circulating tumor cell count. Lower starting doses of cabozantinib are being evaluated in the NRE cohort of CRPC patients treated at a daily dose of 40 mg, and in a dose-ranging study in CRPC patients conducted through an IST. Interim data from this NRE reported at the European Society for Medical Oncology, or ESMO, Annual Meeting in September 2012 suggest that the 40 mg daily dose has similar clinical activity to the 100 mg daily dose NRE cohort for key parameters, including reduction of metastatic bone and soft tissue disease, and reduction of bone pain and narcotic use, with an apparent improvement in tolerability compared to the 100 mg dose cohort. Interim data from the 40 mg cohort of the dose-ranging IST reported at ASCO in June 2012 had demonstrated similar clinical activity.

COMET Pivotal Trials. Two phase 3 pivotal trials, COMET-1 (CabOzantinib MET Inhibition CRPC Efficacy Trial-1) and COMET-2, were designed to provide an opportunity to clinically and commercially differentiate cabozantinib as an oncology agent with a potentially beneficial impact on overall survival, pain, and narcotic usage. We initiated the COMET-1 trial with an overall survival endpoint in May 2012 and we initiated the COMET-2 trial with a pain palliation endpoint in December 2011. In September 2013, COMET-1 reached its enrollment target of 960 patients. We currently believe that the top-line results from the COMET-1 and COMET-2 trials will be available in 2014.

COMET-1 is a double-blinded study comparing cabozantinib and prednisone that includes up to 280 international sites. The trial is designed to enroll 960 patients with CRPC that is metastatic to the bone and who have failed prior docetaxel therapy and have also failed prior abiraterone and/or enzalutamide therapies. There is no limit to the number, order or type of prior treatments. Patients are being randomized 2:1 to receive cabozantinib (60 mg daily, N=640) or prednisone (5 mg twice daily, N=320). Each arm is also receiving placebo to account for the once-daily versus twice-daily dosing regimens of cabozantinib and prednisone, respectively. The trial has 90% power to detect a 25% reduction in the risk of death (HR = 0.75). The final analysis will be event driven, with 578 events (deaths) required. A single interim analysis is planned after 387 events. The secondary endpoint is bone scan response as assessed by an independent radiology facility.

COMET-2 is a double-blinded study comparing cabozantinib and mitoxantrone/prednisone designed to enroll 246 patients with CRPC that is metastatic to the bone, who are suffering from moderate to severe bone pain despite optimized narcotic medication, and who have failed prior docetaxel therapy and have also failed prior abiraterone and/or enzalutamide therapies. The trial is being conducted in English-speaking regions, including the United States, Canada, Australia, and the United Kingdom. Patients are being randomized 1:1 to receive either cabozantinib or mitoxantrone/prednisone. Alleviation of bone pain will be determined by comparing the percentage of patients in the two treatment arms who achieve a pain response at Week 6 that is confirmed at Week 12. The trial design assumes that 25% of patients in the cabozantinib arm will have a pain response while 8% of patients in the mitoxantrone/prednisone arm will have a pain response. Prior to randomization, patients will undergo a period during which their pain medication is optimized using one long acting narcotic medication and one immediate release narcotic medication. This optimization follows a standard approach defined in the National Comprehensive Cancer Network guidelines. Patients in the cabozantinib arm will be dosed at 60 mg per day until the patient no longer

receives clinical benefit. The definition of a responder with respect to the bone pain endpoint is a greater than or equal to 30% decrease from baseline in the average of the daily worst pain intensity collected over seven days in Week 6 and confirmed in Week 12, with neither a

concomitant increase in average daily dose of any narcotic pain medication, nor addition of any new narcotic pain medication. Overall survival will be a secondary endpoint of the COMET-2 trial. The trial will be deemed successful if the primary endpoint of statistically significant pain improvement is met and the overall survival analysis does not show an adverse impact on overall survival in the cabozantinib arm.

Combination Trials. In December 2013 we initiated a phase 2 clinical trial evaluating cabozantinib in combination with abiraterone and prednisone versus abiraterone and prednisone in patients with CRPC that is metastatic to the bone who have not been treated with chemotherapy. The trial will compare abiraterone and prednisone to abiraterone and prednisone in combination with one of the three cabozantinib doses: 40 mg daily, 20 mg daily or 20 mg every other day. The primary endpoint for the randomized, open-label trial is radiographic progression-free survival. The trial is expected to enroll 280 chemotherapy-naïve CRPC patients who have bone metastases and will be conducted at approximately 50 sites in North America. In addition to evaluating radiographic progression-free survival, the trial includes pre-specified outcome measures of safety and tolerability, pharmacokinetics of cabozantinib in combination with abiraterone, overall survival, and bone scan response by computer-aided detection.

We are also planning to initiate a phase 1b clinical trial evaluating cabozantinib in combination with enzalutamide in patients with metastatic CRPC who have not received prior enzalutamide therapy or chemotherapy.

RCC

METEOR (Metastatic RCC Phase 3 Study Evaluating Cabozantinib vs Everolimus), a phase 3 pivotal trial comparing cabozantinib to everolimus in patients with metastatic RCC who have experienced disease progression following treatment with at least one prior VEGFR tyrosine kinase inhibitor, or TKI, was initiated in May 2013. The trial is designed to enroll 650 patients at approximately 200 sites. Patients will be stratified based on the number of prior VEGFR-TKI therapies received and commonly applied RCC risk criteria. Patients will be randomized 1:1 to receive 60 mg of cabozantinib daily or 10 mg of everolimus daily, and no cross-over will be allowed between the study arms. The primary endpoint for METEOR is progression-free survival, and the secondary endpoints are overall survival and objective response rate.

HCC

CELESTIAL (Cabozantinib Phase 3 Controlled Study In Hepatocellular Carcinoma), a phase 3 pivotal trial comparing cabozantinib with placebo in patients with advanced HCC who have previously been treated with sorafenib was initiated in September 2013. The trial is designed to enroll 760 patients at approximately 200 sites. Patients will be randomized 2:1 to receive 60 mg of cabozantinib daily or placebo. The primary endpoint for CELESTIAL is overall survival, and the secondary endpoints include objective response rate and progression-free survival.

NSCLC

We are planning to conduct a single arm trial in patients with non-small cell lung cancer, or NSCLC, who are positive for a RET fusion gene. The trial will enroll approximately 100 patients, and objective response rate will be the primary endpoint. Additionally, we will include exploratory cohorts of patients with other relevant molecular alterations targeted by cabozantinib.

Other Cancer Indications

We are also evaluating the potential initiation of pivotal trials in other tumor types. We believe the potential initiation of pivotal trials in other tumor types may increase the value of the cabozantinib franchise, accelerate potential

revenues, and spread the development and commercialization risk for cabozantinib across multiple opportunities. We have launched two initiatives to expand the cabozantinib development program beyond our internal development efforts: our CRADA with NCI-CTEP and our IST program.

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We entered into our CRADA with NCI-CTEP in November 2011. The proposed clinical trials approved to date under the CRADA include the following:

- Phase 2 clinical trials to help prioritize future pivotal trials of cabozantinib 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, platinum-resistant or refractory ovarian cancer, ocular melanoma, and second line/third line non-small cell lung cancer.

- Additional phase 2 clinical trials to explore cabozantinib s potential utility in other tumor types, including endometrial cancer, bladder cancer, sarcomas, second line non-small cell lung cancer, 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 to further evaluate cabozantinib, 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, a trial to evaluate the safety and pharmacokinetics of cabozantinib in pediatric patients, and a trial of cabozantinib in patients with advanced solid tumors and human immunodeficiency virus.

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. 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.

We launched the IST program in October 2010, 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. Cabozantinib is being evaluated in a variety of ISTs. Currently there is one completed IST, 18 ongoing ISTs, 11 studies undergoing activation, and we expect to continue to consider additional IST proposals for the foreseeable future.

Cobimetinib Collaboration

In December 2006, we entered into a worldwide co-development agreement with Genentech for the development and commercialization of cobimetinib. Cobimetinib is a potent, highly selective inhibitor of MEK, a serine/threonine kinase that is a component of the RAS/RAF/MEK/ERK pathway. This pathway mediates signaling downstream of growth factor receptors, and is prominently activated in a wide variety of human tumors. In preclinical studies, oral dosing of cobimetinib resulted in potent and sustained inhibition of MEK in RAS- or BRAF-mutant tumor models. Exelixis discovered cobimetinib internally and advanced the compound to investigational new drug, or IND, status.

Genentech paid upfront and milestone payments of $25.0 million in December 2006 and $15.0 million in January 2007 upon signing of the co-development agreement and with the submission of the IND for cobimetinib. Under the terms of the agreement, we were responsible for developing cobimetinib through the end of a phase 1 clinical trial,

and Genentech had the option to co-develop cobimetinib, which Genentech could exercise after receipt of certain phase 1 data from us. In March 2008, Genentech exercised its option, triggering a payment to us of $3.0 million, which we received in April 2008. We were responsible for the phase 1 clinical trial until the point that a maximum tolerated dose, or MTD, was determined. After MTD was determined, we granted to Genentech an exclusive worldwide revenue-bearing license to cobimetinib in March 2009, at which point Genentech became responsible for completing the phase 1 clinical trial and subsequent clinical development. We received an additional $7.0 million milestone payment in March 2010.

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Preliminary results from BRIM7, an ongoing phase 1b dose escalation study conducted by Roche and Genentech of the BRAF inhibitor vemurafenib in combination with cobimetinib in patients with locally advanced/unresectable or metastatic melanoma carrying a BRAFV600 mutation were presented at the 2012 ESMO Annual Meeting. Updated data from BRIM7 reported at the European Cancer Congress 2013 suggest that the preliminary safety profile and activity of the investigational combination of cobimetinib and vemurafenib are encouraging in BRAF inhibitor-naïve patients. Although the phase 1b dose escalation study was designed to evaluate the safety and tolerability of cobimetinib in combination with vemurafenib, objective responses (comprising complete or partial responses) were observed in 85% of the patients who had not been previously treated with a BRAF inhibitor.

