EXELIXIS, INC.
Form 424B5
July 24, 2015
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Filed Pursuant to Rule 424(b)(5)

Registration No. 333-205397

CALCULATION OF REGISTRATION FEE

Title of each class of Securities to be registered(1)	Aggregate Offering Price	Registration Fee(2)
Common Stock, par value $0.001 per share	$155,250,000	$18,041

(1) There are being registered hereunder such number of shares of Common Stock as shall have an aggregate offering price not to exceed $155,250,000.
(2) The registration fee is calculated in accordance with Rule 457(o) and 457(r) under the Securities Act of 1933, as amended.

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PROSPECTUS SUPPLEMENT
(To Prospectus dated July 1, 2015)

25,000,000 Shares

Common Stock

We are offering 25,000,000 shares of our common stock. Our common stock is quoted on The NASDAQ Global Select Market under the symbol EXEL. On July 23, 2015, the last reported sale price of our common stock was $5.88 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-16 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	**$ 5.400**	**$ 135,000,000**
Underwriting discount	**$ 0.324**	**$ 8,100,000**
Proceeds, before expenses, to Exelixis	**$ 5.076**	**$ 126,900,000**

The underwriters may also purchase up to an additional 3,750,000 shares from us at the public offering price, less the underwriting discount, within 30 days from the date of this prospectus supplement.

The underwriters expect to deliver the shares against payment in New York, New York on July 29, 2015.

Cowen and Company **William Blair** **Stifel**
July 23, 2015

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Prospectus

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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 July 1, 2015, 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; it 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 biopharmaceutical company committed to developing small molecule therapies for the treatment of cancer. Our two most advanced assets are cabozantinib, our wholly-owned inhibitor of multiple receptor tyrosine kinases, and cobimetinib (GDC-0973/XL518), a selective inhibitor of MEK, a serine/threonine kinase, which we out-licensed to Genentech, Inc. (a member of the Roche Group), or Genentech.

Our development and commercialization efforts are focused primarily on cabozantinib. We are evaluating cabozantinib in a broad development program comprising over forty-five clinical trials, across multiple indications, including two ongoing phase 3 pivotal trials focusing on metastatic renal cell carcinoma, or mRCC, and advanced hepatocellular carcinoma, or HCC. On April 8, 2015, the United States Food and Drug Administration, or FDA, granted Fast Track designation to cabozantinib for the treatment of patients with advanced mRCC, who have received one prior therapy. On July 20, 2015, we announced positive top-line results from the primary analysis of METEOR, the phase 3 pivotal trial comparing cabozantinib to everolimus in 658 patients who experienced disease progression following treatment with a VEGF receptor tyrosine kinase inhibitor, or TKI. The trial demonstrated a statistically significant increase in PFS for cabozantinib over everolimus, reduced the risk of disease progression or death by 42 percent compared to the everolimus arm, and showed a positive trend for the secondary endpoint of overall survival. The trial will continue to the final analysis of overall survival, or OS, anticipated in 2016. Detailed results will be submitted for presentation at an upcoming medical conference. A review of serious adverse event (SAE) data demonstrated that the frequency of SAEs of any Grade regardless of causality was approximately balanced between study arms and the rate of treatment discontinuation due to adverse events was low (10%) in both study arms.

We expect top-line results from CELESTIAL, our phase 3 pivotal trial in advanced HCC, in 2017.

Cabozantinib was approved by the FDA on November 29, 2012, for the treatment of progressive, metastatic medullary thyroid cancer, or MTC, in the United States under the brand name COMETRIQ®. COMETRIQ became commercially available in the United States in January 2013. In March 2014, the European Commission granted cabozantinib conditional marketing authorization for the treatment of adult patients with progressive, unresectable locally advanced or metastatic MTC, also under the brand name COMETRIQ.

Our second most advanced oncology asset, cobimetinib, is being evaluated by Genentech in a broad development program, including coBRIM, a phase 3 pivotal trial evaluating cobimetinib in combination with vemurafenib versus vemurafenib alone in previously untreated patients with

unresectable locally advanced melanoma harboring a BRAF V600 mutation. On September 29, 2014, positive results from this trial were reported at the European Society for Medical Oncology, or ESMO, 2014 Congress. The trial met its primary endpoint of demonstrating a statistically significant increase in investigator-determined progression free survival, or PFS, for cobimetinib in combination with vemurafenib versus vemurafenib alone. Roche has completed the Marketing Authorization Application, or MAA, for cobimetinib in combination with vemurafenib in the European Union. In the United States, Genentech submitted its New Drug Application, or NDA, in December 2014 and the FDA granted the NDA priority review with a projected action date of August 11, 2015. On June 30, 2015, Genentech informed us that, in order to accommodate its review of a supplemental data submission the FDA extended the projected action date for its review of the cobimetinib NDA by the standard extension period of three months, to November 11, 2015.

Our Strategy

Our business strategy focuses predominantly on two Exelixis-discovered compounds, cabozantinib and cobimetinib. Cabozantinib is wholly owned by Exelixis. We are pursuing development and commercialization in multiple tumor indications. Cobimetinib is partnered with Genentech, which is solely responsible for its development and commercialization, although we have exercised our option to co-promote the drug with Genentech in the US.

Cabozantinib is an inhibitor of the activity of tyrosine kinases, including MET, VEGF receptors, AXL and RET. 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. We believe that cabozantinib has the potential to make a meaningful difference in the lives of patients and we believe the emerging clinical data support such a view. Our objective, therefore, is to build cabozantinib into a significant oncology franchise as a single agent, and potentially in combination with other therapies.

Cabozantinib s first regulatory approvals, in the U.S. and EU as COMETRIQ capsules for MTC, presented us with a valuable opportunity to gain experience commercializing this new compound. The results of METEOR in mRCC now offer an opportunity to commercialize cabozantinib more broadly in a tablet formulation in a significantly larger market. We are seeking to partner cabozantinib with a global pharmaceutical organization whose international resources will permit us to explore and exploit the potential opportunity cabozantinib presents on its own and in combination with other agents, in RCC, HCC, and other potential indications.

On the development front, 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, have permitted us to engage with leading clinicians to expand our collective understanding of cabozantinib s potential, while also conserving our internal resources for late stage trials. We believe this staged approach to building cabozantinib s value with a far lesser upfront expenditure of funds has been rational and cost-effective.

A second Exelixis-discovered compound, cobimetinib, a selective inhibitor of MEK, is being developed under a collaboration with Genentech. Following the positive results from the coBRIM phase 3 trial of cobimetinib plus vemurafenib vs vemurafenib alone in BRAF mutation positive metastatic melanoma patients, we exercised our option to co-promote cobimetinib in the US to provide the opportunity for us to further build our commercialization experience in oncology. Genentech is pursuing a broad development program for cobimetinib in combination with multiple agents in its oncology pipeline, including immuno-oncology agents. These studies seek to expand the potential use of cobimetinib in additional melanoma patient populations and into other significant tumor types including NSCLC and CRC. We believe that cobimetinib has the potential to provide us with a second significant source of revenue.

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Beyond our efforts regarding cabozantinib and cobimetinib, we are working with our corporate partners under the terms of our various collaboration agreements to realize the potential value of the compounds and programs we have out-licensed to them. In the aggregate, these partnered compounds could potentially be of significant value to us if their development programs progress successfully.

COMETRIQ (cabozantinib)

The recommended dose of COMETRIQ capsules for progressive, metastatic MTC is 140 mg orally, once daily (one 80 mg capsule and three 20 mg capsules) administered without food. The dose may be withheld in response to certain adverse reactions, and upon resolution of adverse reactions may be reduced stepwise to 100 or 60 mg once daily to adjust to each individual patient s tolerability. Permanent discontinuation is recommended for certain adverse reactions.

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 confirmed by an Independent Radiology Review Committee, or IRRC. This assessment was performed by the 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 TKI. 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 OS. 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 (RECIST) (a widely used set of rules that define when cancer patients improve (respond), stay the same (stabilize) or worsen (progress) during treatments).

EXAM served as the basis for the regulatory approval of COMETRIQ in the U.S. and EU for the treatment of MTC. 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.

In November 2014, we completed the OS analysis for EXAM, a secondary endpoint of the study. Consistent with an earlier interim analysis, there was no statistically significant difference in OS between the treatment arms. The median OS was 26.6 months for the COMETRQ arm and 21.1 months for the placebo arm (HR = 0.85; 95% CI 0.64, 1.12; p = 0.2409). The subgroup analysis by

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RET M918T mutation status, a known negative prognostic factor in MTC, revealed a large improvement in OS of 25.4 months for COMETRIQ-treated patients who were positive for the RET M918T mutation; the median OS was 44.3 months for the COMETRIQ arm and 18.9 months for the placebo arm (HR = 0.60; 95% CI 0.38, 0.95; p = 0.026, not adjusted for multiple subgroup testing). The final results were presented at the 2015 annual meeting of the American Society for Clinical Oncology, or ASCO, and will be submitted to regulatory authorities to satisfy post-marketing commitments.

Post-marketing Commitments

In connection with the approval of COMETRIQ for the treatment of progressive, metastatic MTC, we are subject to the following postmarketing requirements:

- A clinical 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.
- Submission of the overall survival analysis from the EXAM study (see above).
- Two clinical pharmacology studies assessing the pharmacokinetics of COMETRIQ, one to address the effect of administering COMETRIQ in conjunction with agents that increase gastric pH such as proton pump inhibitors, and the other to assess the pharmacokinetics of COMETRIQ in patients with hepatic impairment. Both studies have been completed.
- Four non-clinical studies to further assess the carcinogenicity, mutagenicity and teratogenicity of cabozantinib. The mutagenicity and teratogenicity studies have been completed.

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 May 25, 2015, the wholesale acquisition cost of COMETRIQ is $12,995 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 designed our commercial organization to maintain flexibility in response to market opportunities. At present, our commercial organization is sized at a level commensurate with the size of the market opportunity for progressive, metastatic MTC. We expect to be able to scale up quickly if additional indications for cabozantinib are approved in the future. We believe the design of our commercial organization is efficient, 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 do not 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 of COMETRIQ, our Medical Affairs department is responsible for responding to unsolicited physician inquiries with appropriate scientific and medical information, preparing scientific presentations and publications, and overseeing the process for IST concept review and support.

EMA Marketing Authorization Application for COMETRIQ

In February 2009 COMETRIQ received orphan drug designation in the European Union from the Committee for Orphan Medicinal Products for the treatment of MTC. The European Commission granted COMETRIQ conditional approval for the treatment of adult patients with progressive, unresectable, locally advanced, or metastatic MTC in March 2014. Similar to another drug approved in this setting, the approved COMETRIQ indication in Europe states that for patients in which RET mutation status is not known or is negative, a possible lower benefit should be taken into account before individual treatment decisions.

During 2013, we entered into an agreement with Swedish Orphan Biovitrum, or Sobi, to support the distribution and commercialization of COMETRIQ for the approved MTC indication primarily in the European Union, Switzerland, Norway, Russia and Turkey, and potentially other countries in the event that COMETRIQ is approved for commercial sale in such jurisdictions. In January 2015, the parties amended and restructured their agreement, which was due to expire on December 31, 2015, extending its term to December 31, 2019. The agreement remains limited to the approved MTC indication in the indicated territories, and we continue to maintain commercial rights for all other potential cabozantinib oncology indications on a global basis. Under the amended terms, however, our payments to Sobi transition from fixed fees paid by Exelixis to Sobi to support initial build out of the COMETRIQ European infrastructure to a sales margin-based approach. 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 agreements with Sobi, we have established the infrastructure to make COMETRIQ available globally upon physician request under a named patient use, or NPU, program in countries where the drug is not yet commercially approved. 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 activity profile is compelling and will allow commercial differentiation from other available commercial products in a variety of indications, assuming appropriate regulatory approvals. The cabozantinib clinical development program consists of a wide range of trials. We are the sponsor of some of those trials, including two phase 3 pivotal studies in mRCC and advanced HCC. The remaining trials are being conducted through our CRADA with NCI-CTEP or our IST program.

We developed cabozantinib for MTC using a capsule formulation at the maximum tolerated dose (MTD) of 140 mg per day. In the course of further clinical investigation of cabozantinib for the treatment of other tumors, it was determined that a tablet formulation of at the lower dose of 60 mg per day had improved tolerability while retaining clinical activity. Hence, all ongoing and planned single agent studies now utilize the tablet formulation, with most studies, including METEOR, employing a 60 mg starting dose. A bioequivalence study comparing the two formulations in healthy adult subjects did not meet the requirements for bioequivalence. Therefore, if approved, the tablet formulation of cabozantinib will be launched and marketed as a new and distinct commercial product. The tablet

formulation may confer advantages relative to the current capsule configuration such as improved convenience for patients and their healthcare providers, improved adherence to the dosing schedule, as well as potentially providing flexibility in pricing.