As disclosed on ClinicalTrials.gov (NCT01689519), a multicenter, randomized, double-blind, placebo-controlled phase 3 clinical trial evaluating the combination of vemurafenib with cobimetinib versus vemurafenib in previously untreated BRAFV600 mutation positive patients with unresectable locally advanced or metastatic melanoma was initiated on November 1, 2012. On January 14, 2013, we received notice from Genentech that the first patient was dosed in this phase 3 pivotal trial. Roche and Genentech have provided guidance that they expect top-line data from this trial in 2014.

In addition, as disclosed on ClinicalTrials.gov, on the basis of strong scientific rationale and encouraging preclinical data, Genentech is initiating the following new clinical trials of cobimetinib in combination with other agents under the agreement:

A Phase 1b, Open-Label, Dose-Escalation Study of the Safety, Tolerability, and Pharmacokinetics of MEHD7945A and Cobimetinib in Patients with Locally Advanced or Metastatic Solid Tumors with Mutant KRAS (NCT01986166);

A Phase 1b, Open-Label Study Evaluating the Safety, Tolerability, and Pharmacokinetics of Onartuzumab in Combination with Vemurafenib and/or Cobimetinib in Patients with Advanced Solid Malignancies (NCT01974258); and

A Phase 1b Study of the Safety and Pharmacology of MPDL3280A Administered with Cobimetinib in Patients with Locally Advanced or Metastatic Solid Tumors (NCT01988896).

Under the terms of our agreement with Genentech, we are entitled to an initial equal share of U.S. profits and losses for cobimetinib, which will decrease as sales increase, and will share equally in the U.S. marketing and commercialization costs. The profit share has multiple tiers we are entitled to 50% of profits from the first $200 million of U.S. actual sales, decreasing to 30% of profits from U.S. actual sales in excess of $400 million. We are entitled to low double-digit royalties on ex-U.S. net sales. In November 2013, we exercised our option to co-promote in the U.S. We will provide up to 25% of the total sales force for cobimetinib in the U.S. if commercialized, and will call on customers and otherwise engage in promotional activities using that sales force, consistent with the terms of the co-development agreement and a co-promotion agreement to be entered into by the parties. If Genentech terminates the co-development agreement without cause, all licenses that were granted to Genentech under the agreement terminate and revert to us. Additionally, we would receive, subject to certain conditions, licenses from Genentech to research, develop and commercialize reverted product candidates.

Other Collaborations

We have established collaborations with other leading pharmaceutical and biotechnology companies, including GlaxoSmithKline, Bristol-Myers Squibb Company, or Bristol-Myers Squibb, Sanofi, 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, have no further development cost obligations related to such compounds or programs and may be entitled to receive milestones and royalties or a share of profits from commercialization. Several of these out-licensed compounds are in

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multiple phase 2 studies. These partnered compounds could potentially be of significant value to us if their development progresses successfully.

With respect to these partnered compounds, we are eligible to receive potential milestone payments under our collaborations totaling approximately $2.4 billion in the aggregate on a non-risk adjusted basis, of which approximately 10% are related to clinical development milestones, approximately 41% are related to regulatory milestones and approximately 49% 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 Avenue, 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.

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The Offering

Common stock offered by Exelixis	10,000,000 shares
Underwriter s option to purchase additional shares	1,500,000 shares
Common stock to be outstanding after the offering	194,194,124 shares
Use of proceeds	We currently expect to use the net proceeds from this offering for general corporate purposes, including for clinical trials, research and development, capital expenditures and working capital.
Risk factors	See Risk Factors beginning on page S-13 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 September 30, 2013. As of that date, we had 184,194,124 shares of common stock outstanding, excluding:

- 23,509,515 shares of common stock underlying options outstanding as of September 30, 2013, at a weighted average exercise price of $6.50 per share;
- 1,441,215 shares of common stock underlying warrants outstanding as of September 30, 2013, at a weighted average exercise price of $6.99 per share;
- 2,051,098 shares reserved for future issuance pursuant to unvested restricted stock units as of September 30, 2013;
- 1,489,683 shares available for future grant under our 2011 Equity Incentive Plan, 2,164,717 shares available for future purchase under our 2000 Employee Stock Purchase Plan, 732,656 shares available for future grant under our 2000 Non-Employee Directors Stock Option Plan, and 384,255 shares available for future grant under our 401(k) Retirement Plan, all as of September 30, 2013; and

54,117,649 shares of common stock reserved for issuance upon conversion of our outstanding 4.25% convertible senior subordinated notes due 2019, or the 2019 Notes.

Unless we specifically state otherwise, the information in this prospectus supplement assumes that the underwriter in this offering does not exercise its option to purchase up to 1,500,000 additional shares of our common stock in this offering within 30 days after the date of this prospectus supplement.

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Summary Consolidated Financial Data

We derived the information presented below as of December 31, 2012, and for each of the three years ended December 31, 2010, 2011 and 2012, from our audited consolidated financial statements. We derived the information presented below as of September 30, 2013, and for each of the nine months ended September 30, 2012 and 2013, 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 September 30, 2013, and for each of the nine months ended September 30, 2012 and 2013, have been reflected therein. Operating results for the nine months ended September 30, 2013, 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, 2012, and our Quarterly Report on Form 10-Q for the fiscal quarter ended September 30, 2013.

The as adjusted balance sheet data as of September 30, 2013, reflects receipt of the estimated net proceeds of $78.3 million from the sale of common stock in this offering (assuming no exercise of the underwriter s option to purchase additional shares) at an assumed public offering price of $8.24 per share, the closing price of our common stock on January 21, 2014, after deducting the estimated underwriting discount 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,			Nine Months Ended September 30,	
	2010	2011	2012	2012	2013
				(unaudited)	
	(in thousands, except per share data)				
Consolidated Statement of Operations Data					
Total revenues	$ 185,045	$ 289,636	$ 47,450	$ 39,636	$ 26,991
Total operating expenses	$ 276,442	$ 200,101	$ 169,886	$ 120,098	$ 168,209
Net (loss) income	$ (92,330)	$ 75,697	$ (147,645)	$ (95,452)	$ (174,014)
Net (loss) income per share, basic	$ (0.85)	$ 0.60	$ (0.92)	$ (0.63)	$ (0.95)
Net (loss) income per share, diluted	$ (0.85)	$ 0.58	$ (0.92)	$ (0.63)	$ (0.95)
Shares used in computing basic net (loss) income per share	108,522	126,018	160,138	152,316	183,957
Shares used in computing diluted net (loss) income per share	108,522	130,479	160,138	152,316	183,957

	As of September 30, 2013	
	Actual	As Adjusted(1)(2)
	(unaudited)	
	(in thousands)	
Consolidated Balance Sheet Data		

Cash and cash equivalents, marketable securities, restricted cash and investments and long-term investments	$ 464,721	$ 543,028
Working capital	$ 228,284	$ 306,591
Total assets	$ 555,959	$ 634,266
4.25 % Convertible senior subordinated notes due 2019	$ 161,279	$ 161,279
Debt obligations under our loan and security agreement with Silicon Valley Bank	$ 82,884	$ 82,884
Debt obligations under the Deerfield Notes	$ 97,428	$ 97,428
Additional paid-in-capital	$ 1,560,415	$ 1,638,712
Total stockholders equity	$ 132,763	$ 211,070

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(1) As adjusted to reflect the sale of 10,000,000 shares being offered in this offering and the receipt of the estimated net proceeds of $78.3 million from the sale of these shares, assuming a public offering price of $8.24 per share and after deducting the estimated underwriting discount and estimated offering expenses payable by us.

(2) Each $0.50 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 $4.8 million, assuming that the number of shares offered by us, as set forth on the cover page of this prospectus supplement, remains the same and after deducting the estimated underwriting discount and estimated offering expenses payable by us. We may also increase or decrease the number of shares we are offering. An increase or decrease of 500,000 shares in the number of shares offered by us at the assumed offering price would increase or decrease the as adjusted 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 $3.9 million, after deducting the estimated underwriting discount and estimated offering expenses payable by us.

Our Fiscal Year

We have adopted a 52- or 53-week fiscal year that ends on the Friday closest to December 31st. Fiscal year 2010, a 52-week year, ended on December 31, 2010, fiscal year 2011, a 52-week year, ended on December 30, 2011, fiscal year 2012, a 52-week year, ended on December 28, 2012, and fiscal year 2013, a 52-week year, ended on December 27, 2013. For convenience, references in this prospectus supplement as of and for the fiscal years ended December 31, 2010, December 30, 2011, and December 28, 2012, and as of and for the fiscal quarters ended September 28, 2012, and September 27, 2013, are indicated on a calendar year basis as ended December 31, 2010, 2011 and 2012, and calendar quarter basis as ended September 30, 2012 and 2013, respectively.

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RISK FACTORS

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

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

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

We may need to raise additional capital to:

- fund our operations and clinical trials;
- continue our research and development efforts;
- commercialize cabozantinib or any other future product candidates, if such candidates receive regulatory approval for commercial sale; and
- fund the U.S. marketing and commercialization costs for cobimetinib (GDC-0973/XL518) we are obligated to share under our collaboration with Genentech or any similar costs we are obligated to fund under collaborations we may enter into in the future.

As of September 30, 2013, we had $464.7 million in cash and investments, which included short- and long-term restricted cash and investments of $12.2 million and $15.9 million, respectively, and short- and long-term unrestricted investments of $187.2 million and $157.4 million, respectively. We are required to maintain on deposit with Silicon Valley Bank or one of its affiliates short- and long-term unrestricted investments of $2.2 million and $82.4 million, respectively, pursuant to covenants in our loan and security agreement with Silicon Valley Bank. We anticipate that our current cash and cash equivalents, short- and long-term investments, and product revenues, together with the anticipated proceeds from this offering, will enable us to maintain our operations through at least 2014. However, our future capital requirements will be substantial, and we may 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 development and commercialization activities with respect to COMETRIQ® (cabozantinib);

repayment of $287.5 million aggregate principal amount of the 2019 Notes that mature on August 15, 2019, unless earlier converted, redeemed or repurchased;

repayment of the $104.0 million principal amount of the secured convertible notes, or the Deerfield Notes, issued to entities affiliated with Deerfield Management Company, L.P., or Deerfield, for which we will be required to make a mandatory prepayment in 2015, and if we elect to extend the maturity of the Deerfield Notes and Deerfield so elects, mandatory prepayments in each of 2016, 2017 and 2018, in each case equal to 15% of specified payments from our collaborative arrangements (other than intercompany arrangements) received during the applicable prior fiscal year, and subject to a maximum annual prepayment amount that will be no greater than $27.5 million, unless we are able to repay them with our common stock, which we are only able to do under specified conditions;

repayment of our term loan and line of credit from Silicon Valley Bank, which had an outstanding balance at September 30, 2013, of $82.9 million;

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the commercial success of COMETRIQ and the revenues we generate;

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 COMETRIQ) 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, short- and long-term investments that serve as collateral for bank lines of credit;

future clinical trial results;

our need to expand our product and clinical development efforts;

the cost and timing of regulatory approvals;

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

our obligation to share U.S. marketing and commercialization costs for cobimetinib under our collaboration with Genentech;

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

the effect of competing technological and market developments;

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

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

We may seek to raise funds, in addition to the proceeds of this offering, 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 our loan and security agreement with Silicon Valley Bank. This agreement contains covenants or events of default requiring us to maintain specified collateral balances. The failure to comply with these covenants could result in an acceleration of the underlying debt obligations. If we are unable 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.

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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 the fiscal quarter ended September 30, 2013, with the exception of the fiscal year ended December 31, 2011. In 2011, we had net income 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 nine months ended September 30, 2013, we had a net loss of $174.0 million; as of September 30, 2013, we had an accumulated deficit of $1.4 billion. We commercially launched COMETRIQ for the treatment of progressive, metastatic MTC in the United States in late January 2013. From the commercial launch through September 30, 2013, we have generated $10.7 million in net revenues from the sale of COMETRIQ. We have derived substantially all of our revenues to date from collaborative research and development agreements. Revenues from research and development collaborations depend on 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 sales of COMETRIQ for progressive, metastatic MTC, 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 for each year other than 2011, and we expect to spend significant additional amounts to fund the continued 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 whether or when we will become profitable.

Our significant level of indebtedness could limit cash flow available for our operations and expose us to risks that could adversely affect our business, financial condition and results of operations.

We incurred significant additional indebtedness and substantial debt service requirements as a result of our offering of the 2019 Notes in August 2012. As of September 30, 2013, our total consolidated indebtedness through maturity was $467.8 million (excluding trade payables). We may also incur additional indebtedness to meet future financing needs. If we incur additional indebtedness, it would increase our interest expense, leverage and operating and financial costs.

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 2019 Notes, the Deerfield Notes, our loan and security agreement with Silicon Valley Bank or 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 loan and security agreement with Silicon Valley Bank;

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

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clinical trials, research and development, capital expenditures, working capital 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 2019 Notes in the event we are required to do so following a Fundamental Change as specified in the indenture governing the 2019 Notes, or to settle conversions of the 2019 Notes in cash;

dilution experienced by our existing stockholders as a result of the conversion of the 2019 Notes or the Deerfield 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.

We cannot assure you that we will continue to maintain sufficient cash reserves or that our business will continue to generate cash flow from operations at levels sufficient to permit us to pay principal, premium, if any, and interest on our indebtedness, or that our cash needs will not increase. 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 2019 Notes, the Deerfield Notes, our loan and security agreement with Silicon Valley Bank, or any indebtedness which we have incurred or may incur in the future, we would be in default, which would permit the holders or the Trustee of the 2019 Notes or other indebtedness to accelerate the maturity of such notes or other indebtedness and could cause defaults under the 2019 Notes, the Deerfield Notes, our loan and security agreement with Silicon Valley Bank or our other indebtedness. Any default under the 2019 Notes, the Deerfield Notes, our loan and security agreement with Silicon Valley Bank, 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.

If a Fundamental Change occurs, holders of the 2019 Notes may require us to purchase for cash all or any portion of their 2019 Notes at a purchase price equal to 100% of the principal amount of the Notes to be purchased plus accrued and unpaid interest, if any, to, but excluding, the Fundamental Change purchase date. We may not have sufficient funds to purchase the notes upon a Fundamental Change. In addition, the terms of any borrowing agreements which we may enter into from time to time may require early repayment of borrowings under circumstances similar to those constituting a Fundamental Change. Furthermore, any repurchase of 2019 Notes by us may be considered an event of default under such borrowing agreements.

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, and 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 the restructurings, which resulted in an aggregate reduction in headcount of 429 employees. We have recorded aggregate restructuring charges of $52.9 million in connection with the restructurings and anticipate that we will incur additional restructuring charges related to the exit of all or portions of certain of our buildings in South San Francisco, California. These charges will be recorded through the end of the building lease terms, the last of which ends in 2017.

As part of these restructurings, we have entered into sublease agreements for certain of our facilities in South San Francisco. 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 September 30, 2013, 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 COMETRIQ® (cabozantinib)

We are dependent on the successful development and commercialization of COMETRIQ.

The success of our business is dependent upon the successful development and commercialization of COMETRIQ. As part of our strategy, we are dedicating substantially all of our proprietary resources to advance COMETRIQ as aggressively as possible. On November 29, 2012, the FDA approved COMETRIQ for the treatment of progressive, metastatic MTC in the United States and we commercially launched COMETRIQ in late January 2013. In December 2013, the European Committee for Medicinal Products for Human Use, or CHMP, issued a positive opinion of the MAA, submitted to the EMA, for COMETRIQ for the proposed indication of progressive, unresectable, locally advanced, or metastatic MTC. The CHMP s positive opinion will be reviewed by the European Commission, which has the authority to approve medicines for the European Union. We view the approval of COMETRIQ by the FDA for the treatment of progressive, metastatic MTC as a transitional event towards our objective of developing COMETRIQ into a major oncology franchise. Our ability to realize this objective or the value of our investment is contingent on, among other things, successful clinical development, regulatory approval and market acceptance of COMETRIQ. If we encounter difficulties in the development of COMETRIQ in other indications beyond progressive, metastatic MTC due to any of the factors discussed in this Risk Factors section or otherwise, or we do not receive regulatory approval in such indications or are unable to successfully commercialize COMETRIQ in progressive, metastatic MTC or such other indications if approved, we will not have the resources necessary to continue our business in its current form.

The commercial success of COMETRIQ will depend upon the degree of market acceptance of COMETRIQ among physicians, patients, health care payors, and the medical community.

Our ability to commercialize COMETRIQ for the treatment of progressive, metastatic MTC and potentially other indications, if approved, will be highly dependent upon the extent to which COMETRIQ gains market

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acceptance among physicians, patients, health care payors such as Medicare and Medicaid, and the medical community. If COMETRIQ does not achieve an adequate level of acceptance, we may not generate significant future product revenues, and we may not become profitable. The degree of market acceptance of COMETRIQ will depend upon a number of factors, including:

- the effectiveness, or perceived effectiveness, of COMETRIQ in comparison to competing products;
- the existence of any significant side effects of COMETRIQ, 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 COMETRIQ is approved;
- the ability to offer COMETRIQ for sale at competitive prices;
- relative convenience and ease of administration;
- the strength of sales, marketing and distribution support; and
- sufficient third-party coverage or reimbursement.

If we are unable to establish and maintain adequate sales, marketing and distribution capabilities or enter into or maintain agreements with third parties to do so, we may be unable to successfully commercialize COMETRIQ.

We have established a small internal commercial organization that we believe is commensurate with the size of the market opportunity for progressive, metastatic MTC. We have also designed our commercial organization to maintain flexibility, and to enable us to quickly scale up if additional indications are approved in the future. We believe we have created an efficient commercial organization, taking advantage of outsourcing options where prudent to maximize the effectiveness of our commercial expenditures. However, we may not be able to correctly judge the size and experience of the sales and marketing force and the scale of distribution necessary to successfully market and sell COMETRIQ. Establishing and maintaining sales, marketing and distribution capabilities are expensive and time-consuming. Such expenses may be disproportional compared to the revenues we may be able to generate on sales of COMETRIQ and have an adverse impact on our results of operations. If we are unable to establish and maintain adequate sales, marketing and distribution capabilities, independently or with others, we may not be able to generate product revenues and our business may be adversely affected.

We currently rely on a single third party logistics provider to handle shipping and warehousing of our commercial supply of COMETRIQ and a single specialty pharmacy to dispense COMETRIQ to patients in fulfillment of prescriptions in the United States. We will also rely on a third party, Swedish Orphan Biovitrum, or Sobi, to distribute and commercialize COMETRIQ for the treatment of metastatic MTC primarily in the European Union and potentially other countries in the event that COMETRIQ is approved for commercial sale in those jurisdictions. Sobi is currently supporting access to cabozantinib under a Named Patient Use program in the European Union and other regions outside of the United States. Our current and anticipated future dependence upon these third parties may adversely affect our future profit margins and our ability to supply COMETRIQ to the marketplace on a timely and competitive basis. For example, if our third party logistics provider s warehouse suffers a fire or damage from another type of disaster, the commercial supply of COMETRIQ could be destroyed, resulting in a disruption in our commercialization efforts. These third parties may not be able to provide services in the time we require to meet our commercial timelines and objectives or to meet regulatory requirements. We may not be able to maintain or renew our arrangements with these third parties, or enter into new arrangements, on acceptable terms, or at all. These third parties could terminate or decline to renew our arrangements based on their own business priorities, at a time that is costly or inconvenient for us. If we are unable to contract for logistics services or distribution of COMETRIQ on acceptable terms, our commercialization efforts may be delayed or otherwise adversely affected.