To date, we have observed encouraging objective tumor responses in patients treated with cabozantinib in 15 individual tumor types investigated as part of our randomized discontinuation trial, or RDT, and in phase 1 and 2 clinical trials, reflecting the broad potential clinical activity and commercial opportunity of this product candidate. It is our intention to expand the cabozantinib development program to other tumor indications, based on encouraging interim data that have emerged from our randomized discontinuation trial, or RDT, as well as other clinical trials. In addition we have observed resolution of metastatic bone lesions on bone scan in patients with metastatic castration-resistant prostate cancer, or mCRPC, metastatic breast cancer or melanoma in the RDT, in patients with RCC and differentiated thyroid cancer in a phase 1 clinical trial, and in patients with bladder cancer in an NCI-CTEP-sponsored phase 2 clinical trial.

Our cabozantinib IST program is critical to advancing our understanding of cabozantinib and supporting its future development. Our Medical Affairs department is responsible for reviewing IST requests for support and managing the provision of such support, if warranted. 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.

mRCC

METEOR (Metastatic RCC Phase 3 Study Evaluating Cabozantinib vs. Everolimus), a phase 3 pivotal trial comparing cabozantinib to everolimus in patients with mRCC who have experienced disease progression following treatment with at least one prior VEGFR TKI, was initiated in May 2013. On July 20, 2015, we announced that the trial had met its primary endpoint of demonstrating a statistically significant increase in PFS for cabozantinib versus everolimus in the first 375 randomized patients as determined by an independent radiology committee, or IRC. Cabozantinib reduced the risk of disease progression or death by 42 percent compared to the everolimus arm (hazard ratio [HR]=0.58, 95 percent CI 0.45-0.75, p<0.0001).

Data pertaining to overall survival (OS) in the entire study population of 658 patients, a secondary endpoint of the trial, were immature at the data cutoff. A prespecified interim analysis, triggered by the primary analysis for PFS, showed a trend in OS favoring cabozantinib (HR = 0.67, unadjusted 95 percent CI 0.51 0.89; p=0.005). At the time of the interim analysis, the pre-specified p-value of 0.0019 to achieve statistical significance was not reached. The trial will continue to the final analysis of OS anticipated in 2016. Detailed results of the trial will be submitted for presentation at an upcoming medical conference.

METEOR s primary analysis included a review of serious adverse event (SAE) data. Based on this analysis the frequency of SAEs of any Grade regardless of causality was approximately balanced between study arms. The rate of treatment discontinuation due to adverse events was low (10%) in both study arms.

In April 2015, cabozantinib received Fast Track designation by the FDA for the potential treatment of advanced RCC patients who have received one prior therapy. Based on the outcome of METEOR, we plan to complete regulatory filings in the United States and European Union in early 2016.

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HCC

CELESTIAL (Cabozantinib Phase 3 Controlled Study In Hepatocellular Carcinoma), a phase 3 pivotal trial comparing cabozantinib to 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 are being randomized 2:1 to receive 60 mg of cabozantinib daily or placebo. The primary endpoint for CELESTIAL is OS, and the secondary endpoints include objective response rate and PFS. We expect top-line results from CELESTIAL in 2017.

NSCLC

In November 2014, we announced positive top-line results from a randomized phase 2 trial of cabozantinib and erlotinib alone or in combination as second- or third-line therapy in patients with stage IV EGFR wild-type non-small cell lung cancer, or NSCLC. This trial (Study E1512) is sponsored through our CRADA with NCI-CTEP. Study E1512 was designed and is being conducted by the ECOG-ACRIN Cancer Research Group.

The results of study E1512 were presented at the 2015 ASCO annual meeting. Study E1512 met its primary endpoint, demonstrating significant increases in PFS for cabozantinib and the combination of cabozantinib plus erlotinib when individually compared to the erlotinib arm. The median PFS for the combination of cabozantinib and erlotinib was 4.7 months versus 1.9 months for erlotinib alone, a more than two-fold increase that corresponds to a 65% reduction in the risk of disease worsening (hazard ratio [HR]=0.35, 80% CI 0.23-0.52, p=0.0005). The median PFS for cabozantinib monotherapy was 4.2 months versus 1.9 months for erlotinib alone, a more than doubling that corresponds to a 62% reduction in the risk of disease worsening (HR=0.38, 80% CI 0.27-0.55, p=0.0004).

OS was a secondary endpoint of the trial. Median OS was 13.3 months for the combination of cabozantinib and erlotinib, and 9.2 months for cabozantinib alone, as compared to 4.1 months for erlotinib alone. These results correspond to a 56% reduction in the risk of death (HR=0.44, p=0.004) for the combination of cabozantinib plus erlotinib, and a 41% reduction in the risk of death (HR=0.59, p=0.03) for the cabozantinib monotherapy arm, respectively, when individually compared to the erlotinib arm. Objective response rate, another secondary endpoint, was 8% for the combination arm (2 partial responses [PR]), 14% (4 PRs) for the cabozantinib monotherapy arm, and 3% (1 PR) for the erlotinib arm. Stable disease as a best response was observed in 42% in the combination arm and 45% in the cabozantinib monotherapy arm, compared with 17% in the erlotinib arm.

118 patients were evaluable for safety. The most common treatment-related adverse events (AEs), grade 3 or higher, for the combination arm (n=39) were: diarrhea (27%), fatigue (15%), and syncope (8%). For the cabozantinib monotherapy arm, the most common AEs, grade 3 or higher, were: hypertension (26%), fatigue (15%), mucositis (10%) and thromboembolic events (8%). The most common AEs, grade 3 or higher, for the erlotinib arm were fatigue (12%) and diarrhea (8%). Overall, the rate of grade 3 or higher worst grade adverse events was 72% in the combination arm and 67% in the cabozantinib monotherapy arm, compared with the erlotinib arm (35%).

Urothelial (Bladder) Cancer and Other Genitourinary Tumors

Given reported single agent activity in urothelial cancers with immune checkpoint inhibitors including anti-PD-1 and anti-PD-L1 monoclonal antibodies, the single agent clinical anti-tumor activity observed with cabozantinib, and preclinical data indicating that cabozantinib may result in a more immunopermissive tumor microenvironment, the combination of cabozantinib with the immunotherapies nivolumab and ipilimumab is being evaluated. On July 14, 2015, we announced the

initiation of a phase 1 trial of cabozantinib in combination with nivolumab alone or in combination with nivolumab plus ipilimumab in patients with advanced/metastatic urothelial (bladder) and other genitourinary tumors. The study is being sponsored through our CRADA with NCI-CTEP with our support and support from Bristol-Myers Squibb. Preliminary data on objective tumor responses were presented at the annual ASCO conference in June 2014. The primary endpoint of the trial is the determination of dose-limiting toxicities (DLT) and a recommended phase 2 dose (RP2D) for the combination of cabozantinib and nivolumab, and separately, for the combination of cabozantinib, nivolumab and ipilimumab, in patients with genitourinary solid tumors. Secondary endpoints include evaluating the activity of the two combinations by objective response rate, as well as PFS and OS, in cohorts of patients with urothelial carcinoma of the bladder, urethra, ureter or renal pelvis.

Other Cancer Indications

We are evaluating the initiation of pivotal trials with cabozantinib in other tumor types, based on our belief that these will increase the commercial value of cabozantinib, 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.

In addition to other trials reviewed above, proposed clinical trials approved to date under our CRADA with NCI-CTEP and our IST program include the following:

- Phase 2 or phase 1/2 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, ocular melanoma, prostate cancer and second line/third line EGFR-wt NSCLC.
- Additional phase 2 or phase 1/2 clinical trials to explore cabozantinib s potential utility in other tumor types, including endometrial cancer, bladder cancer, sarcomas, NSCLC (EGFR-activating mutation positive), differentiated thyroid cancer, triple-negative breast cancer, hormone-receptor-positive breast cancer, cutaneous melanoma (molecularly selected patients), colorectal cancer and pancreatic neuroendocrine tumors/carcinoid. 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 the above mentioned combination trial of cabozantinib and immunotherapy (nivolumab with or without ipilumumab) in genitourinary tumors, 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, each representing a substantial unmet medical need. 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.

Under our IST program, initiated in October 2010, patients have enrolled in 24 trials, 16 of which are currently accruing patients. An additional three studies are expected to initiate accrual soon.

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XL888

XL888 is an Exelixis-discovered highly potent small molecule oral inhibitor of Heat Shock Protein 90 (HSP90), a molecular chaperone protein that affects the activity and stability of a range of key regulatory proteins, including kinases such as BRAF, MET, and VEGFR2, which are implicated in cancer cell proliferation and survival. After completing phase 1 testing, we deprioritized XL888 and our other pipeline assets to focus our limited resources on our lead compound, cabozantinib. Investigators at the H. Lee Moffitt Cancer Center subsequently conducted additional preclinical work showing activity of XL888 in vemurafenib-resistant melanoma models, the results of which provided the rationale for the initiation of an investigator-sponsored phase 1 trial conducted by investigators at the Moffitt Cancer Center.

In November 2014, we announced positive preliminary results from this phase 1 trial, which evaluated the safety and activity of XL888 in combination with vemurafenib in patients with unresectable stage III/IV BRAF V600 mutation-positive melanoma. The primary endpoint of the trial was to determine the safety and tolerability of the combination, including determination of a maximum tolerated dose, or MTD, of XL888. Secondary endpoints included objective response rate (RECIST-1 criteria), estimates of PFS and OS, and analysis of pharmacodynamic biomarkers. The trial had enrolled fifteen subjects, and at the time of data cut-off, objective tumor regression was observed in 11 of 12 response-evaluable patients (two complete responses and nine partial responses), for an objective response rate of 92%. Safety data for the combination identified tolerable dose levels of XL888 with full dose vemurafenib.

Based on these results, as well as findings from coBRIM, the phase 3 pivotal trial of cobimetinib, an Exelixis-discovered MEK inhibitor, and vemurafenib in previously untreated metastatic melanoma patients with a BRAF V600 mutation, investigators at the Moffitt Cancer Center plan to initiate a phase 1b IST of the triple combination of vemurafenib, cobimetinib, and XL888 in a similar patient population.

Collaborations

We have established a collaboration with Genentech for cobimetinib, and other collaborations with leading pharmaceutical companies including 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 compounds and programs in our portfolio. Pursuant to these collaborations, we have fully out-licensed compounds or programs to a partner for further development and commercialization. We have no further development cost obligations under our collaborations and may be entitled to receive milestones and royalties, or in the case of cobimetinib, a share of profits (or losses) from commercialization.

Cobimetinib Collaboration

Our collaboration with Genentech for cobimetinib continues to be of increasing importance to us as cobimetinib is our most advanced partnered compound in development and has the greatest near-term commercial potential. In addition to the coBRIM trial, of which data has been submitted for regulatory approval and marketing authorizations in the U.S. and EU, the following clinical trials of cobimetinib in combination with other agents are ongoing, as disclosed on clinicaltrials.gov:

- A Study of MEHD7945A and Cobimetinib (GDC-0973) in Patients With Locally Advanced or Metastatic Cancers With Mutant KRAS (NCT01986166);

- A Phase 1b Study of MPDL3280A (an Engineered Anti-PDL1 Antibody) in Combination With Cobimetinib in Patients With Locally Advanced or Metastatic Solid Tumors (NCT01988896);

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- Trial of Vemurafenib/Cobimetinib With or Without Bevacizumab in Patients With Stage IV BRAF V600 Mutant Melanoma (NCT01495988);
- A Phase 1b Study of MPDL3280A (an Engineered Anti-PDL1 Antibody) in Combination With Vemurafenib (Zelboraf®) or Vemurafenib Plus Cobimetinib in Patients With Previously Untreated BRAF V600-Mutation Positive Metastatic Melanoma (NCT01656642);
- A Study of Cobimetinib in Combination With Paclitaxel as First-line Treatment for Patients With Metastatic Triple-negative Breast Cancer (NCT02322814);
- A Study of Neo-adjuvant Use of Vemurafenib Plus Cobimetinib for BRAF Mutant Melanoma With Palpable Lymph Node Metastases (NCT02036086);
- A Phase II Study of Cobimetinib in Combination with Vemurafenib in Active Melanoma Brain Metastases (CoBRIM-B) (NCT02230306);
- Neoadjuvant Vemurafenib + Cobimetinib in Melanoma: NEO-VC (NCT02303951);
- Vemurafenib Plus Cobimetinib in Metastatic Melanoma (REPOSIT) (NCT02414750); and
- A Phase Ib, Open-Label, Dose-Escalation Study Of The Safety, Tolerability, and Pharmacokinetics of Cobimetinib and GDC-0994 In Patients With Locally Advanced or Metastatic Solid Tumors (NCT02457793).

Under the terms of our collaboration agreement with Genentech for cobimetinib, we are entitled to an initial equal share of U.S. profits and losses for cobimetinib, with our share decreasing as sales increase, and we 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 an option under the collaboration agreement to co-promote in the United States. As a result of exercising our option to co-promote, we may 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 collaboration agreement and a co-promotion agreement to be entered into by the parties.