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We are subject to certain healthcare laws, regulation and enforcement; our failure to comply with those laws could have a material adverse effect on our results of operations and financial condition.

We are subject to certain healthcare laws and regulations and enforcement by the federal government and the states in which we conduct our business. The laws that may affect our ability to operate include, without limitation:

the federal healthcare programs Anti-Kickback Law, which constrains our marketing practices, educational programs, pricing policies, and relationships with healthcare providers or other entities, by prohibiting, among other things, persons from knowingly and willfully soliciting, receiving, offering or paying remuneration, directly or indirectly, in exchange for or to induce either the referral of an individual for, or the purchase, order or recommendation of, any good or service for which payment may be made under federal healthcare programs such as the Medicare and Medicaid programs;

federal civil and criminal false claims laws and civil monetary penalty laws, which prohibit, among other things, individuals or entities from knowingly presenting, or causing to be presented, claims for payment from Medicare, Medicaid, or other third-party payors that are false or fraudulent;

federal criminal laws that prohibit executing a scheme to defraud any healthcare benefit program or making false statements relating to healthcare matters;

state law equivalents of each of the above federal laws, such as anti-kickback and false claims laws which may apply to items or services reimbursed by any third-party payor, including commercial insurers, and state laws governing the privacy and security of health information in certain circumstances, many of which differ from each other in significant ways and may not have the same effect, thus complicating compliance efforts;

the Foreign Corrupt Practices Act, a U.S. law which regulates certain financial relationships with foreign government officials (which could include, for example, certain medical professionals);

federal and state consumer protection and unfair competition laws, which broadly regulate marketplace activities and activities that potentially harm consumers;

state and federal government price reporting laws that require us to calculate and report complex pricing metrics to government programs, where such reported priced may be used in the calculation of reimbursement and/or discounts on our marketed drugs (participation in these programs and compliance with the applicable requirements may subject us to potentially significant discounts on our products, increased infrastructure costs, and potentially limit our ability to offer certain marketplace discounts); and

state and federal marketing expenditure tracking and reporting laws, which generally require certain types of expenditures in the United States to be tracked and reported (compliance with such requirements may require

investment in infrastructure to ensure that tracking is performed properly, and some of these laws result in the public disclosure of various types of payments and relationships, which could potentially have a negative effect on our business and/or increase enforcement scrutiny of our activities).

In addition, certain marketing practices, including off-label promotion, may also violate false claims laws. If our operations are found to be in violation of any of the laws described above or any other governmental regulations that apply to us, we, or our officers or employees, may be subject to penalties, including civil and criminal penalties, damages, fines, withdrawal of regulatory approval, the curtailment or restructuring of our operations, the exclusion from participation in federal and state healthcare programs and imprisonment, any of which could adversely affect our ability to sell COMETRIQ or operate our business and also adversely affect our financial results.

Numerous federal and state laws, including state security breach notification laws, state health information privacy laws and federal and state consumer protection laws, govern the collection, use and disclosure of personal information. Other countries also have, or are developing, laws governing the collection, use and transmission of personal information. In addition, most healthcare providers who are expected to prescribe our products and from whom we obtain patient health information are subject to privacy and security requirements

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under the Health Insurance Portability and Accountability Act of 1996, as amended by the Health Information Technology and Clinical Health Act, or HIPAA. Although we are not directly subject to HIPAA, we could be subject to criminal penalties if we knowingly obtain individually identifiable health information from a HIPAA-covered entity in a manner that is not authorized or permitted by HIPAA. The legislative and regulatory landscape for privacy and data protection continues to evolve, and there has been an increasing amount of focus on privacy and data protection issues with the potential to affect our business, including recently enacted laws in a majority of states requiring security breach notification. These laws could create liability for us or increase our cost of doing business. International laws, such as the EU Data Privacy Directive (95/46/EC) and Swiss Federal Act on Data Protection, regulate the processing of personal data within Europe and between European countries and the United States. Failure to provide adequate privacy protections and maintain compliance with Safe Harbor mechanisms could jeopardize business transactions across borders and result in significant penalties.

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

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

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 COMETRIQ to other available therapies. The conduct of such a clinical trial could be expensive and result in delays in the commercialization of COMETRIQ. 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 COMETRIQ. Cost-control initiatives could decrease the price we might establish for COMETRIQ, 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 COMETRIQ profitably.

The United States 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 COMETRIQ profitably. Among policy makers and payors in the United States 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 United States, the pharmaceutical industry has been a particular focus of these efforts and has been significantly affected by major legislative initiatives.

For example, under the Patient Protection and Affordable Care Act of 2010, as amended by the Health Care and Education Affordability Reconciliation Act, or collectively, PPACA, substantial changes may be made to the way healthcare is financed by both governmental and private insurers, and those changes may significantly affect the

pharmaceutical industry. Among other things, PPACA creates a new system of health insurance exchanges, designed to make health policies available to individuals and certain groups though state- or federally-administered marketplaces, beginning in 2014. In connection with such exchanges, certain essential health benefits are intended to be made more consistent across plans, setting basically a baseline coverage level. While prescription drugs are broadly considered essential, there is some discretion to the plans as to what categories of prescription drug products will be covered (and the scope of coverage in each category). We cannot predict at

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this time whether COMETRIQ would be covered by the health plans offered in any or all of the exchanges. Failure to be covered by plans offered in the exchanges could have a material adverse impact on our business. 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 COMETRIQ and any subsequently approved product, and could seriously harm our business. Under the Budget Control Act of 2011, as amended, federal budget sequestration became effective in March 2013, automatically reducing payments under various government programs, including, for example, certain Medicare provider and supplier reimbursement payments. Sequestration may have a material adverse effect on our customers and accordingly, our financial operations. 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 COMETRIQ will successfully be placed on the list of drugs covered by particular commercial or government health plan formularies, nor can we predict the negotiated price for COMETRIQ, which will be determined by market factors. Many states have also created preferred drug lists for their Medicaid programs, and include drugs on those lists only when the manufacturers agree to pay a supplemental rebate. If COMETRIQ 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 COMETRIQ.

As a result of the overall 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 COMETRIQ by placing it 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 COMETRIQ. We also anticipate pricing pressures in connection with the sale of COMETRIQ due to 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 for the treatment of additional tumor types beyond progressive, metastatic MTC could allow our competitors to bring products to market before us, which would impair our ability to commercialize cabozantinib in such tumor types. Our future success will depend upon our ability to maintain a competitive position with respect to technological advances. The markets for which we intend to pursue regulatory approval of cabozantinib are highly competitive. 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 commercial 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, cabozantinib may compete with existing therapies that have long histories of use, such as chemotherapy and radiation treatments in cancer indications.

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We believe that the principal competing anti-cancer therapy to COMETRIQ in progressive, metastatic MTC is AstraZeneca s RET, VEGFR and EGFR inhibitor vandetanib, which has been approved by the FDA and the EMA for the treatment of symptomatic or progressive MTC in patients with unresectable, locally advanced, or metastatic disease. In addition, we believe that COMETRIQ also faces competition as a treatment for progressive, metastatic MTC from off-label use of Bayer s and Onyx Pharmaceuticals (a wholly-owned subsidiary of Amgen) multikinase inhibitor sorafenib, Pfizer s multikinase inhibitor sunitinib, and Ariad Pharmaceutical s multikinase inhibitor ponatinib.

We believe that if cabozantinib is approved for the treatment of the indications for which we currently have ongoing phase 3 pivotal trials, its potential principal competition in such indications may include the following:

- CRPC (castration-resistant prostate cancer): Bayer s and Algeta s alpha-pharmaceutical (radium 223); Janssen Biotech s CYP17 inhibitor abiraterone; Medivation s androgen receptor inhibitor enzalutamide; and chemotherapeutic agents, including Sanofi s cabazitaxel and generic docetaxel;

- RCC (renal cell cancer): Pfizer s axitinib, sunitinib and temsirolimus; Novatis everolimus; Bayer s and Onyx Pharmaceuticals sorafenib; GlaxoSmithKline s pazopanib; and Genentech s bevacizumab; and

- HCC (hepatocellular cancer): Bayer s and Onyx Pharmaceuticals sorafenib; Bayer s regorafenib; ImClone System s ramucirumab; and ArQule s tivantinib.

Examples of potential competition for cabozantinib in other cancer indications include: other VEGF pathway inhibitors, including Genentech s bevacizumab; other RET inhibitors including Eisai s lenvatinib; and other MET inhibitors, including Amgen s AMG 208, Pfizer s crizotinib, ArQule s tivantinib, GlaxoSmithKline s foretinib (XL880), and Genentech s onartuzumab.

We lack the manufacturing capabilities and experience necessary to enable us to produce COMETRIQ for clinical development or for commercial sale and rely on third parties to do so, which subjects us to various risks.

We do not have the manufacturing capabilities or experience necessary to enable us to produce materials for our clinical trials or for commercial sale of COMETRIQ and rely on third party contractors to do so. These third-parties 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 parties may adversely affect our future profit margins and our ability to develop and commercialize COMETRIQ on a timely and competitive basis. These third parties 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 and commercial timelines and applicable regulatory requirements. We may not be able to maintain or renew our existing third party manufacturing and supply arrangements, or enter into new arrangements, on acceptable terms, or at all. Our third party manufacturers and suppliers could terminate or decline to renew our manufacturing and supply 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 and commercialization efforts may be delayed or otherwise adversely affected.