Other Collaborations

With respect to our partnered compounds, other than cobimetinib, we are eligible to receive potential contingent payments totaling approximately $2.3 billion in the aggregate on a non-risk adjusted basis, of which 10% are related to clinical development milestones, 42% are related to regulatory milestones and 48% are related to commercial milestones, all to be achieved by the various licensees, which may not be paid, if at all, until certain conditions are met.

Recent Financial Information

We have not finalized our consolidated financial statements for the quarter ended July 3, 2015. Based on our current estimates, as of July 3, 2015, we had $167.0 million in cash and investments, which included $76.6 million available for operations, $6.1 million of short-term restricted investments for public debt service obligations, $81.6 million of compensating balance investments that we are required to maintain on deposit with Silicon Valley Bank, and $2.7 million of long-term restricted investments. The actual amounts that we report will be subject to our financial closing procedures and any final adjustments that may be made prior to the time our financial results for the quarter ended July 3, 2015, are finalized.

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Corporate Information

We were incorporated in Delaware in November 1994 as Exelixis Pharmaceuticals, Inc. and we changed our name to Exelixis, Inc. in February 2000. Our principal executive offices are located at 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	25,000,000 shares
Underwriters option to purchase additional shares	3,750,000 shares
Common stock to be outstanding after the offering	221,020,856 shares
Use of proceeds	We currently expect to use the net proceeds from this offering for general corporate purposes, including for clinical trials, build-out of commercial infrastructure, research and development, capital expenditures and working capital.
Risk factors	See Risk Factors beginning on page S-16 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 March 31, 2015. As of that date, we had 196,020,856 shares of common stock outstanding, excluding:

- 28,601,848 shares of common stock underlying options outstanding as of March 31, 2015, at a weighted average exercise price of $4.44 per share;
- 1,000,000 shares of common stock underlying warrants outstanding as of March 31, 2015, at a weighted average exercise price of $3.445 per share;
- 825,486 shares reserved for future issuance pursuant to unvested restricted stock units as of March 31, 2015;
- 10,190,819 shares available for future grant under our 2014 Equity Incentive Plan, 1,371,274 shares available for future purchase under our 2000 Employee Stock Purchase Plan, and 516,715 shares available for future grant under our 401(k) Retirement Plan, all as of March 31, 2015; 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 underwriters in this offering do not exercise their option to purchase up to 3,750,000 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, 2014, and for each of the three years ended December 31, 2012, 2013 and 2014, from our audited consolidated financial statements. We derived the information presented below as of March 31, 2015, and for each of the three months ended March 31, 2014 and 2015, 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 March 31, 2015, and for each of the three months ended March 31, 2014 and 2015, have been reflected therein. Operating results for the three months ended March 31, 2015, 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, 2014, and our Quarterly Report on Form 10-Q for the fiscal quarter ended March 31, 2015.

The as adjusted balance sheet data as of March 31, 2015, reflects receipt of the estimated net proceeds of $126.5 million from the sale of the common stock in this offering (assuming no exercise of the underwriters option to purchase additional shares), after deducting the 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,			Three Months Ended March 31,	
	2012	2013	2014	2014	2015
				(unaudited)	
	(in thousands, except per share data)				
Consolidated Statement of Operations Data					
Total revenues	$ 47,450	$ 31,338	$ 25,111	$ 4,905	$ 9,388
Total operating expenses	$ 169,886	$ 232,070	$ 249,569	$ 69,893	$ 32,148
Net loss	$ (147,645)	$ (244,760)	$ (268,542)	$ (74,619)	$ (35,170)
Net loss per share, basic and diluted	$ (0.92)	$ (1.33)	$ (1.38)	$ (0.39)	$ (0.18)
Shares used in computing basic and diluted net loss per share amounts	160,138	184,062	194,299	191,699	195,904

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	As of March 31, 2015	
	Actual	As adjusted (1)
	(unaudited) (in thousands)	
Consolidated Balance Sheet Data		
Cash and cash equivalents, short- and long-term investments, and short- and long-term restricted cash and investments	$ 197,634	$ 324,089
Working capital	$ 66,360	$ 192,815
Total assets	$ 282,934	$ 409,389
4.25 % Convertible senior subordinated notes due 2019	$ 186,940	$ 186,940
Debt obligations under the Deerfield Notes (defined herein)	$ 101,326	$ 101,326
Debt obligations under our loan and security agreement with Silicon Valley Bank	$ 80,164	$ 80,164
Additional paid-in-capital	$ 1,655,580	$ 1,782,010
Total stockholders deficit	$ (146,759)	$ (20,304)

(1) As adjusted to reflect the sale of 25,000,000 shares being offered in this offering and the receipt of the estimated net proceeds of $126.5 million from the sale of these shares, after deducting the 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 2012, a 52-week year, ended on December 28, 2012, fiscal year 2013, a 52-week year, ended on December 27, 2013, fiscal year 2014, a 53-week year, ended on January 2, 2015, and fiscal year 2015, a 52-week year, will end on January 1, 2016. For convenience, references in this prospectus supplement as of and for the fiscal years ended December 28, 2012, December 27, 2013, and January 2, 2015, and as of and for the fiscal quarters ended March 28, 2014, and April 3, 2015, are indicated on a calendar year basis as ended December 31, 2012, 2013 and 2014, and calendar quarter basis as ended March 31, 2014 and 2015, 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 at this time 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 access additional capital to:

- fund our operations and clinical trials;
- continue our research and development efforts;
- commercialize cabozantinib or other future product candidates, if any such candidates receive regulatory approval for commercial sale; and
- fund the portion of U.S. marketing and commercialization costs for cobimetinib that we are obligated to fund 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 March 31, 2015, we had $197.6 million in cash and investments, which included $107.2 million available for operations, $6.1 million of short-term restricted investments available for public debt service obligations, $81.6 million of compensating balance investments that we are required to maintain on deposit with Silicon Valley Bank, and $2.7 million of long-term restricted investments. We anticipate that our current cash and cash equivalents, and short-term investments available for operations, and product revenues together with the proceeds from this offering will enable us to maintain our operations through at least the next 12 months. While a forecast of future events is inherently uncertain, our ability to sustain our business operations for approximately 12 months is highly dependent on the commercial success of COMETRIQ and the revenues we generate as well as the commercial success of cobimetinib and our share of related net profits and losses, and royalties under our collaboration with Genentech. Consistent with the actions we have taken in the past, we will prioritize necessary and appropriate steps to ensure the continued operation of our business and preservation of the value of our assets. 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 cabozantinib development and commercialization activities;
- the commercial success of COMETRIQ and the revenues we generate;
- our obligation to share U.S. marketing and commercialization costs for cobimetinib under our collaboration with Genentech;
-

the commercial success of cobimetinib and our share of related profits and losses for the commercialization of cobimetinib in the U.S. and receipt of royalties from cobimetinib sales outside the U.S. under our collaboration with Genentech;

- our ability to obtain regulatory approval for cabozantinib for the treatment of advanced RCC and other indications;

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- whether we enter into new collaboration agreements, licensing agreements or other arrangements with respect to cabozantinib or other product candidates that provide additional capital;
- future clinical trial results, notably the results from CELESTIAL, our phase 3 pivotal trial in patients with advanced HCC;
- repayment of the $100.0 million principal amount outstanding under our Secured Convertible Notes which mature on July 1, 2018, referred to herein as the Deerfield Notes, subject to a requirement to make a mandatory prepayment in each of 2016, 2017 and 2018 equal to 15% of certain revenues from collaborative arrangements (other than intercompany arrangements) received during the prior fiscal year, subject to a maximum annual prepayment amount of $27.5 million;
- our ability to repay the Deerfield Notes with our common stock, which we are only able to do under specified conditions;
- repayment of our $287.5 million aggregate principal amount of the 2019 Notes, which mature on August 15, 2019, unless earlier converted, redeemed or repurchased;
- repayment of our term loan and line of credit from Silicon Valley Bank, which had an outstanding balance at March 31, 2015, of $80.1 million;
- 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;
- our need to expand our product and clinical development efforts;
- the cost and timing of regulatory approvals;
- the cost of clinical and research drug supply for our clinical trials;
- the effect of economic and scientific developments in the market for oncologic therapeutics and the timing of regulatory approvals for competing oncologic therapies; and
- the filing, maintenance, prosecution, defense and enforcement of patent claims and other intellectual property rights.

In addition, we may need to obtain additional funding in order to stay in compliance with 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.

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 three months ended March 31, 2015, with the exception of the 2011 fiscal year. We anticipate net losses and negative operating cash flow for the foreseeable future. For the three months ended March 31, 2015, we incurred a net loss of $35.2 million and as of March 31, 2015, we had an accumulated deficit of $1.8 billion. These losses have had, and will continue to have, an adverse effect on our stockholders deficit and working capital. 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, if at all. Our research and development expenditures and selling, 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 and commercialization 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.

We commercially launched COMETRIQ for the treatment of progressive, metastatic MTC in the United States in late January 2013 and from the commercial launch through March 31, 2015, we have

generated $49.5 million in net revenues from the sale of COMETRIQ. Other than revenues from COMETRIQ, we have derived substantially all of our revenues since inception from collaborative research and development agreements that depend on research funding, the achievement of milestones, and royalties we earn from any future products developed from the collaborative research. If the amount of research funding we receive from our collaborators decreases, if our collaborators fail to develop successful products, if we are unable to successfully achieve the milestones under our collaboration agreements, or if sales of products to which we are entitled to royalties under such agreements are weak, our revenues and financial condition would be materially adversely affected.

The amount of our net losses will depend, in part, on our sales of COMETRIQ, our share of the net profits and losses for the commercialization for cobimetinib in the U.S., if any, the receipt of royalties from cobimetinib sales outside the U.S., if any, partnering activities for cabozantinib, other license and contract revenues, and the level of expenses with respect to development and commercialization activities, including for cabozantinib.

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 have significant indebtedness and substantial debt service requirements as a result of the Deerfield Notes, our loan and security agreement with Silicon Valley Bank and the 2019 Notes. As of March 31, 2015, our total consolidated indebtedness through maturity was $471.7 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 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 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.

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We cannot assure you that we will continue to maintain sufficient cash reserves or that our business will 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, as defined in the indenture governing the 2019 Notes, 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 that 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 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 March 31, 2015, 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 Cabozantinib and Cobimetinib

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

The success of our business is dependent upon the successful development and commercialization of cabozantinib. As part of our strategy, we are dedicating substantially all of our proprietary resources to

advance cabozantinib as aggressively as possible and are seeking to partner cabozantinib with a global pharmaceutical organization whose international resources will permit us to explore and exploit fully the potential opportunity cabozantinib presents on its own and in combination with other agents, in mRCC, advanced HCC, and other potential indications. On November 29, 2012, the FDA approved a capsule formulation of cabozantinib for the treatment of progressive, metastatic MTC in the United States under the brand name COMETRIQ, and we commercially launched COMETRIQ in late January 2013. In March 2014, the European Commission approved cabozantinib for the treatment of adult patients with progressive, unresectable locally advanced or metastatic MTC, also in a capsule formulation under the brand name COMETRIQ. The European Commission granted conditional marketing authorization following a positive opinion from the Committee for Medicinal Products for Human Use issued in December 2013. We view the approvals of COMETRIQ by the FDA and European Commission for MTC as transitional events towards our objective of developing cabozantinib capsules and tablets into a significant oncology franchise. Our ability to realize this objective is contingent on, among other things, successful clinical development, regulatory approval and market acceptance of cabozantinib. The failure of COMET-1 and COMET-2, our two phase 3 pivotal trials of cabozantinib in mCRPC, to meet their respective primary endpoints negatively impacted our ability to achieve our development and commercialization goals for cabozantinib in prostate cancer. On July 20, 2015, we announced that METEOR, a phase 3 pivotal trial comparing cabozantinib to everolimus in patients with mRCC who have experienced disease progression following treatment with at least one prior VEGFR TKI, met its primary endpoint of demonstrating a statistically significant increase in PFS for cabozantinib versus everolimus in the first 375 randomized patients as determined by an IRC. See Prospectus Supplement Summary Cabozantinib Development Program mRCC. Data pertaining to OS in the entire study population of 658 patients, a secondary endpoint of the trial, were immature at the data cutoff, and we cannot be certain that the final analysis of OS anticipated in 2016 will be consistent with the trend in OS favoring cabozantinib that was observed in our interim analysis. Although we plan to complete regulatory filings in the United States and European Union in early 2016 for treatment of such patients with mRCC, we cannot be certain that such filings will be made when expected, or at all, or that we will ultimately receive regulatory approval for cabozantinib for that indication by the FDA or the EMA. In addition, even if such approvals are obtained, the commercial potential of cabozantinib for the treatment of such patients will be affected by a variety of factors, including the final analysis of OS expected in 2016, the perceived benefits associated with the median PFS of patients receiving cabozantinib as compared to everolimus, and the availability and benefits of competitive treatments. We believe that if cabozantinib is approved for the treatment of 2nd or later-line mRCC, its potential principal competition in this indication could include axitinib and everolimus, which are already approved in this indication, as well as other agents approved for 1st-line mRCC including sunitinib, sorafenib, pazopanib, temsirolimus, and bevacizumab. Other agents being investigated in 2nd line mRCC, including nivolumab, may also become competitive treatments if they are approved for mRCC. In particular, on July 20, 2015, Bristol-Myers Squibb announced that the phase 3 trial comparing nivolumab to everolimus in 2nd or later-line metastatic RCC patients (Checkmate 025) had met its primary endpoint of showing an improvement in overall survival for patients treated with nivolumab. We anticipate that nivolumab may be approved for use in 2nd or later-line patients in 2016 and will provide immediate direct competition for cabozantinib in this market. In addition, if we fail to enter into a suitable collaboration agreement with respect to cabozantinib for indications beyond MTC, or otherwise encounter additional difficulties in the development of cabozantinib in such other indications due to any of the factors discussed in this Risk Factors section or otherwise, or if we do not receive regulatory approval in such indications, including mRCC, or are unable to successfully commercialize cabozantinib in such other indications, if approved, we will not have the resources necessary to continue our business in its current form.

In addition, if we fail to enter into a suitable collaboration agreement with respect to cabozantinib for indications beyond MTC, or otherwise encounter additional difficulties in the development of cabozantinib in such other indications beyond MTC due to any of the factors discussed in this Risk Factors section or otherwise, or if we do not receive regulatory approval in such indications, including

mRCC, or are unable to successfully commercialize cabozantinib in such other indications, if approved, we will not have the resources necessary to continue our business in its current form.

We are dependent on the successful development and commercialization of cobimetinib, and rely heavily on our partner, Genentech, for achieving that success.

We have entered into a worldwide collaboration agreement with Genentech for the development and commercialization of cobimetinib, a compound discovered by Exelixis and licensed to Genentech in 2009 after determination of the maximum tolerated dose in a phase 1 clinical trial. Genentech is responsible for cobimetinib s clinical development and, if cobimetinib is approved, for worldwide commercialization. Under the terms of our collaboration agreement, we are entitled to an initial equal share of U.S. profits and losses for cobimetinib, with our share decreasing as sales increase, and we will share equally in the U.S. marketing and commercialization costs. Pursuant to our collaboration agreement, we may provide up to 25% of the total sales force for cobimetinib in the United States, if cobimetinib is commercialized.

On September 29, 2014, positive results from coBRIM, a phase 3 pivotal trial evaluating cobimetinib in combination with vemurafenib in previously untreated patients with unresectable locally advanced melanoma harboring a BRAF V600 mutation, were reported at the ESMO 2014 Congress. The trial met its primary endpoint of demonstrating a statistically significant increase in investigator-determined PFS for the combination of cobimetinib and vemurafenib versus vemurafenib alone. On the basis of data from the coBRIM trial, Roche submitted a MAA for cobimetinib in combination with vemurafenib in the European Union in September 2014. In the United States, Genentech submitted its NDA in December 2014 and the FDA has granted the NDA priority review, with a projected action date of August 11, 2015. On June 30, 2015, Genentech informed us that, in order to accommodate its review of a supplemental data submission the FDA extended the projected action date for its review of the cobimetinib NDA by the standard extension period of three months, to November 11, 2015.

Under the terms of our collaboration agreement, we rely heavily upon Genentech s leadership and expertise to further develop cobimetinib. Any significant changes to Genentech s business strategy and priorities, over which we have no control, could adversely affect Genentech s willingness or ability to complete their obligations under our agreement and result in harm to our business and operations. Genentech has complete financial responsibility for cobimetinib s development program, and we are not able to control the amount or timing of resources that Genentech will devote to the product. Of particular significance are Genentech s development efforts with respect to the combination of cobimetinib with immune-oncology agents, a promising and competitive area of clinical research. While Genentech is currently conducting a phase 1b clinical trial combining cobimetinib with the Genentech PD-L1 antibody (MPDL3280A), we are dependent on Genentech for all future development of cobimetinib in combination with MPDL3280A or any other immune-oncology agents. Regardless of Genentech s efforts toward the further development of cobimetinib, such additional clinical investigation may not provide positive data supporting product label expansions or approval in additional indications.

We are similarly dependent upon Genentech s strategic and tactical planning and decision-making with regard to the commercialization of cobimetinib; and, in addition, during the period prior to commercialization, we are obligated to reimburse half of Genentech s costs for commercializing the drug in the U.S. Furthermore, regardless of the level of Genentech s investment in cobimetinib, the compound may not be accepted by physicians, patients, health care payers, such as Medicare and Medicaid, and the medical community.

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The commercial success of cabozantinib, as COMETRIQ capsules for MTC, or if approved in a tablet formulation for additional indications in the future, will depend upon the degree of market acceptance of cabozantinib among physicians, patients, health care payers, and the medical community.

Our ability to commercialize cabozantinib, as COMETRIQ capsules for the approved MTC indication or if approved in a tablet formulation for additional indications, will be highly dependent upon the extent to which cabozantinib gains market acceptance among physicians, patients, health care payers such as Medicare and Medicaid, and the medical community. If cabozantinib 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 and other cabozantinib products, if approved, will depend upon a number of factors, including:

- the effectiveness, or perceived effectiveness, of cabozantinib in comparison to competing products;
- the existence of any significant side effects of cabozantinib, as well as their severity in comparison to those of any competing products;
- potential advantages or disadvantages in relation to alternative treatments;
- the timing of market entry relative to competitive treatments;
- indications for which cabozantinib is approved;
- the ability to offer cabozantinib for sale at competitive prices;
- relative convenience and ease of administration;
- the strength of sales, marketing and distribution support; and
- sufficient third-party coverage and reimbursement.

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

We have designed our commercial organization and strategic commercial approach to maintain flexibility in response to market opportunities. At present, our U.S. commercial organization is sized at a level commensurate with the size of the market opportunity for progressive, metastatic MTC. We expect to be able to scale up quickly if additional indications for cabozantinib are approved in the future, or to scale down if necessary. Our distribution arrangements with Sobi are also right-sized for the EU MTC opportunity and retain strategic flexibility. Overall, we believe the design of our commercial organization, and our strategic commercial approach, are efficient, taking advantage of outsourcing options where prudent to maximize the effectiveness of our commercial expenditures.

However, should the commercial opportunity for cabozantinib grow over time, we may not correctly judge the proper size and level of and experience of the sales and marketing force or the scale of distribution necessary to market and sell cabozantinib successfully. Maintaining sales, marketing, and distribution capabilities is expensive and time-consuming. Such expenses may be disproportionate compared to the revenues we may be able to generate on sales of cabozantinib and have an adverse impact on our results of operations. If we are unable to 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 also rely on a third party, Sobi, to distribute and commercialize COMETRIQ for the treatment of the approved MTC indication primarily in the European Union and potentially other countries in the event that COMETRIQ is approved for commercial sale in those jurisdictions. Our current and anticipated future dependence upon the

activities, and legal and regulatory compliance, of these or other 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 or other 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 third parties, or enter into new arrangements, on acceptable terms, or at all. 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.

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 Anti-Kickback Law, which constrains our business activities, including our marketing practices, educational programs, pricing policies, and relationships with healthcare providers or other entities, by prohibiting, among other things, persons and entities 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 payers 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;
- the federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act, and their implementing regulations, which impose certain requirements relating to the privacy, security and transmission of individually identifiable health information;
- 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 payer, 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

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- 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 certain federal and state health regulatory fraud and abuse laws as well as 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 administrative 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 under 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 both adequate coverage and adequate reimbursement from third-party payers for cabozantinib, our revenues and prospects for profitability will suffer.

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

In addition, in some foreign countries, particularly the countries in the European Union, the pricing of prescription pharmaceuticals is subject to governmental control. In these countries, price negotiations with governmental authorities can take six to twelve months or longer after the receipt of regulatory marketing approval for a product. To obtain reimbursement and/or pricing approval in some countries, we may be required to conduct a clinical trial that compares the cost effectiveness of cabozantinib to other available therapies. The conduct of such a clinical trial could be expensive and

result in delays in the commercialization of cabozantinib. Third-party payers are challenging the prices charged for medical products and services, and many third-party payers limit reimbursement for newly-approved health care products. In particular, third-party payers may limit the indications for which they will reimburse patients who use cabozantinib. Cost-control initiatives could decrease the price we might establish for cabozantinib, which would result in lower product revenues to us.

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

The 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 cabozantinib profitably. Among policy makers and payers 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, as amended by the Health Care and Education Reconciliation Act of 2010, collectively referred to as the PPACA, enacted in March 2010, substantial changes have been made, and may continue to be made, to the way healthcare is financed by both governmental and private insurers, and those changes are significantly impacting the pharmaceutical industry. Provisions of the PPACA relevant to the pharmaceutical industry include the following:

- an annual, nondeductible fee on any entity that manufactures or imports certain branded prescription drugs and biologic agents, apportioned among these entities according to their market share in certain government healthcare programs, not including orphan drug sales;
- an increase in the rebates a manufacturer must pay under the Medicaid Drug Rebate Program to 23.1% and 13% of the average manufacturer price for most branded and generic drugs, respectively;
- a new Medicare Part D coverage gap discount program, in which manufacturers must agree to offer 50% point-of-sale discounts on negotiated prices of applicable brand drugs to eligible beneficiaries during their coverage gap period, as a condition for the manufacturer s outpatient drugs to be covered under Medicare Part D;
- extension of manufacturers Medicaid rebate liability to covered drugs dispensed to individuals who are enrolled in Medicaid managed care organizations;
- expansion of eligibility criteria for Medicaid programs by, among other things, allowing states to offer Medicaid coverage to additional individuals with income at or below 133% of the Federal Poverty Level, thereby potentially increasing manufacturers Medicaid rebate liability;
- expansion of the entities eligible for discounts under the Public Health Service pharmaceutical pricing program;
- new requirements to report annually under the federal Open Payments program certain financial arrangements with physicians and teaching hospitals, as defined in PPACA and its implementing regulations, including reporting any payment or transfer of value provided to physicians and teaching hospitals and any ownership and investment interests held by physicians and their immediate family members during the preceding calendar year;
- expansion of healthcare fraud and abuse laws, including the federal False Claims Act and the federal Anti-Kickback Statute, new government investigative powers and enhanced penalties for noncompliance; and
-

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

The PPACA may change in the future. In August 2011, the President signed into law the Budget Control Act of 2011, which, among other things, created the Joint Select Committee on Deficit Reduction to recommend proposals in spending reductions to Congress. The Joint Select Committee on Deficit Reduction did not achieve its targeted deficit reduction of at least $1.2 trillion for the years 2013 through 2021, triggering the legislation s automatic reductions to several government programs. These reductions include aggregate reductions to Medicare payments to providers of up to 2% per fiscal year, starting in 2013 and will stay in effect through 2024 unless additional Congressional action is taken. In January 2013, President Obama signed into law the American Taxpayer Relief Act of 2012, which, among other things, reduced Medicare payments to several providers and increased the statute of limitations period for the government to recover overpayments to providers from three to five years. These laws, and others that may affect our business that have been recently enacted or may in the future be enacted, may result in additional reductions in Medicare and other healthcare funding, which could have a material adverse effect on our customers and accordingly, our financial operations. Further, under the recently enacted Drug Quality and Security Act, drug manufacturers will be subject to a number of requirements, including, product identification, tracing and verification, among others, that are designed to improve the detection and removal of counterfeit, stolen, contaminated or otherwise potentially harmful drugs from the U.S. drug supply chain. These requirements will be phased in over several years and compliance with this new law will likely increase the costs of the manufacture and distribution of drug products, which could have an adverse effect on our financial condition.

As a result of the overall trend towards cost-effectiveness criteria and managed healthcare in the United States, third-party payers 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 cabozantinib 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 payers 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 payers outside of the United States for coverage and reimbursement of cabozantinib. We also anticipate pricing pressures in connection with the sale of cabozantinib due to the increasing influence of health maintenance organizations and additional legislative proposals.

Our competitors may develop products and technologies that impair the value of cabozantinib and cobimetinib.

The pharmaceutical, biopharmaceutical and biotechnology industries are highly fragmented and are 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, biopharmaceutical 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 cobimetinib, and cabozantinib for the treatment of additional tumor types, could allow our competitors to bring products to market before us, which would impair the commercialization of cobimetinib or 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 and for which Roche and Genentech intend to pursue regulatory approval for cobimetinib 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 cobimetinib and cabozantinib. In addition, cobimetinib and cabozantinib may compete with existing therapies that have long histories of use, such as chemotherapy and radiation treatments in cancer indications.

Competition for cabozantinib

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, Ariad Pharmaceutical s multikinase inhibitor ponatinib, Novartis multikinase inhibitor pazopanib and Eisai s multikinase inhibitor lenvatinib.