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 manufacturing or supply arrangements, we may not be able to obtain approval from the FDA of any alternate

manufacturer or supplier in a timely manner, or at all, which could delay or prevent the clinical development and commercialization of COMETRIQ. Failure of our third party manufacturers or suppliers 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 COMETRIQ, 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 effect on our business. In addition, COMETRIQ 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

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product testing or delivery, cost overruns or other problems that could have also a significant adverse effect on our business.

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

Cabozantinib is being evaluated in a comprehensive development program for the treatment of CRPC, RCC, HCC and a variety of other indications beyond progressive, metastatic MTC. Clinical trials are inherently risky and may reveal that cabozantinib is ineffective or has unacceptable toxicity or other side effects that may significantly decrease the likelihood of regulatory approval in such indications.

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 for the treatment of CRPC, RCC, HCC and other indications, 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 cabozantinib, 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 and our ability to generate revenues 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 or regulatory authorities in other jurisdictions, including those identified based on our discussions with the FDA or such other regulatory authorities. Our planned clinical trials may not begin on time, or at all, may not be completed on schedule, or at all, may not be sufficient for registration of cabozantinib or may not result in an approvable product.

Completion of clinical trials may take several years or more, but the length of time generally varies substantially according to the type, complexity, novelty and intended use of cabozantinib. 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 who ultimately participate in the clinical trial;

the duration of patient follow-up that is appropriate in view of the results or required by regulatory authorities;

the number of clinical sites included in the trials; and

the length of time required to enroll suitable patient subjects.

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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 for the treatment of additional indications beyond progressive, metastatic MTC.

We do not have the ability to independently conduct clinical trials for cabozantinib, including our postmarketing commitments for COMETRIQ for the treatment of progressive, metastatic MTC, and we rely on third parties we do not control such as the federal government (including NCI-CTEP, with whom we have our CRADA), 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 commercialize cabozantinib for additional indications beyond progressive, metastatic MTC.

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 cabozantinib.

Cabozantinib, as well as the activities associated with its research, development and commercialization, are subject to extensive regulation by the FDA and other regulatory agencies in the United States and by comparable authorities in other countries. Failure to obtain regulatory approval for cabozantinib would prevent us from promoting its use. We have only limited experience in preparing and filing the applications necessary to gain regulatory approvals. The process of obtaining regulatory approvals in the United States and other foreign jurisdictions 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. For example, before a New Drug Application, or NDA, or NDA supplement can be submitted to the FDA, or MAA to the EMA or any application or submission to regulatory authorities in other jurisdictions, the product candidate must undergo extensive clinical trials, which can take many years and require substantial expenditures.

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 Special Protocol Assessment, or 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;

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; and

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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 an NDA, 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 or regulatory authorities in other jurisdictions. 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 jurisdiction 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. For example, in connection with the FDA s approval of COMETRIQ for the treatment of progressive, metastatic MTC, we are subject to the various postmarketing requirements, including a requirement to conduct a phase 2 clinical trial comparing a lower dose of COMETRIQ to the approved dose of 140 mg daily COMETRIQ in progressive, metastatic MTC and to conduct other clinical pharmacology and preclinical studies. 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 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, GlaxoSmithKline, Merck (known as MSD outside of the United States and Canada) and Daiichi Sankyo, for the development and ultimate commercialization of a significant number of compounds generated from our research and development efforts. We may 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 may not be able to control the amount of U.S. marketing and commercialization costs for cobimetinib we are obligated to share under our collaboration with Genentech;

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we are not able to control the amount and timing of resources that our collaborators or potential future collaborators will devote to the development or commercialization of drug candidates or to their marketing and distribution;

collaborators may delay clinical trials, provide insufficient funding for a clinical trial program, stop a clinical trial or abandon a drug candidate, repeat or conduct new clinical trials or require a new formulation of a drug candidate for clinical testing;

disputes may arise between us and our collaborators that result in the delay or termination of the research, development or commercialization of our drug candidates or that result in costly litigation or arbitration that diverts management s attention and resources;

collaborators may experience financial difficulties;

collaborators may not be successful in their efforts to obtain regulatory approvals in a timely manner, or at all;

collaborators may not properly maintain or defend our intellectual property rights or may use our proprietary information in such a way as to invite litigation that could jeopardize or invalidate our proprietary information or expose us to potential litigation;

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 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 on 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 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, 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.

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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 Our Intellectual Property

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

Our success will depend in part upon our ability to obtain patents and maintain adequate protection of the intellectual property related to our technologies and products. The patent positions of biotechnology companies, including our patent position, are generally uncertain and involve complex legal and factual questions. We will be able to protect our intellectual property rights from unauthorized use by third parties only to the extent that our technologies are covered by valid and enforceable patents or are effectively maintained as trade secrets. We will continue to apply for patents covering our technologies and products as, where 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 closely related 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 our products or 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 some of 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.

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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 and the technologies of third parties. 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 or other biotechnology or pharmaceutical companies, including our competitors or potential competitors. We may be subject to claims that these employees, independent contractors or we have inadvertently or otherwise used or disclosed trade secrets or other proprietary information of their former employers, or used or sought to use patent inventions belonging to 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 we have engaged in 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.

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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, subject us to liability 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 subject us to liability and have a material adverse impact on our business, operating results and financial condition. Additionally, any break-in or trespass at 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 subject us to liability and 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.

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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 third parties 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 and commercial activities for cabozantinib in the amount of $15.0 million per occurrence and $15.0 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. 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 this Offering

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 development and commercialization activities;
- the commercial success of COMETRIQ and the revenues we generate;
- recognition of upfront licensing or other fees or revenues;
- payments of non-refundable upfront or licensing fees, or payment for cost-sharing expenses, to third parties;
- acceptance of our technologies and platforms;
- the success rate of our efforts leading to milestone payments and royalties;
- the introduction of new technologies or products by our competitors;

the timing and willingness of collaborators to further develop or, if approved, commercialize our product candidates 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 restructuring activities; 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 expiration or

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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 commercial success of COMETRIQ and the revenues we generate;
- 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 or conversion of our convertible notes, or the perception that such sales or conversions may occur, may depress our stock price.

A substantial number of shares of our common stock is reserved for issuance upon conversion of the 2019 Notes, upon the exercise of stock options, upon vesting of restricted stock unit awards, upon sales under our employee stock purchase program, upon exercise of certain warrants issued to Deerfield and upon conversion of the Deerfield Notes. The issuance and sale of substantial amounts of our common stock, including upon conversion of the 2019 Notes or the Deerfield Notes, 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 or equity-related securities in the future at a time and price that we deem appropriate. Trading of the 2019 Notes is likely to influence and be influenced by 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 2019 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.

The accounting method for convertible debt securities that may be settled in cash, such as the 2019 Notes, could have a material effect on our reported financial results.

Under Accounting Standards Codification, or ASC, Subtopic 470-20, issuers of certain convertible debt instruments that have a net settlement feature and may be settled in cash upon conversion, including partial cash settlement, are required to separately account for the liability (debt) and equity (conversion option) components of the instrument. As a result of the application of ASC 470-20, we recognized $143.2 million as the initial debt discount with a corresponding increase to paid-in capital, the equity component, for the 2019 Notes. We will be required to record the amortization of this debt discount over the terms of the 2019 Notes, which may adversely affect our reported or future financial results and the market price of our common stock. In addition, if the 2019 Notes become convertible, we could be required under applicable accounting rules to reclassify all or a portion of the outstanding principal of the 2019 Notes as a current rather than long-term liability, which would result in a material reduction of our net working capital. Finally, we use the if-converted method to compute earnings per share, which could be more dilutive than using the treasury stock method.

Certain provisions applicable to the 2019 Notes and the Deerfield Notes could delay or prevent an otherwise beneficial takeover or takeover attempt.

Certain provisions applicable to the 2019 Notes and the indenture pursuant to which the 2019 Notes were issued, and the Deerfield Notes and the note purchase agreement governing the Deerfield Notes, could make it more difficult or more expensive for a third party to acquire us. For example, if an acquisition event constitutes a Fundamental Change under the indenture for the 2019 Notes or a Major Transaction under the note purchase agreement governing the Deerfield Notes, holders of the 2019 Notes or the Deerfield Notes, applicable, will have the right to require us to purchase their notes in cash. In addition, if an acquisition event constitutes a Make-Whole Fundamental Change under the indenture for the 2019 Notes, we may be required to increase the conversion rate for holders who convert their

2019 Notes in connection with such Make-Whole Fundamental Change. In any of these cases, and in other cases, our obligations under the 2019 Notes and the indenture pursuant to which such notes were issued and the Deerfield Notes and the note purchase agreement governing the Deerfield Notes, as well as provisions of our organizational documents and other agreements, could increase the cost of acquiring us or otherwise discourage a third party from acquiring us or removing incumbent management.

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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;
- 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.

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 $8.24 per share, you will experience immediate dilution of $7.48 per share, representing the difference between the assumed public offering price and our as adjusted net tangible book value per share as of September 30, 2013, 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 may not use them effectively.

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

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FORWARD-LOOKING STATEMENTS

Some of the statements in this prospectus supplement, the accompanying prospectus, the documents incorporated by reference and any free writing prospectus that we have authorized for use in connection with this offering are forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, as amended, and Section 21E of the Securities Exchange Act of 1934, as amended. These statements 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 potential of other of our compounds or those of collaborators. 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 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-13 of this prospectus supplement, in the documents incorporated by reference, in any free writing prospectus that we have authorized for use in connection with this offering or as a result of other circumstances beyond our control. The forward-looking statements made in this prospectus supplement, the accompanying prospectus and any free writing prospectus that we have authorized for use in connection with this offering speak only as of the date on which the statements are made.