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:

- RCC: Pfizer s axitinib, sunitinib and temsirolimus; Novartis everolimus and pazopanib; Bayer s and Onyx Pharmaceuticals sorafenib; Genentech s bevacizumab; Eisai s lenvatinib; and Bristol-Myers Squibb s nivolumab; and
- HCC: Bayer s and Onyx Pharmaceuticals sorafenib; Bayer s regorafenib; ArQule s tivantinib; and Eisai s lenvatinib.

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 Ariad s ponatinib; and other MET inhibitors, including Amgen s AMG 208, Pfizer s crizotinib, ArQule s tivantinib, and Mirati s MGCD265; and immunotherapies such as Bristol-Myers Squibb s ipilimumab and nivolimab and Merck s pembrolizumab.

Competition for cobimetinib

We believe that if cobimetinib is approved for the treatment of advanced melanoma, its potential principal competition amongst targeted agent s may include Novartis trametinib and dabrafenib, and Array s encorafenib and binimetinib; and within the class of immunotherapies, Bristol-Myers Squibb s ipilimumab and nivolumab and Merck s pembrolizumab. The second category, immunotherapies, are of particular competitive importance vis-a-vis cobimetinib in advanced melanoma as they are already FDA approved in melanoma patient populations that overlap with those that may be eligible for cobimetinib, they have been rapidly incorporated into the National Comprehensive Cancer Network treatment guidelines, and they are viewed with a high degree of enthusiasm by physicians and key opinion leaders. Ongoing and future trials incorporating immune-oncology agents, including combination trials, may further impact usage of cobimetinib in melanoma and potentially in additional tumor types in which cobimetinib may ultimately gain approval.

We lack the manufacturing capabilities and experience necessary to enable us to produce cabozantinib 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 expertise 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 cGMP and the European Commission s Guidelines on Good Distribution Practice. Our current and anticipated future dependence upon these third parties may adversely affect our future profit margins and our ability to develop and commercialize cabozantinib 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.

The manufacturing process for pharmaceutical products is highly regulated and our third party vendors are subject to cGMP. Our third-party manufacturers may not be able to comply with the cGMP 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 cabozantinib. 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 cabozantinib, injunctions, delays, suspension or withdrawal of approvals, license revocation, seizures or recalls of products and compounds, operating restrictions and criminal prosecutions, any of which could have a significant adverse effect on our business. Our third party manufacturers are subject to routine regulatory inspections. Failure of our third party manufacturers to meet these appropriate standards and/or perform manufacturing as required could result in a batch not passing quality inspection or meeting regulatory approval. This could result in product recalls or withdrawals, delays or failures in 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 mRCC, advanced HCC and a variety of other indications beyond the approved MTC indication. 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. For example, COMET-1 and COMET-2, our two phase 3 pivotal trials of cabozantinib in mCRPC, failed to meet their respective primary endpoints of demonstrating a statistically significant increase in overall survival for patients treated with cabozantinib as compared to prednisone and to demonstrate improvement in pain response for patients treated by cabozantinib as compared to mitoxantrone/prednisone. Based on the outcome of the COMET trials, we deprioritized the clinical development of cabozantinib in mCRPC.

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.

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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 mRCC, advanced 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.

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 the approved MTC indication.

We do not have the ability to independently conduct clinical trials for cabozantinib, including our post-marketing commitments in connection with the approvals of COMETRIQ in 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), third-party 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 their 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 the approved MTC indication in the United States and European Union.

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 an 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.

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 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 or any individual, additional indications.

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 post-marketing requirements, including a requirement to conduct a clinical study comparing a lower dose of cabozantinib to the approved dose of 140 mg daily cabozantinib in progressive, metastatic MTC and to conduct other clinical pharmacology and preclinical studies. Failure to complete any post-marketing requirements in accordance with the timelines and conditions set forth by the FDA could significantly increase costs or delay, limit or eliminate the commercialization of cabozantinib. Further, these agencies may also

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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 Genentech, Bristol-Myers Squibb, Sanofi, Merck (known as MSD outside of the United States and Canada) and Daiichi Sankyo, for the development and ultimate commercialization of certain compounds generated from our research and development efforts. Our dependence on our relationships with existing collaborators for the development and commercialization of compounds under the collaborations 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;
- 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 diminish or delay receipt of the economic benefits we are entitled to receive under the collaboration, 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;
- collaborators may not comply with applicable healthcare regulatory laws;
- 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, we may not receive collaboration revenue or otherwise realize anticipated benefits from such collaborations, our product development efforts could be delayed and our business, operating results and financial condition could be adversely affected.

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We may be unable to establish a collaboration for cabozantinib outside of the U.S. or other collaborations for selected preclinical and clinical compounds.

To enable us to capitalize on a potential indication in mRCC and other potential cabozantinib opportunities most effectively, we intend to seek a partner for cabozantinib outside of the U.S. We may also pursue 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. However, 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.

Risks Related to Our Intellectual Property

Data breaches and cyber-attacks could compromise our intellectual property or other sensitive information and cause significant damage to our business and reputation.

In the ordinary course of our business, we collect, maintain and transmit sensitive data on our networks and systems, including our intellectual property and proprietary or confidential business information (such as research data and personal information) and confidential information with respect to our customers, clinical trial patients and our business partners. We have also outsourced significant elements of our information technology infrastructure and, as a result, third parties may or could have access to our confidential information. The secure maintenance of this information is critical to our business and reputation. We believe that companies have been increasingly subject to a wide variety of security incidents, cyber-attacks and other attempts to gain unauthorized access. These threats can come from a variety of sources, ranging in sophistication from an individual hacker to a state-sponsored attack and motive (including corporate espionage). Cyber threats may be generic, or they may be custom-crafted against our information systems. Over the past year, cyber-attacks have become more prevalent and much harder to detect and defend against. Our network and storage applications and those of our vendors may be subject to unauthorized access by hackers or breached due to operator error, malfeasance or other system disruptions. It is often difficult to anticipate or immediately detect such incidents and the damage caused by such incidents. These data breaches and any unauthorized access or disclosure of our information or intellectual property could compromise our intellectual property and expose sensitive business information. A data security breach could also lead to public exposure of personal information of our clinical trial patients, customers and others. Cyber-attacks could cause us to incur significant remediation costs, result in product development delays, disrupt key business operations and divert attention of management and key information technology resources. Our network security and data recovery measures and those of our vendors may not be adequate to protect against such security breaches and disruptions. These incidents could also subject us to liability, expose us to significant expense and cause significant harm to our reputation and business.

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 biopharmaceutical 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, third parties may have 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.

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, biopharmaceutical 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 operate and expand our operations.

We are highly dependent upon the principal members of our management, clinical 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 that we have experienced since 2010 have had and may continue to have an adverse impact on our ability to retain and recruit qualified personnel. Competition is intense for experienced clinical personnel, and we may be unable to retain or recruit clinical personnel with the expertise or experience necessary to allow us to pursue collaborations, develop our products and core technologies or expand our operations to the extent otherwise possible. Further, all of our employees are employed at will and, therefore, may leave our employment at any time.

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

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

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

Our headquarters are located in South San Francisco, California, and therefore our facilities are vulnerable to damage from earthquakes. We do not carry earthquake insurance. We are also vulnerable to damage from other types of disasters, including fire, floods, power loss, communications

failures, terrorism and similar events since any insurance we may maintain may not be adequate to cover our losses. If any disaster were to occur, our ability to operate our business at our facilities could be seriously, or potentially completely, impaired. In addition, the unique nature of our research activities could cause significant delays in our programs and make it difficult for us to recover from a disaster. Accordingly, an earthquake or other disaster could materially and adversely harm our ability to conduct business.

Facility security breaches may disrupt our operations, subject us to liability and harm our operating results.

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.

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, biopharmaceutical and biotechnology industries, in general, have been subject to significant medical malpractice litigation. A successful

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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 the development and commercialization activities for cabozantinib and our other compounds;

- the commercial success of COMETRIQ and the revenues we generate;
- future clinical trial results, notably the results from CELESTIAL, our phase 3 pivotal trial in patients with advanced HCC;
- the inability to obtain adequate product supply for any approved drug product or inability to do so at acceptable prices;
- 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;
- whether we enter into new collaboration agreements, licensing agreements or other arrangements with respect to cabozantinib or other product candidates;
- the termination or non-renewal of existing collaborations or third party vendor relationships;
- regulatory actions with respect to our product candidates and any approved products or our competitors products;
- disputes or other developments relating to proprietary rights, including patents, litigation matters and our ability to obtain patent protection for our technologies;
- 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;
- additions and departures of key personnel;
- general and industry-specific economic conditions that may affect our or our collaborators research and development expenditures; and
- other factors described in this Risk Factors section.

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 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, and as a result, you may not be able to resell your shares at or above the public offering price.

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 cabozantinib or any of our other programs or 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, biopharmaceutical 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 coverage and 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.

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.

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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, as 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 us, a change in control, or attempts by our stockholders to replace or remove members of our current Board of Directors. Because our Board of Directors is responsible for appointing the members of our management team, these provisions could in turn affect any attempt by our stockholders to replace current members of our management team. These provisions include:

- a classified Board of Directors;
- a prohibition on actions by our stockholders by written consent;
- the inability of our stockholders to call special meetings of stockholders;
- the ability of our Board of Directors to issue preferred stock without stockholder approval, which could be used to institute a poison pill that would work to dilute the stock ownership of a potential hostile acquirer, effectively preventing acquisitions that have not been approved by our Board of Directors;
- 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 deficit per share of our common stock. If you purchase shares of our common stock in this offering, you will experience immediate dilution of $5.78 per share, representing the difference between the public offering price and our as adjusted net tangible deficit per share as of March 31, 2015, 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.

Our ability to use net operating losses to offset future taxable income may be subject to limitations.

Under the Internal Revenue Code, or the Code, and similar state provisions, certain substantial changes in our ownership could result in an annual limitation on the amount of net operating loss carry-forwards that can be utilized in future years to offset future taxable income. The annual limitation may result in the expiration of net operating losses and credit carry-forwards before utilization. We concluded, as of December 31, 2014, that an ownership change, as defined under Section 382, had not occurred. However, if there is an ownership change in connection with or after this offering under Section 382 of the Code, we may not be able to utilize a material portion of our NOLs. Furthermore, our ability to utilize our NOLs is conditioned upon our attaining profitability and generating United States federal taxable income. As described above, we have incurred significant net losses since our inception and anticipate that we will continue to incur significant losses for the foreseeable future; thus, we do not know whether or when we will generate the United States federal taxable income necessary to utilize our NOLs. A full valuation allowance has been provided for the entire amount of our NOLs.

Because we do not anticipate paying any cash dividends on our capital stock in the foreseeable future, capital appreciation, if any, will be your sole source of gain and you may never receive a return on your investment.

We do not anticipate that we will pay any dividends to holders of our common stock in the foreseeable future and investors seeking cash dividends should not purchase our common stock. We plan to retain any earnings to invest in the development of our product candidates and commercialization of products and to maintain and expand our operations. Therefore, capital appreciation, or an increase in your stock price, which may never occur, may be the only way to realize any return on your investment.

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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-16 of this prospectus supplement, in the documents incorporated by reference, in any free writing prospectus that we have authorized for use in connection with this offering or as a result of other circumstances beyond our control. The forward-looking statements made in this prospectus supplement, the accompanying prospectus and any free writing prospectus that we have authorized for use in connection with this offering speak only as of the date on which the statements are made.

USE OF PROCEEDS

We estimate that the net proceeds from the sale of the 25,000,000 shares of common stock we are offering will be approximately $126.5 million, after deducting the underwriting discount and estimated offering expenses payable by us. If the underwriters exercise in full their option to purchase additional shares, we estimate that the net proceeds to us will be approximately $145.5 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, build-out of commercial infrastructure, research and development, capital expenditures and working capital. We also expect to invest the net proceeds in investment grade, interest-bearing securities.

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PRICE RANGE OF OUR COMMON STOCK

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

	Common Stock Price	
	High	**Low**
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 Ended January 2, 2015		
Fiscal quarter ended March 28, 2014	$ 8.41	$ 3.37
Fiscal quarter ended June 27, 2014	3.84	3.02
Fiscal quarter ended September 26, 2014	4.55	1.51
Fiscal quarter ended January 2, 2015	1.88	1.26
Fiscal Year Ending January 1, 2016		
Fiscal quarter ending April 3, 2015	$ 3.16	$ 1.54
Fiscal quarter ended July 3, 2015	4.18	2.51
Fiscal quarter ending October 2, 2015 (through July 23, 2015)	$ 6.38	$ 3.31

The reported last sale price of our common stock on the NASDAQ Global Select Market on July 23, 2015, was $5.88 per share. As of July 20, 2015, there were approximately 476 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.

DILUTION

Our net tangible deficit on March 31, 2015, was $210.4 million, or $(1.07) per share. Net tangible deficit per share is equal to the amount of our total tangible assets, less total liabilities, divided by the aggregate number of shares of common stock outstanding as of March 31, 2015. Dilution in net tangible deficit per share represents the difference between the amount per share paid by purchasers of shares of common stock in this offering and the net tangible deficit per share of our common stock immediately after this offering. After giving effect to the purchase from us of 25,000,000 shares of common stock in this offering, and after deducting the underwriting discount and estimated offering expenses payable by us, our net tangible deficit on March 31, 2015, would have been approximately

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$(84.0) million, or approximately $(0.38) per share. This represents an immediate dilution of $5.78 per share to investors purchasing shares of common stock in this offering. The following table illustrates this dilution:

Public offering price per share		$ 5.40
Net tangible deficit per share as of March 31, 2015	$ (1.07)	
Increase per share attributable to new investors	0.69	
Less net tangible deficit per share as of March 31, 2015, after giving effect to this offering		(0.38)
Dilution per share to investors in this offering		$ 5.78

The foregoing discussion and table do not take into account further dilution to new investors that could occur upon the exercise of the underwriters option to purchase up to an additional 3,750,000 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 public offering price per share in this offering. If the underwriters exercise in full their option to purchase 3,750,000 additional shares, our net tangible deficit on March 31, 2015, after giving effect to this offering, would have been approximately $(65.0) million, or approximately $(0.29) per share, representing an immediate dilution of $5.69 per share to new investors purchasing shares of common stock in this offering.

The number of shares of common stock to be outstanding after the offering is based on the number of shares outstanding as of March 31, 2015. As of that date, we had 196,020,856 shares of common stock outstanding, excluding:

- 28,601,848 shares of common stock underlying options outstanding as of March 31, 2015, at a weighted average exercise price of $4.44 per share;
- 1,000,000 shares of common stock underlying warrants outstanding as of March 31, 2015, at a weighted average exercise price of $3.445 per share;
- 825,486 shares reserved for future issuance pursuant to unvested restricted stock units as of March 31, 2015;
- 10,190,819 shares available for future grant under our 2014 Equity Incentive Plan, 1,371,274 shares available for future purchase under our 2000 Employee Stock Purchase Plan, and 516,715 shares available for future grant under our 401(k) Retirement Plan, all as of March 31, 2015; 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.

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 March 31, 2015:

- on an actual basis; and
- on an as adjusted basis to give effect to the receipt of the estimated net proceeds of $126.5 million from the sale of the common stock in this offering (assuming no exercise of the underwriters option to purchase additional shares), after deducting the underwriting discounts and estimated offering expenses payable by us as described under Use of Proceeds.

You should read the data set forth in the table below in conjunction with (i) our consolidated financial statements, including the related notes, and Management s Discussion and Analysis of Financial Condition and Results of Operations from our Annual Report on Form 10-K for the fiscal year ended December 31, 2014, 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 March 31, 2015, which are incorporated by reference into this prospectus supplement.

	As of March 31, 2015	
(In thousands, except share and per share amounts)	**Actual**	**As Adjusted(1)**
Current portion of debt obligations under the loan and security agreement with Silicon Valley Bank	$ 164	$ 164
Current portion of debt obligations under the Deerfield Notes	$ 3,911	$ 3,911
Long-term debt, less current portion:		
4.25% Convertible senior subordinated notes due 2019	$ 186,940	$ 186,940
Long-term portion of debt obligations under the loan and security agreement with Silicon Valley Bank	80,000	80,000
Long-term portion of debt obligations under the Deerfield Notes(2)	97,415	97,415
Total long-term debt	364,355	364,355
Stockholders deficit:		
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; 196,020,856 shares issued and outstanding, actual, 221,020,856 shares issued and outstanding as adjusted(3)	196	221
Additional paid-in capital	1,655,580	1,782,010
Accumulated other comprehensive loss	(61)	(61)
Accumulated deficit	(1,802,474)	(1,802,474)
Total stockholders deficit	(146,759)	(20,304)

Total capitalization	$ 217,596	$ 344,051

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(1) As adjusted to reflect the sale of 25,000,000 shares being offered in this offering and the receipt of the estimated net proceeds of $126.5 million from the sale of these shares, after deducting the underwriting discount and estimated offering expenses payable by us.

(2) On March 9, 2015, we provided Deerfield notice that we elected to (i) require certain affiliates of Deerfield to acquire $100.0 million principal amount of Deerfield Notes and (ii) extend the maturity date of the Deerfield Notes to July 1, 2018. On July 1, 2015, such Deerfield affiliates acquired the $100.0 million principal amount of Deerfield Notes and we made a $4.0 million payment in respect of the Deerfield Notes. After giving effect to such transactions, $100.0 million principal amount of Deerfield Notes remained outstanding. The Deerfield Notes, as amended as result of these transactions, will bear interest on and after July 2, 2015, at the rate of 7.5% per annum to be paid in cash, quarterly in arrears, and 7.5% per annum to be paid in kind, quarterly in arrears, for a total interest rate of 15% per annum and will mature on July 1, 2018.

(3) The common stock shown as issued and outstanding in the table above is based on 196,020,856 shares of common stock outstanding as of March 31, 2015, and excludes the shares of common stock reserved for issuance upon conversion of the 2019 Notes, and also excludes, as of March 31, 2015: (i) 28,601,848 shares of common stock underlying options outstanding as of March 31, 2015, at a weighted average exercise price of $4.44 per share; (ii) 1,000,000 shares of common stock underlying warrants outstanding as of March 31, 2015, at a weighted average exercise price of $3.445 per share; (iii) 825,486 shares reserved for future issuance pursuant to unvested restricted stock units as of March 31, 2015; (iv) 10,190,819 shares available for future grant under our 2014 Equity Incentive Plan, 1,371,274 shares available for future purchase under our 2000 Employee Stock Purchase Plan, and 516,715 shares available for future grant under our 401(k) Retirement Plan, all as of March 31, 2015; and (v) 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.

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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, corporations organized outside of United States, any state thereof or the District of Columbia that are nonetheless treated as United States income taxpayers for United States federal tax purposes, 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, subject to the discussion below regarding foreign accounts. 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 IRS Form W-8BEN-E, 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. 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

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any gain on your disposition is taxable because we are a United States real property holding corporation and your ownership of our common stock exceeds 5%, you will be taxed on such disposition generally in the manner applicable to U.S. persons and in addition, a purchaser of your common stock may be required to withhold a tax equal to 10% of the amount realized on the sale.

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.

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 IRS Form W-8BEN-E or otherwise establishes an exemption.

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 IRS Form W-8BEN-E 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 to 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 to 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. An intergovernmental agreement between the United States and an applicable foreign country may modify these requirements. 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 withholding provisions described above currently apply to payments of dividends, and will apply 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 the underwriters for the offering named below have entered into an underwriting agreement with respect to the common stock being offered. Subject to the terms and conditions of the underwriting agreement, each underwriter has severally agreed to purchase from us the number of shares of our common stock set forth opposite its name below. Cowen and Company, LLC, William Blair & Company, L.L.C. and Stifel, Nicolaus & Company, Incorporated are the representatives of the underwriters.

Underwriters	Number of Shares
Cowen and Company, LLC	12,500,000
William Blair & Company, L.L.C.	7,500,000
Stifel, Nicolaus & Company, Incorporated	5,000,000
Total	25,000,000

The underwriting agreement provides that the obligations of the underwriters are subject to certain conditions precedent and that the underwriters have agreed, severally and not jointly, 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 option described below. If an underwriter defaults, the underwriting agreement provides that the purchase commitments of the non-defaulting underwriters may be increased or the underwriting agreement may be terminated, depending on the number of shares that remain unpurchased.

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

The underwriters are offering the shares, subject to prior sale, when, as and if issued to and accepted by them, subject to the receipt of certain legal opinions and other conditions specified in the underwriting agreement. The underwriters reserve the right to withdraw, cancel or modify offers to the public and to reject orders in whole or in part.

Option to Purchase Additional Shares. We have granted to the underwriters an option to purchase up to 3,750,000 additional shares of common stock at the public offering price, less the underwriting discount. This option is exercisable for a period of 30 days. To the extent that the underwriters exercise this option, the underwriters will purchase additional shares from us in approximately the same proportion as shown in the table above.

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 underwriters option to purchase additional shares.

We estimate that the total expenses of the offering, excluding underwriting discount, will be approximately $445,000 and are payable by us.

	Per Share	Total

		Without Option to Purchase Additional Shares	With Option to Purchase Additional Shares
Public offering price	$ 5.400	$ 135,000,000	$ 155,250,000
Underwriting discount	$ 0.324	$ 8,100,000	$ 9,315,000
Proceeds, before expenses, to Exelixis	$ 5.076	$ 126,900,000	$ 145,935,000

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The underwriters propose to offer the shares of common stock to the public at the public offering price set forth on the cover of this prospectus. The underwriters may offer the shares of common stock to securities dealers at the public offering price less a concession not in excess of $0.1944 per share. If all of the shares are not sold at the public offering price, the underwriters may change the offering price and other selling terms.

Discretionary Accounts. The underwriters do not intend to confirm sales of the shares to any accounts over which they have discretionary authority.

Stabilization. In connection with this offering, the underwriters may engage in stabilizing transactions, overallotment transactions, syndicate covering transactions, penalty bids 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 underwriters of shares of common stock in excess of the number of shares the underwriters are obligated to purchase. This creates a syndicate 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 underwriters is not greater than the number of shares that they may purchase in the option to purchase additional shares. In a naked short position, the number of shares involved is greater than the number of shares in the option to purchase additional shares. The underwriters may close out any short position by exercising their option to purchase additional shares and/or purchasing shares in the open market.
- Syndicate covering transactions involve purchases of common stock in the open market after the distribution has been completed in order to cover syndicate short positions. In determining the source of shares to close out the short position, the underwriters will consider, among other things, the price of shares available for purchase in the open market as compared with the price at which they may purchase shares through exercise of the option to purchase additional shares. If the underwriters sell more shares than could be covered by exercise of the option to purchase additional shares and, therefore, have 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 underwriters are 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.
- Penalty bids permit the representatives to reclaim a selling concession from a syndicate member when the common stock originally sold by that syndicate member is purchased in stabilizing or syndicate covering transactions to cover syndicate short positions.

These stabilizing transactions, syndicate covering transactions and penalty bids 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 underwriters make 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, underwriters 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, or (c) issue common stock 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. 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, (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 and (d) in the case of one individual, pursuant to a plan under Rule 10b5-1 under the Exchange Act, sell shares subject to expiring options during the last 45 days of the 90-day lock-up period solely to cover the exercise price of such options and any withholding tax payable upon exercise of such options.

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. Each of the underwriters 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 does 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 any 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.

Israel. In the State of Israel this prospectus shall not be regarded as an offer to the public to purchase shares of common stock under the Israeli Securities Law, 5728 1968, which requires a prospectus to be published and authorized by the Israel Securities Authority, if it complies with certain provisions of Section 15 of the Israeli Securities Law, 5728 1968, including, inter alia, if: (i) the offer is made, distributed or directed to not more than 35 investors, subject to certain conditions (the Addressed Investors); or (ii) the offer is made, distributed or directed to certain qualified investors defined in the First Addendum of the Israeli Securities Law, 5728 1968, subject to certain conditions (the Qualified Investors). The Qualified Investors shall not be taken into account in the count of the Addressed Investors and may be offered to purchase securities in addition to the 35 Addressed Investors. The company has not and will not take any action that would require it to publish a prospectus in accordance with and subject to the Israeli Securities Law, 5728 1968. We have not and will not distribute this prospectus or make, distribute or direct an offer to subscribe for our common stock to any person within the State of Israel, other than to Qualified Investors and up to 35 Addressed Investors.

Qualified Investors may have to submit written evidence that they meet the definitions set out in of the First Addendum to the Israeli Securities Law, 5728 1968. In particular, we may request, as a condition to be offered common stock, that Qualified Investors will each represent, warrant and certify to us and/or to anyone acting on our behalf: (i) that it is an investor falling within one of the categories listed in the First Addendum to the Israeli Securities Law, 5728 1968; (ii) which of the categories listed in the First Addendum to the Israeli Securities Law, 5728 1968 regarding Qualified Investors is applicable to it; (iii) that it will abide by all provisions set forth in the Israeli Securities Law, 5728 1968 and the regulations promulgated thereunder in connection with the offer to be issued common stock; (iv) that the shares of common stock that it will be issued are, subject to exemptions available under the Israeli Securities Law, 5728 1968: (a) for its own account; (b) for investment purposes only; and (c) not issued with a view to resale within the State of Israel, other than in accordance with the provisions of the Israeli Securities Law, 5728 1968; and (v) that it is willing to provide further evidence of its Qualified Investor status. Addressed Investors may have to submit written evidence in respect of their identity and may have to sign and submit a declaration containing, inter alia, the Addressed Investor s name, address and passport number or Israeli identification number.

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 underwriters and their 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 underwriters, is authorized to make any further offer of shares on our behalf or on behalf of the underwriters.