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USE OF PROCEEDS

Based upon an assumed public offering price of $8.24 per share, we estimate that the net proceeds from the sale of the 10,000,000 shares of common stock we are offering will be approximately $78.3 million, after deducting the estimated underwriting discount and estimated offering expenses payable by us. If the underwriter exercises in full its option to purchase additional shares, we estimate that the net proceeds to us will be approximately $90.1 million.

We will retain broad discretion over the use of the net proceeds from this offering. We currently expect to use the net proceeds from this offering for general corporate purposes, including for clinical trials, research and development, capital expenditures and working capital.

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

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
Fiscal Year Ended December 28, 2012		
Fiscal quarter ended March 30, 2012	$ 6.57	$ 4.47
Fiscal quarter ended June 29, 2012	5.59	4.37
Fiscal quarter ending September 28, 2012	6.95	4.19
Fiscal quarter ended December 28, 2012	5.39	4.29
Fiscal Year Ended December 27, 2013		
Fiscal quarter ended March 29, 2013	$ 5.06	$ 4.32
Fiscal quarter ended June 28, 2013	5.30	4.33
Fiscal quarter ended September 27, 2013	5.88	4.58
Fiscal quarter ended December 27, 2013	6.14	4.66
Fiscal Year Ending January 2, 2015		
Fiscal quarter ending March 28, 2014 (through January 21, 2014)	$ 8.38	$ 5.83

The reported last sale price of our common stock on the NASDAQ Global Select Market on January 21, 2014, was $8.24 per share. As of January 17, 2014, there were approximately 510 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 Silicon Valley Bank restricts our ability to pay dividends and make distributions. In addition, our note purchase agreement with Deerfield restricts our ability to make distributions.

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DILUTION

Our net tangible book value on September 30, 2013, was approximately $69.1 million, or approximately $0.38 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 September 30, 2013. 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 10,000,000 shares of common stock in this offering at an assumed public offering price of $8.24 per share (which was the last reported sale price of our common stock on January 21, 2014), and after deducting the estimated underwriting discount and estimated offering expenses payable by us, our net tangible book value on September 30, 2013, would have been approximately $147.4 million, or approximately $0.76 per share. This represents an immediate dilution of $7.48 per share to investors purchasing shares of common stock in this offering. The following table illustrates this dilution:

Assumed public offering price per share		$ 8.24
Net tangible book value per share as of September 30, 2013	$ 0.38	
Increase per share attributable to new investors	0.38	
Net tangible book value per share as of September 30, 2013, after giving effect to this offering		0.76
Dilution per share to investors in this offering		$ 7.48

The foregoing discussion and table do not take into account further dilution to new investors that could occur upon the exercise of the underwriter s option to purchase up to an additional 1,500,000 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 underwriter exercises in full its option to purchase 1,500,000 additional shares, our net tangible book value on September 30, 2013, after giving effect to this offering, would have been approximately $159.2 million, or approximately $0.81 per share, representing an immediate dilution of $7.43 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 $8.24 per share would increase (decrease) our as adjusted net tangible book value by $4.8 million, or $0.02 per share, and the dilution per share to investors in this offering by $0.48 per share, assuming that the number of shares offered by us, as set forth on the cover page of this prospectus supplement, remains the same and after deducting the estimated underwriting discount and estimated offering expenses payable by us. We may also increase or decrease the number of shares we are offering. An increase of 500,000 shares in the number of shares offered by us, to a total of 10,500,000 million shares, together with a concomitant $0.50 increase in the assumed public offering price of $8.24 per share, would increase our as adjusted net tangible book value by $8.9 million, or $0.04 per share, and the dilution per share to investors in this offering by $0.46 per share. Similarly, a decrease of 500,000 shares in the number of shares offered by us, to a total of 9,500,000 million shares, together with a concomitant $0.50 decrease in the assumed public offering price of $8.24 per share, would decrease our as adjusted net tangible book value by $8.5 million, or $0.04 per share, and the dilution per share to investors in this offering by $0.46 per share. The as adjusted information discussed above is illustrative only and will be adjusted based on the actual public offering price and other terms of this offering determined at pricing.

The number of shares of common stock to be outstanding after the offering is based on the number of shares outstanding as of September 30, 2013. As of that date, we had 184,194,124 shares of common stock outstanding,

excluding:

- 23,509,515 shares of common stock underlying options outstanding as of September 30, 2013, at a weighted average exercise price of $6.50 per share;

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1,441,215 shares of common stock underlying warrants outstanding as of September 30, 2013, at a weighted average exercise price of $6.99 per share;

2,051,098 shares reserved for future issuance pursuant to unvested restricted stock units as of September 30, 2013;

1,489,683 shares available for future grant under our 2011 Equity Incentive Plan, 2,164,717 shares available for future purchase under our 2000 Employee Stock Purchase Plan, 732,656 shares available for future grant under our 2000 Non-Employee Directors Stock Option Plan, and 384,255 shares available for future grant under our 401(k) Retirement Plan, all as of September 30, 2013; and

54,117,649 shares of common stock reserved for issuance upon conversion of the outstanding 2019 Notes.

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.

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CAPITALIZATION

The following table sets forth our capitalization as of September 30, 2013:

- on an actual basis; and
- on an as adjusted basis to give effect to the receipt of the estimated net proceeds of $78.3 million from the sale of the common stock in this offering (assuming no exercise of the underwriter s option to purchase additional shares) at an assumed public offering price of $8.24 per share, after deducting the estimated underwriting discount 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, 2012, 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 September 30, 2013, which are incorporated by reference into this prospectus supplement.

	As of September 30, 2013	
(In thousands, except share and per share amounts)	**Actual**	**As Adjusted(1)(2)**
Current portion of debt obligations under the loan and security agreement with Silicon Valley Bank	$ 2,127	$ 2,127
Current portion of debt obligations under the Deerfield Notes	$ 10,000	$ 10,000
Long-term debt, less current portion:		
4.25% Convertible senior subordinated notes due 2019	$ 161,279	$ 161,279
Long-term portion of debt obligations under the loan and security agreement with Silicon Valley Bank	$ 80,757	$ 80,757
Long-term portion of debt obligations under the Deerfield Notes	$ 87,428	$ 87,428
Total long-term debt	$ 329,464	$ 329,464
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; 184,194,124 shares issued and outstanding, actual, 194,194,124 shares issued and outstanding as adjusted(2)	184	194
Additional paid-in capital	1,560,415	1,638,712
Accumulated other comprehensive income	180	180
Accumulated deficit	(1,428,016)	(1,428,016)

Total stockholders equity	132,763	211,070
Total capitalization	$ 462,227	$ 540,534

(1) As adjusted to reflect the sale of 10,000,000 shares being offered in this offering and the receipt of the estimated net proceeds of $78.3 million from the sale of these shares, assuming a public offering price of $8.24 per share and after deducting the estimated underwriting discount and estimated offering expenses payable by us.

(2) The common stock shown as issued and outstanding in the table above is based on 184,194,124 shares of common stock outstanding as of September 30, 2013, and excludes the shares of common stock reserved for issuance upon conversion of the 2019 Notes, and also excludes, as of September 30, 2013: (i) 23,509,515 shares of common stock issuable upon the exercise of outstanding stock options, having a weighted average exercise price of $6.50 per share; (ii) 1,441,215 shares of common stock underlying warrants outstanding as

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of September 30, 2013, at a weighted average exercise price of $6.99 per share; (iii) 2,051,098 shares of common stock issuable upon the vesting of outstanding restricted stock units, stock appreciation rights and performance share awards; (iv) an aggregate of up to 4,771,311 shares of common stock reserved for future issuance under our equity incentive plans and our 401(k) retirement plan; and (v) 54,117,649 shares of common stock reserved for issuance upon conversion of the 2019 Notes.

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

The following summary describes the material U.S. federal income tax consequences of the acquisition, ownership and disposition of our common stock acquired in this offering by Non-U.S. Holders (as defined below). This discussion does not address all aspects of U.S. federal income tax and does not deal with foreign, state and local consequences that may be relevant to Non-U.S. Holders in light of their particular circumstances, nor does it address U.S. federal tax consequences other than income taxes. Special rules different from those described below may apply to certain Non-U.S. Holders that are subject to special treatment under the Internal Revenue Code of 1986, as amended, or 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 or other risk reduction strategy persons subject to the alternative minimum tax or Medicare contribution tax, partnerships and other pass-through entities, and investors in such pass-through entities. Such Non-U.S. Holders are urged to consult their own tax advisors to determine the U.S. federal, state, local and other tax consequences that may be relevant to them. Furthermore, the discussion below is based upon the provisions of the Code, and Treasury regulations, rulings and judicial decisions thereunder as of the date hereof, and such authorities may be repealed, revoked or modified, perhaps retroactively, so as to result in U.S. federal income tax consequences different from those discussed below. We have not requested a ruling from the U.S. Internal Revenue Service, or IRS, with respect to the statements made and the conclusions reached in the following summary, and there can be no assurance that the IRS will agree with such statements and conclusions. This discussion assumes that the Non-U.S. Holder holds our common stock as a capital asset within the meaning of Section 1221 of the Code (generally, property held for investment).

Persons considering the purchase of our common stock pursuant to this offering should consult their own tax advisors concerning the U.S. federal income and tax consequences of acquiring, owning and disposing of our common stock in light of their particular situations as well as any consequences arising under the laws of any other taxing jurisdiction, including any state, local or foreign tax consequences.