Electronic Offer, Sale and Distribution of Shares. A prospectus in electronic format may be made available on the websites maintained by one or more of the underwriters or selling group members, if any, participating in this offering and one or more of the underwriters participating in this offering may distribute prospectuses electronically. The representatives may agree to allocate a number of shares to underwriters and selling group members for sale to their online brokerage account holders. Internet distributions will be allocated by the underwriters 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 or the registration statement of which this prospectus forms a part, has not been approved or endorsed by us or any underwriter in its capacity as underwriter, and should not be relied upon by investors.

Other Relationships. Certain of the underwriters and their affiliates have provided, and may in the future provide, various investment banking, 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

Cooley LLP, San Francisco, California, will pass upon the validity of the common stock offered hereby. Sullivan & Cromwell LLP, Palo Alto, California, will pass upon the validity of the common stock offered hereby for the underwriters.

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, 2014, and the effectiveness of our internal control over financial reporting as of December 31, 2014, 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.

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. 000-30235):

- our Annual Report on Form 10-K for the fiscal year ended January 2, 2015, which was filed on March 2, 2015;
- the information specifically incorporated by reference into our Annual Report on Form 10-K for the fiscal year ended January 2, 2015, from our definitive proxy statement on Schedule 14A which was filed on April 16, 2015;
- our Quarterly Report on Form 10-Q which was filed on April 30, 2015;
- our Current Reports on Form 8-K or Form 8-K/A filed on February 11, 2015, March 9, 2015, April 30, 2015 (Form 8-K/A only), May 28, 2015, July 1, 2015, July 15, 2015 and July 20, 2015; 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 30, 2015, the last reported sale price of our common stock was $3.76 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 July 1, 2015.

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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.

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The information appearing in this prospectus, any applicable prospectus supplement or any related free writing prospectus is accurate only as of the date on the front of the document and any information we have incorporated by reference is accurate only as of the date of the document incorporated by reference, regardless of the time of delivery of this prospectus, any applicable prospectus supplement or any related free writing prospectus, or any sale of a security. Our business, financial condition, results of operations and prospects may have changed since those dates.

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

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

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

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PROSPECTUS SUMMARY

This summary highlights selected information contained elsewhere in this prospectus or incorporated by reference in this prospectus, and does not contain all of the information that you need to consider in making your investment decision. You should carefully read the entire prospectus, the applicable prospectus supplement and any related free writing prospectus, including the risks of investing in our securities discussed under the heading Risk Factors contained in the applicable prospectus supplement and any related free writing prospectus, and under similar headings in the other documents that are incorporated by reference into this prospectus. You should also carefully read the information incorporated by reference into this prospectus, including our financial statements, and the exhibits to the registration statement of which this prospectus is a part.

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

Exelixis, Inc.

Overview

We are a biopharmaceutical company committed to developing small molecule therapies for the treatment of cancer. Our most advanced asset is cabozantinib, our wholly-owned inhibitor of multiple receptor tyrosine kinases. Cabozantinib was approved by the United States Food and Drug Administration (FDA) on November 29, 2012, for the treatment of progressive, metastatic medullary thyroid cancer (MTC) in the United States under the brand name COMETRIQ®. In March 2014, the European Commission granted cabozantinib conditional marketing authorization for the treatment of adult patients with progressive, unresectable locally advanced or metastatic MTC, also under the brand name COMETRIQ. We are also evaluating cabozantinib in a broad development program comprising over forty-five clinical trials, across multiple indications, including two ongoing phase 3 pivotal trials focusing on metastatic renal cell carcinoma and advanced hepatocellular carcinoma.

Our second most advanced asset is cobimetinib (GDC-0973/XL518), a selective inhibitor of MEK, a serine/threonine kinase, which we out-licensed to our collaboration partner, Genentech (a member of the Roche Group). Cobimetinib is being evaluated by Genentech in a broad development program, including coBRIM, a phase 3 pivotal trial evaluating cobimetinib in combination with vemurafenib in patients with unresectable locally advanced melanoma harboring a BRAF V600 mutation. Genentech submitted a New Drug Application (NDA) to the FDA for the combination in December 2014, for which the FDA has granted priority review. On June 30, 2015, Genentech informed us that, in order to accommodate its review of a supplemental data submission, the FDA extended the Prescription Drug User Fee Act action date for its review of the NDA by the standard extension period of three months, from August 11, 2015 to November 11, 2015.

Company Information

We were incorporated in Delaware in November 1994 as Exelixis Pharmaceuticals, Inc., and we changed our name to Exelixis, Inc. in February 2000.

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

The Securities We May Offer

We may offer shares of our common stock and preferred stock, various series of debt securities and/or warrants to purchase any of such securities, either individually or in combination, from time to time under this prospectus, together with the applicable prospectus supplement and any related free writing prospectus, at prices and on terms to be determined by market conditions at the time of any offering. We may also offer common stock, preferred stock and/or debt securities upon the exercise of warrants. This prospectus provides you with a general description of the

securities we may offer. Each time we offer a type or series of securities under this prospectus, we will provide a prospectus supplement that will describe the specific amounts, prices and other important terms of the securities, including, to the extent applicable:

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

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

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

- the names of those agents or underwriters;
- applicable fees, discounts and commissions to be paid to them;
- details regarding over-allotment options, if any; and
- the net proceeds to us.

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

Common Stock. We may issue shares of our common stock from time to time. The holders of our common stock are entitled to one vote for each share held of record on all matters submitted to a vote of stockholders. Subject to preferences that may be applicable to any outstanding shares of preferred stock, the holders of common stock are

entitled to receive ratably such dividends as may be declared by our board of directors out of legally available funds. Upon our liquidation, dissolution or winding up, holders of our common stock are entitled to share ratably in all assets remaining after payment of liabilities and the liquidation preferences of any outstanding shares of preferred stock. Holders of common stock have no preemptive rights and no right to convert their common stock into any other securities. There are no redemption or sinking fund provisions applicable to our common stock. In this prospectus, we have summarized certain general features of the common stock under Description of Capital Stock Common stock. We urge you, however, to read the applicable prospectus supplement (and any related free writing prospectus that we may authorize to be provided to you) related to any common stock being offered.

Preferred Stock. We may issue shares of our preferred stock from time to time, in one or more series. Our board of directors will determine the designations, voting powers, preferences and rights of the preferred stock, as well as the qualifications, limitations or restrictions thereof, including dividend rights, conversion rights, preemptive rights, terms of redemption or repurchase, liquidation preferences, sinking fund terms and the number of shares constituting any series or the designation of any series. Convertible preferred stock will be convertible into our common stock or exchangeable for other securities. Conversion may be mandatory or at your option and would be at prescribed conversion rates.

If we sell any series of preferred stock under this prospectus, we will fix the designations, voting powers, preferences and rights of the preferred stock of each series we issue under this prospectus, as well as the qualifications, limitations or restrictions thereof, in the certificate of designation relating to that series. We will file as an exhibit to the registration statement of which this prospectus is a part, or will incorporate by reference from reports that we file with the SEC, the form of any certificate of designation that contains the terms of the series of preferred stock we are offering. In this prospectus, we have summarized certain general features of the preferred stock under Description of Capital Stock Preferred stock. We urge you, however, to read the applicable prospectus supplement (and any related free writing prospectus that we may authorize to be provided to you) related to the series of preferred stock being offered, as well as the complete certificate of designation that contains the terms of the applicable series of preferred stock.

Debt Securities. We may issue debt securities from time to time, in one or more series, as either senior or subordinated debt or as senior or subordinated convertible debt. The senior debt securities will rank equally with any other unsecured and unsubordinated debt. The subordinated debt securities will be subordinate and junior in right of payment, to the extent and in the manner described in the instrument governing the debt, to all of our senior indebtedness. Convertible debt securities will be convertible into or exchangeable for our common stock or other securities. Conversion may be mandatory or at your option and would be at prescribed conversion rates.

Any debt securities issued under this prospectus will be issued under one or more documents called indentures, which are contracts between us and a national banking association or other eligible party, as trustee. In this prospectus, we have summarized certain general features of the debt securities under Description of Debt Securities. We urge you, however, to read the applicable prospectus supplement (and any free writing prospectus that we may authorize to be provided to you) related to the series of debt securities being offered, as well as the complete indentures that contain the terms of the debt securities. We have filed the form of indenture as an exhibit to the registration statement of which this prospectus is a part, and supplemental indentures and forms of debt securities containing the terms of the debt securities being offered will be filed as exhibits to the registration statement of which this prospectus is a part or will be incorporated by reference from reports that we file with the SEC.

Warrants. We may issue warrants for the purchase of common stock, preferred stock and/or debt securities in one or more series. We may issue warrants independently or in combination with common stock, preferred stock and/or debt securities. In this prospectus, we have summarized certain general features of the warrants under Description of

Warrants. We urge you, however, to read the applicable prospectus supplement (and any related free writing prospectus that we may authorize to be provided to you) related to the particular series of warrants being offered, as well as any warrant agreements and warrant certificates that contain the terms of the warrants. We have filed forms of the warrant agreements and forms of warrant certificates containing the terms of the warrants that may be offered as exhibits to the registration statement of which this prospectus is a part. We will file as exhibits to the

registration statement of which this prospectus is a part, or will incorporate by reference from reports that we file with the SEC, the form of warrant and/or the warrant agreement and warrant certificate, as applicable, that contain the terms of the particular series of warrants we are offering, and any supplemental agreements, before the issuance of such warrants.

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

Use of Proceeds

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

The NASDAQ Global Select Market Listing

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

Financial Presentation

Exelixis adopted a 52- or 53-week fiscal year that generally ends on the Friday closest to December 31st. Fiscal year 2015, a 52-week year, will end on January 1, 2016, and fiscal year 2014, a 53-week year, ended on January 2, 2015. For convenience, references of and for the fiscal periods ended April 3, 2015, and as of and for the fiscal years ended January 2, 2015, December 27, 2013, December 28, 2012, December 30, 2011, December 31, 2010, are indicated as being as of and for the periods ended March 31, 2015, and December 31, 2014, 2013, 2012, 2011 and 2010, respectively.

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RISK FACTORS

Investing in our securities involves a high degree of risk. Before deciding whether to invest in our securities, you should consider carefully the risks and uncertainties described under the heading Risk Factors contained in the applicable prospectus supplement and any related free writing prospectus, and discussed under the section entitled Risk Factors contained in our most recent Annual Report on Form 10-K and in our most recent Quarterly Report on Form 10-Q, as well as any amendments thereto reflected in subsequent filings with the SEC, which are incorporated by reference into this prospectus in their entirety, together with other information in this prospectus, the documents incorporated by reference and any free writing prospectus that we may authorize for use in connection with this offering. The risks described in these documents are not the only ones we face, but those that we consider to be material. There may be other unknown or unpredictable economic, business, competitive, regulatory or other factors that could have material adverse effects on our future results. Past financial performance may not be a reliable indicator of future performance, and historical trends should not be used to anticipate results or trends in future periods. If any of these risks actually occurs, our business, financial condition, results of operations or cash flow could be seriously harmed. This could cause the trading price of our common stock to decline, resulting in a loss of all or part of your investment. Please also read carefully the section below entitled Special Note Regarding Forward-Looking Statements.

SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

This prospectus and the documents we have filed with the SEC that are incorporated by reference contain forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, as amended, or the Securities Act, and Section 21E of the Securities Exchange Act of 1934, as amended, or the Exchange Act. These statements relate to future events or to our future operating or financial performance and involve known and unknown risks, uncertainties and other factors which may cause our actual results, performance or achievements to be materially different from any future results, performances or achievements expressed or implied by the forward-looking statements. Forward-looking statements include, but are not limited to, statements about:

- our business strategy and our expectations with respect to the implementation of our business strategy;
- our expectations with respect to the potential therapeutic and commercial value of cabozantinib, cobimetinib and any other of our product candidates;
- our expectations with respect to regulatory submissions and approvals and our clinical trials;
- our expectations with respect to our intellectual property position; and
- our estimates regarding our capital requirements and our need for additional financing.

In some cases, you can identify forward-looking statements by terms such as may, will, should, could, would, plan, anticipate, believe, estimate, project, predict, potential and similar expressions intended to identify forward-looking statements. These statements reflect our current views with respect to future events and are based on assumptions and are subject to risks and uncertainties. Given these uncertainties, you should not place undue reliance

on these forward-looking statements. We discuss in greater detail many of these risks under the heading Risk Factors contained in the applicable prospectus supplement, in any free writing prospectuses we may authorize for use in connection with a specific offering, and in our most recent annual report on Form 10-K and in our most recent quarterly report on Form 10-Q, as well as any amendments thereto reflected in subsequent filings with the SEC, which are incorporated by reference into this prospectus in their entirety. Also, these forward-looking statements represent our estimates and assumptions only as of the date of the document containing the applicable statement. Unless required by law, we undertake no obligation to update or revise any forward-looking statements to reflect new information or future events or developments. Thus, you should not assume that our silence over time means that actual events are bearing out as expressed or implied in such forward-looking statements. You should read this prospectus, any applicable prospectus supplement, together with the documents we have filed with the SEC that are incorporated by reference and any free writing prospectus that we may authorize for use in connection with this offering completely and with the understanding that our actual future results may be materially different from what we expect. We qualify all of the forward-looking statements in the foregoing documents by these cautionary statements.