For the purposes of this discussion, a Non-U.S. Holder is, for U.S. federal income tax purposes, a beneficial owner of common stock that is neither a U.S. Holder, nor a partnership (or other entity treated as a partnership for U.S. federal income tax purposes regardless of its place of organization or formation). A U.S. Holder means a beneficial owner of our common stock that is for U.S. federal income tax purposes (a) an individual who is a citizen or resident of the U.S., (b) a corporation or other entity treated as a corporation created or organized in or under the laws of the U.S., any state thereof or the District of Columbia, (c) an estate the income of which is subject to U.S. federal income taxation regardless of its source or (d) a trust if it (1) is subject to the primary supervision of a court within the U.S. and one or more U.S. persons have the authority to control all substantial decisions of the trust or (2) has a valid election in effect under applicable U.S. Treasury regulations to be treated as a U.S. person.

Distributions

Subject to the discussion below, distributions, if any, made on our common stock to a Non-U.S. Holder of our common stock to the extent made out of our current or accumulated earnings and profits (as determined under U.S. federal income tax principles) generally will constitute dividends for U.S. tax purposes and will be subject to withholding tax at a 30% rate or such lower rate as may be specified by an applicable income tax treaty. To obtain a reduced rate of withholding under a treaty, a Non-U.S. Holder generally will be required to provide us with a properly executed IRS Form W-8BEN, or other appropriate form, certifying the Non-U.S. Holder s entitlement to benefits under that treaty. In the case of a Non-U.S. Holder that is an entity, Treasury Regulations and the relevant tax treaty provide rules to determine whether, for purposes of determining the applicability of a tax treaty, dividends will be treated as

paid to the entity or to those holding an interest in that entity. If a Non-U.S. Holder holds stock through a financial institution or other agent acting on the holder s behalf, the holder will be required to provide appropriate documentation to such agent. The holder s agent will then be required to provide certification to us or our paying agent, either directly or through other intermediaries.

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If you are eligible for a reduced rate of U.S. federal withholding tax under an income tax treaty, you may be able to obtain a refund or credit of any excess amounts withheld by timely filing an appropriate claim for a refund with the IRS.

We generally are not required to withhold tax on dividends paid to a Non-U.S. Holder that are effectively connected with the Non-U.S. Holder s conduct of a trade or business within the U.S. (and, if required by an applicable income tax treaty, are attributable to a permanent establishment that such holder maintains in the U.S.) if a properly executed IRS Form W-8ECI, stating that the dividends are so connected, is furnished to us (or, if stock is held through a financial institution or other agent, to such agent). In general, such effectively connected dividends will be subject to U.S. federal income tax, on a net income basis at the regular graduated rates applicable to U.S. residents. A corporate Non-U.S. Holder receiving effectively connected dividends may also be subject to an additional branch profits tax, which is imposed, under certain circumstances, at a rate of 30% (or such lower rate as may be specified by an applicable treaty) on the corporate Non-U.S. Holder s effectively connected earnings and profits, subject to certain adjustments.

To the extent distributions on our common stock, if any, exceed our current and accumulated earnings and profits, they will first reduce the Non-U.S. Holder s adjusted basis in our common stock, but not below zero, and then will be treated as gain to the extent of any excess, and taxed in the same manner as gain realized from a sale or other disposition of common stock as described in the next section.

Gain on Disposition of Our Common Stock

Subject to the discussion below regarding backup withholding and foreign accounts, a Non-U.S. Holder generally will not be subject to U.S. federal income tax with respect to gain realized on a sale or other disposition of our common stock unless (a) the gain is effectively connected with a trade or business of such holder in the U.S. (and, if required by an applicable income tax treaty, is attributable to a permanent establishment that such holder maintains in the U.S.), (b) the Non-U.S. Holder is a nonresident alien individual and is present in the U.S. for 183 or more days in the taxable year of the disposition and certain other conditions are met or (c) we are or have been a United States real property holding corporation within the meaning of Code Section 897(c)(2) at any time within the shorter of the five-year period preceding such disposition or such holder s holding period. In general, we would be a U.S. real property holding corporation if interests in U.S. real estate comprised (by fair market value) at least half of our business assets. We believe that we have not been, we are not, and do not anticipate becoming, a U.S. real property holding corporation. Even if we are treated as a U.S. real property holding corporation, gain realized by a Non-U.S. Holder on a disposition of our common stock will not be subject to U.S. federal income tax so long as (1) the Non-U.S. Holder owned, directly, indirectly and constructively, no more than five percent of our common stock at all times within the shorter of (i) the five-year period preceding the disposition or (ii) the holder s holding period and (2) our common stock is regularly traded on an established securities market. There can be no assurance that our common stock will continue to qualify as regularly traded on an established securities market.

If you are a Non-U.S. Holder described in (a) above, you will be required to pay tax on the net gain derived from the sale at regular graduated U.S. federal income tax rates, and corporate Non-U.S. Holders described in (a) above may be subject to the additional branch profits tax at a 30% rate or such lower rate as may be specified by an applicable income tax treaty. If you are an individual Non-U.S. Holder described in (b) above, you will be required to pay a flat 30% tax on the gain derived from the sale, which gain may be offset by U.S. source capital losses (even though you are not considered a resident of the U.S.).

Information Reporting Requirements and Backup Withholding

Generally, we must report information to the IRS with respect to any dividends we pay on our common stock (even if the payments are exempt from withholding), including the amount of any such dividends, the name and address of the recipient, and the amount, if any, of tax withheld. A similar report is sent to the holder to whom any such dividends are paid. Pursuant to tax treaties or certain other agreements, the IRS may make its reports available to tax authorities in the recipient s country of residence.

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Dividends paid by us (or our paying agents) to a Non-U.S. Holder may also be subject to U.S. backup withholding. U.S. backup withholding generally will not apply to a Non-U.S. Holder who provides a properly executed IRS Form W-8BEN or otherwise establishes an exemption.

Under current U.S. federal income tax law, U.S. information reporting and backup withholding requirements generally will apply to the proceeds of a disposition of our common stock effected by or through a U.S. office of any broker, U.S. or foreign, except that information reporting and such requirements may be avoided if the holder provides a properly executed IRS Form W-8BEN or otherwise meets documentary evidence requirements for establishing Non-U.S. Holder status or otherwise establishes an exemption. Generally, U.S. information reporting and backup withholding requirements will not apply to a payment of disposition proceeds to a Non-U.S. Holder where the transaction is effected outside the U.S. through a non-U.S. office of a non-U.S. broker. Information reporting and backup withholding requirements may, however, apply to a payment of disposition proceeds if the broker has actual knowledge, or reason to know, that the holder is, in fact, a U.S. person. For information reporting purposes, certain brokers with substantial U.S. ownership or operations will generally be treated in a manner similar to U.S. brokers.

Any amounts of tax withheld under the backup withholding rules may be credited against the tax liability of persons subject to backup withholding, provided that the required information is timely furnished to the IRS.

Foreign Accounts

A U.S. federal withholding tax of 30% may apply on dividends on and the gross proceeds of a disposition of our common stock paid to a foreign financial institution (as specifically defined by applicable rules) unless such institution enters into an agreement with the U.S. government to withhold on certain payments and to collect and provide to the U.S. tax authorities substantial information regarding U.S. account holders of such institution (which includes certain equity holders of such institution, as well as certain account holders that are foreign entities with U.S. owners). This U.S. federal withholding tax of 30% will also apply on dividends on and the gross proceeds of a disposition of our common stock to a non-financial foreign entity unless such entity provides the withholding agent with either a certification that it does not have any substantial direct or indirect U.S. owners or provides information regarding substantial direct and indirect U.S. owners of the entity. The withholding tax described above will not apply if the foreign financial institution or non-financial foreign entity otherwise qualifies for an exemption from the rules. Under certain circumstances, a Non-U.S. Holder might be eligible for refunds or credits of such taxes. Holders are encouraged to consult with their own tax advisors regarding the possible implications of these rules for their investment in our common stock.

The IRS has issued guidance providing that the withholding provisions described above will generally apply to payments of dividends made on or after July 1, 2014, and to payments of gross proceeds from a sale or other disposition of common stock on or after January 1, 2017.

EACH PROSPECTIVE INVESTOR SHOULD CONSULT ITS OWN TAX ADVISOR REGARDING THE TAX CONSEQUENCES OF PURCHASING, HOLDING AND DISPOSING OF OUR COMMON STOCK, INCLUDING THE CONSEQUENCES OF ANY PROPOSED CHANGE IN APPLICABLE LAW.

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UNDERWRITING

We and Cowen and Company, LLC have entered into an underwriting agreement with respect to the common stock being offered. Subject to the terms and conditions of the underwriting agreement, Cowen and Company, LLC, as the underwriter for the offering, has agreed to purchase from us 10,000,000 shares of our common stock.

The underwriting agreement provides that the obligations of the underwriter are subject to certain conditions precedent and that the underwriter has agreed to purchase all of the shares sold under the underwriting agreement if any of these shares are purchased, other than those shares covered by the overallotment option described below.

We have agreed to indemnify the underwriter against specified liabilities, including liabilities under the Securities Act of 1933, and to contribute to payments the underwriter may be required to make in respect thereof.

The underwriter is offering the shares, subject to prior sale, when, as and if issued to and accepted by it, subject to conditions specified in the underwriting agreement. The underwriter reserves the right to withdraw, cancel or modify offers to the public and to reject orders in whole or in part.

Overallotment Option to Purchase Additional Shares. We have granted to the underwriter an option to purchase up to 1,500,000 additional shares of common stock at the public offering price, less the underwriting discount. This option is exercisable for a period of 30 days.

Discounts and Commissions. The following table shows the public offering price, underwriting discount and proceeds, before expenses, to us. These amounts are shown assuming both no exercise and full exercise of the underwriter s option to purchase additional shares.

We estimate that our share of the total expenses of the offering, excluding the underwriting discount, will be approximately $385,000.

	Per Share	Total Without Overallotment	With Overallotment
Public offering price			
Underwriting discount			
Proceeds, before expenses, to Exelixis			

The underwriter proposes to offer the shares of common stock to the public at the public offering price set forth on the cover page of this prospectus supplement. The underwriter may offer the shares of common stock to securities dealers at the public offering price less a concession not in excess of $ per share. If all of the shares are not sold at the public offering price, the underwriter may change the offering price and other selling terms.

Discretionary Accounts. The underwriter does not intend to confirm sales of the shares to any accounts over which it has discretionary authority.

Stabilization. In connection with this offering, the underwriter may engage in stabilizing transactions, overallotment transactions, covering transactions and purchases to cover positions created by short sales.

Stabilizing transactions permit bids to purchase shares of common stock so long as the stabilizing bids do not exceed a specified maximum, and are engaged in for the purpose of preventing or retarding a decline in the market price of the common stock while the offering is in progress.

Overallotment transactions involve sales by the underwriter of shares of common stock in excess of the number of shares the underwriter is obligated to purchase. This creates a short position which may be either a covered short position or a naked short position. In a covered short position, the number of shares over-allotted by the underwriter is not greater than the number of shares that it may purchase in the overallotment option. In a naked short position, the number of shares involved is greater than the number

of shares in the overallotment option. The underwriter may close out any short position by exercising its overallotment option and/or purchasing shares in the open market.

Covering transactions involve purchases of common stock in the open market after the distribution has been completed in order to cover short positions. In determining the source of shares to close out the short position, the underwriter will consider, among other things, the price of shares available for purchase in the open market as compared with the price at which it may purchase shares through exercise of the overallotment option. If the underwriter sells more shares than could be covered by exercise of the overallotment option and, therefore, has a naked short position, the position can be closed out only by buying shares in the open market. A naked short position is more likely to be created if the underwriter is concerned that after pricing there could be downward pressure on the price of the shares in the open market that could adversely affect investors who purchase in the offering.

These transactions may have the effect of raising or maintaining the market price of our common stock or preventing or retarding a decline in the market price of our common stock. As a result, the price of our common stock in the open market may be higher than it would otherwise be in the absence of these transactions. Neither we nor the underwriter makes any representation or prediction as to the effect that the transactions described above may have on the price of our common stock. These transactions may be effected on the Nasdaq Stock Market, in the over-the-counter market or otherwise and, if commenced, may be discontinued at any time.

Passive Market Making. In connection with this offering, the underwriter and selling group members may engage in passive market making transactions in our common stock on the Nasdaq Stock Market in accordance with Rule 103 of Regulation M under the Securities Exchange Act of 1934, as amended, during a period before the commencement of offers or sales of common stock and extending through the completion of the distribution. A passive market maker must display its bid at a price not in excess of the highest independent bid of that security. However, if all independent bids are lowered below the passive market maker s bid, that bid must then be lowered when specified purchase limits are exceeded.

Lock-Up Agreements. Pursuant to certain lock-up agreements, we and our executive officers and directors have agreed, subject to certain exceptions, not to offer, sell, contract to sell, grant any option to purchase or otherwise transfer or dispose of, and in our case, also not to file with the SEC a registration statement under the Securities Act or publicly disclose the intention to make any offer, sale, grant, transfer, disposition or filing relating to, any shares of common stock, or any options or warrants to purchase any shares of common stock, or any securities convertible into, exchangeable for or that represent the right to receive shares of common stock without the prior written consent of Cowen and Company, LLC, for a period of 90 days after the date of the pricing of the offering.

The lock-up agreements apply to common stock, or any options or warrants to purchase any shares of common stock, or any securities convertible into, exchangeable for or that represent the right to receive shares of common stock. In the case of our executive officers and directors, the lock-up agreements also apply to common stock owned now or acquired later by the person executing the agreement or for which the person executing the agreement now possesses or later acquires the power of disposition. The exceptions permit us, among other things and subject to restrictions, to: (a) issue common stock or options pursuant to employee benefit plans, (b) issue common stock upon exercise of outstanding options or warrants, (c) following the date 45 days after the date of this prospectus supplement, issue up to an aggregate of 10% of our outstanding common stock (as of immediately after this offering) in connection with any strategic transaction that includes a commercial relationship involving us and other entities, provided that the recipients of such stock shall be bound by the transfer restrictions described in this and the previous paragraph, or (d) file a shelf registration statement and any related prospectus supplement for the purpose of registering for resale up to 1,000,000 shares of our common stock issuable pursuant to warrants issued to Deerfield Partners, L.P. and

Deerfield International Master Fund, L.P. or any of their affiliated entities. The exceptions permit our executive officers and directors, among other things and subject to restrictions, to: (a) make certain gifts, (b) make certain transfers to trusts for the direct or indirect benefit of the person executing the agreement or the immediate family of the person executing the agreement, and (c) in the case of some individuals, make 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.

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Cowen and Company, LLC, in its sole discretion, may release our common stock and other securities subject to the lock-up agreements described above in whole or in part at any time. When determining whether or not to release our common stock and other securities from lock-up agreements, Cowen and Company, LLC will consider, among other factors, the holder s reasons for requesting the release, the number of shares for which the release is being requested and market conditions at the time of the request.

United Kingdom. The underwriter has represented and agreed that:

- it has not made or will not make an offer of the securities to the public in the United Kingdom within the meaning of section 102B of the Financial Services and Markets Act 2000 (as amended) (FSMA) except 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 or otherwise in circumstances which do not require the publication by us of a prospectus pursuant to the Prospectus Rules of the Financial Services Authority (FSA);

- 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 FSMA) to persons who have professional experience in matters relating to investments falling within Article 19(5) of the Financial Services and Markets Act 2000 (Financial Promotion) Order 2005 or in circumstances in which section 21 of FSMA does not apply to us; and

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

Switzerland. The securities will not be offered, directly or indirectly, to the public in Switzerland and this prospectus supplement and the accompanying prospectus do not constitute a public offering prospectus as that term is understood pursuant to article 652a or 1156 of the Swiss Federal Code of Obligations.

European Economic Area. In relation to each Member State of the European Economic Area (the EEA) which has implemented the European Prospectus Directive (each, a Relevant Member State), an offer of our shares may not be made to the public in a Relevant Member State other than:

- to any legal entity which is a qualified investor, as defined in the European Prospectus Directive;

- to fewer than 100 or, if the Relevant Member State has implemented the relevant provision of the 2010 PD Amending Directive, 150 natural or legal persons (other than qualified investors as defined in the European Prospectus Directive), subject to obtaining the prior consent of the relevant dealer or dealers nominated by us for any such offer, or;

- in any other circumstances falling within Article 3(2) of the European Prospectus Directive,

provided that no such offer of our shares shall require us or the underwriter to publish a prospectus pursuant to Article 3 of the European Prospectus Directive or supplement prospectus pursuant to Article 16 of the European Prospectus Directive.

For the purposes of this description, the expression an offer to the public in relation to the securities 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 securities to be offered so as to enable an investor to decide to purchase or subscribe for the securities, as the expression may be varied in that Relevant Member State by any measure implementing the European Prospectus Directive in that member state, and the expression European Prospectus Directive means Directive 2003/71/EC (and amendments hereto, including the 2010 PD Amending Directive, to the extent implemented in the Relevant Member State) and includes any relevant implementing measure in each Relevant Member State. The expression 2010 PD Amending Directive means Directive 2010/73/EU.

We have not authorized and do not authorize the making of any offer of securities through any financial intermediary on our behalf, other than offers made by the underwriter and its respective affiliates, with a view to the final placement of the securities as contemplated in this document. Accordingly, no purchaser of the shares, other than the underwriter, is authorized to make any further offer of shares on our behalf or on behalf of the underwriter.

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Electronic Offer, Sale and Distribution of Shares. A prospectus in electronic format may be made available on the websites maintained by the underwriter or selling group members, if any, participating in this offering and the underwriter may distribute prospectuses electronically. The underwriter may allocate a number of shares to itself and selling group members for sale to their online brokerage account holders. Internet distributions will be allocated by the underwriter and selling group members that will make internet distributions on the same basis as other allocations. Other than the prospectus in electronic format, the information on these websites is not part of this prospectus supplement or the accompanying prospectus or the registration statement of which this prospectus supplement and the accompanying prospectus form a part, has not been approved or endorsed by us or the underwriter in its capacity as underwriter, and should not be relied upon by investors.

Other Relationships. The underwriter and its affiliates have provided, and may in the future provide, various investment banking and/or commercial banking and other financial services for us and our affiliates for which they have received, and may in the future receive, customary fees.

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VALIDITY OF COMMON STOCK

The validity of the common stock offered hereby will be passed upon for us by Cooley LLP, San Francisco, California, and for the underwriter 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, 2012, and the effectiveness of our internal control over financial reporting as of December 31, 2012, 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.

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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 supplement and the accompanying prospectus. Information in this prospectus supplement supersedes information in the accompanying prospectus or incorporated by reference that we filed with the SEC prior to the date of this prospectus supplement, while information that we file later with the SEC will automatically update and supersede the information in this prospectus supplement and the accompanying prospectus. We incorporate by reference into this prospectus supplement, the accompanying 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 fiscal year ended December 28, 2012, filed on February 21, 2013;
- the information specifically incorporated by reference into our Annual Report on Form 10-K for the fiscal year ended December 28, 2012, from our definitive proxy statement on Schedule 14A filed on April 10, 2013;
- our Quarterly Reports on Form 10-Q filed on May 7, 2013, August 6, 2013, and October 30, 2013;
- our Current Reports on Form 8-K filed on January 16, 2013, January 25, 2013, February 8, 2013, May 23, 2013, September 19, 2013, September 20, 2013, November 22, 2013, December 2, 2013, December 20, 2013, and January 22, 2014; 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, until we file a post-effective amendment that indicates the termination of the offering of the securities made by this prospectus supplement and the accompanying prospectus, and such future filings will become a part of this prospectus supplement and the accompanying 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 supplement and the accompanying 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: Corporate Secretary

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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 informatio