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USE OF PROCEEDS

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

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

RATIO OF EARNINGS TO FIXED CHARGES

The following table sets forth, for each of the periods presented, our ratio of earnings to fixed charges or our deficiency of earnings to cover fixed charges. Our earnings were insufficient to cover fixed charges for the three months ended March 31, 2015, and the years ended December 31, 2014, 2013, 2012 and 2010. The following table sets forth our ratio of earnings to fixed charges for the year ended December 31, 2011, and our deficiency of earnings to cover fixed charges for the three months ended March 31, 2015, and the years ended December 31, 2014, 2013, 2012 and 2010.

	Three Months Ended March 31, 2015	Year Ended December 31, 2014	2013	2012	2011	2010
			(In thousands, except ratio)			
Ratio of earnings to fixed charges					5.57	
Deficiency of earnings available to cover fixed charges (in thousands)	$ (35,170)	$ (268,724)	$ (244,856)	$ (147,538)		$ (92,402)

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

DESCRIPTION OF CAPITAL STOCK

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

Common stock

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

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

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

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

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

Preferred stock

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

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

- the title and stated value;
- the number of shares we are offering;

the liquidation preference per share;

the purchase price;

the dividend rate, period and payment date and method of calculation for dividends;

whether dividends will be cumulative or non-cumulative and, if cumulative, the date from which dividends will accumulate;

the procedures for any auction and remarketing, if applicable;

the provisions for a sinking fund, if applicable;

the provisions for redemption or repurchase, if applicable, and any restrictions on our ability to exercise those redemption and repurchase rights;

any listing of the preferred stock on any securities exchange or market;

whether the preferred stock will be convertible into our common stock, and, if applicable, the conversion price, or how it will be calculated, and the conversion period;

whether the preferred stock will be exchangeable into debt securities, and, if applicable, the exchange price, or how it will be calculated, and the exchange period;

voting rights of the preferred stock;

preemptive rights, if any;

restrictions on transfer, sale or other assignment;

whether interests in the preferred stock will be represented by depositary shares;

a discussion of material United States federal income tax considerations applicable to the preferred stock;

the relative ranking and preferences of the preferred stock as to dividend rights and rights if we liquidate, dissolve or wind up our affairs;

any limitations on the issuance of any class or series of preferred stock ranking senior to or on a parity with the series of preferred stock as to dividend rights and rights if we liquidate, dissolve or wind up our affairs; and

any other specific terms, preferences, rights or limitations of, or restrictions on, the preferred stock.

Outstanding warrants

As of June 30, 2015, we had warrants outstanding to purchase an aggregate of 1,000,000 shares of common stock with an exercise price of $3.445 per share expiring on July 1, 2018.

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

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

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

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

Section 203 of the Delaware General Corporation Law

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

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

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

Transfer Agent and Registrar

The transfer agent and registrar for our common stock is Computershare Trust Company, N.A.: 1-866-416-6111.

Listing on The NASDAQ Global Select Market

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

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DESCRIPTION OF DEBT SECURITIES

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

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

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

General

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

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

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

- the title of the series of debt securities;
- any limit upon the aggregate principal amount that may be issued;

the maturity date or dates;

the form of the debt securities of the series;

the applicability of any guarantees;

whether or not the debt securities will be secured or unsecured, and the terms of any secured debt;

whether the debt securities rank as senior debt, senior subordinated debt, subordinated debt or any combination thereof, and the terms of any subordination;

if the price (expressed as a percentage of the aggregate principal amount thereof) at which such debt securities will be issued is a price other than the principal amount thereof, the portion of the principal amount thereof payable upon declaration of acceleration of the maturity thereof, or if applicable, the portion of the principal amount of such debt securities that is convertible into another security or the method by which any such portion shall be determined;

the interest rate or rates, which may be fixed or variable, or the method for determining the rate and the date interest will begin to accrue, the dates interest will be payable and the regular record dates for interest payment dates or the method for determining such dates;

our right, if any, to defer payment of interest and the maximum length of any such deferral period;

if applicable, the date or dates after which, or the period or periods during which, and the price or prices at which, we may, at our option, redeem the series of debt securities pursuant to any optional or provisional redemption provisions and the terms of those redemption provisions;

the date or dates, if any, on which, and the price or prices at which we are obligated, pursuant to any mandatory sinking fund or analogous fund provisions or otherwise, to redeem, or at the holder s option to purchase, the series of debt securities and the currency or currency unit in which the debt securities are payable;

the denominations in which we will issue the series of debt securities, if other than denominations of $1,000 and any integral multiple thereof;

any and all terms, if applicable, relating to any auction or remarketing of the debt securities of that series and any security for our obligations with respect to such debt securities and any other terms which may be advisable in connection with the marketing of debt securities of that series;

whether the debt securities of the series shall be issued in whole or in part in the form of a global security or securities; the terms and conditions, if any, upon which such global security or securities may be exchanged in whole or in part for other individual securities; and the depositary for such global security or securities;

if applicable, the provisions relating to conversion or exchange of any debt securities of the series and the terms and conditions upon which such debt securities will be so convertible or exchangeable, including the conversion or exchange price, as applicable, or how it will be calculated and may be adjusted, any mandatory or optional (at our option or the holders option) conversion or exchange features, the applicable

conversion or exchange period and the manner of settlement for any conversion or exchange;

if other than the full principal amount thereof, the portion of the principal amount of debt securities of the series which shall be payable upon declaration of acceleration of the maturity thereof;

additions to or changes in the covenants applicable to the particular debt securities being issued, including, among others, the consolidation, merger or sale covenant;

additions to or changes in the events of default with respect to the securities and any change in the right of the trustee or the holders to declare the principal, premium, if any, and interest, if any, with respect to such securities to be due and payable;

- additions to or changes in or deletions of the provisions relating to covenant defeasance and legal defeasance;
- additions to or changes in the provisions relating to satisfaction and discharge of the indenture;
- additions to or changes in the provisions relating to the modification of the indenture both with and without the consent of holders of debt securities issued under the indenture;
- the currency of payment of debt securities if other than U.S. dollars and the manner of determining the equivalent amount in U.S. dollars;
- whether interest will be payable in cash or additional debt securities at our or the holders option and the terms and conditions upon which the election may be made;
- the terms and conditions, if any, upon which we will pay amounts in addition to the stated interest, premium, if any and principal amounts of the debt securities of the series to any holder that is not a United States person for federal tax purposes;
- any restrictions on transfer, sale or assignment of the debt securities of the series; and
- any other specific terms, preferences, rights or limitations of, or restrictions on, the debt securities, any other additions or changes in the provisions of the indenture, and any terms that may be required by us or advisable under applicable laws or regulations.

Conversion or Exchange Rights

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

Consolidation, Merger or Sale

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

Events of Default under the Indenture

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

- if we fail to pay any installment of interest on any series of debt securities, as and when the same shall become due and payable, and such default continues for a period of 90 days; provided, however, that a valid extension of an interest payment period by us in accordance with the terms of any indenture supplemental thereto shall not constitute a default in the payment of interest for this purpose;

- if we fail to pay the principal of, or premium, if any, on any series of debt securities as and when the same shall become due and payable whether at maturity, upon redemption, by declaration or otherwise, or in any payment required by any sinking or analogous fund established with respect to such series; provided, however, that a valid extension of the maturity of such debt securities in accordance with the terms of any indenture supplemental thereto shall not constitute a default in the payment of principal or premium, if any;

- if we fail to observe or perform any other covenant or agreement contained in the debt securities or the indenture, other than a covenant specifically relating to another series of debt securities, and our failure continues for 90 days after we receive written notice of such failure, requiring the same to be remedied and stating that such is a notice of default thereunder, from the trustee or holders of at least 25% in aggregate principal amount of the outstanding debt securities of the applicable series; and

- if specified events of bankruptcy, insolvency or reorganization occur.

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

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

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

- the direction so given by the holder is not in conflict with any law or the applicable indenture; and

- subject to its duties under the Trust Indenture Act, the trustee need not take any action that might involve it in personal liability or might be unduly prejudicial to the holders not involved in the proceeding.

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

- the holder has given written notice to the trustee of a continuing event of default with respect to that series;

- the holders of at least 25% in aggregate principal amount of the outstanding debt securities of that series have made written request,

such holders have offered to the trustee indemnity satisfactory to it against the costs, expenses and liabilities to be incurred by the trustee in compliance with the request; and

the trustee does not institute the proceeding, and does not receive from the holders of a majority in aggregate principal amount of the outstanding debt securities of that series other conflicting directions within 90 days after the notice, request and offer.

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

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

Modification of Indenture; Waiver

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

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

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

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

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Discharge

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

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

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

Form, Exchange and Transfer

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

At the option of the holder, subject to the terms of the indenture and the limitations applicable to global securities described in the applicable prospectus supplement, the holder of the debt securities of any series can exchange the

debt securities for other debt securities of the same series, in any authorized denomination and of like tenor and aggregate principal amount.

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

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

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

- issue, register the transfer of, or exchange any debt securities of that series during a period beginning at the opening of business 15 days before the day of mailing of a notice of redemption of any debt securities that may be selected for redemption and ending at the close of business on the day of the mailing; or

- register the transfer of or exchange any debt securities so selected for redemption, in whole or in part, except the unredeemed portion of any debt securities we are redeeming in part.

Information Concerning the Trustee

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

Payment and Paying Agents

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

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

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

Governing Law

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

DESCRIPTION OF WARRANTS

The following description, together with the additional information that we include in any applicable prospectus supplement and in any related free writing prospectus that we may authorize to be distributed to you, summarizes the

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

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

General

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

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

the dates on which the right to exercise the warrants will commence and expire;

the manner in which the warrant agreements and warrants may be modified;

a discussion of any material or special U.S. federal income tax considerations of holding or exercising the warrants;

the terms of the securities issuable upon exercise of the warrants; and

any other specific terms, preferences, rights or limitations of or restrictions on the warrants.

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

- in the case of warrants to purchase debt securities, the right to receive payments of principal of, or premium, if any, or interest on, the debt securities purchasable upon exercise or to enforce covenants in the applicable indenture; or

- in the case of warrants to purchase common stock or preferred stock, the right to receive dividends, if any, or, payments upon our liquidation, dissolution or winding up or to exercise voting rights, if any.

Exercise of Warrants

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

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

Governing Law

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

Enforceability of Rights by Holders of Warrants

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

LEGAL OWNERSHIP OF SECURITIES

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

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

Book-Entry Holders

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

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

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

Street Name Holders

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

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

Legal Holders

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

For example, once we make a payment or give a notice to the holder, we have no further responsibility for the payment or notice even if that holder is required, under agreements with depositary participants or customers or by law, to pass it along to the indirect holders but does not do so. Similarly, we may want to obtain the approval of the holders to amend an indenture, to relieve us of the consequences of a default or of our obligation to comply with a particular provision of the indenture or for other purposes. In such an event, we would seek approval only from the holders, and not the indirect holders, of the securities. Whether and how the holders contact the indirect holders is up to the holders.

Special Considerations For Indirect Holders

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

the performance of third party service providers;

how it handles securities payments and notices;

whether it imposes fees or charges;

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how it would handle a request for the holders consent, if ever required;

whether and how you can instruct it to send you securities registered in your own name so you can be a holder, if that is permitted in the future;

how it would exercise rights under the securities if there were a default or other event triggering the need for holders to act to protect their interests; and

if the securities are in book-entry form, how the depositary s rules and procedures will affect these matters.

Global Securities

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

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

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

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

Special Considerations For Global Securities

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

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

an investor cannot cause the securities to be registered in his or her name, and cannot obtain non-global certificates for his or her interest in the securities, except in the special situations we describe below;

an investor will be an indirect holder and must look to his or her own bank or broker for payments on the securities and protection of his or her legal rights relating to the securities, as we describe above;

an investor may not be able to sell interests in the securities to some insurance companies and to other institutions that are required by law to own their securities in non-book-entry form;

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- an investor may not be able to pledge his or her interest in a global security in circumstances where certificates representing the securities must be delivered to the lender or other beneficiary of the pledge in order for the pledge to be effective;

- the depositary s policies, which may change from time to time, will govern payments, transfers, exchanges and other matters relating to an investor s interest in a global security;

- we and any applicable trustee have no responsibility for any aspect of the depositary s actions or for its records of ownership interests in a global security, nor do we or any applicable trustee supervise the depositary in any way;

- the depositary may, and we understand that DTC will, require that those who purchase and sell interests in a global security within its book-entry system use immediately available funds, and your broker or bank may require you to do so as well; and

- financial institutions that participate in the depositary s book-entry system, and through which an investor holds its interest in a global security, may also have their own policies affecting payments, notices and other matters relating to the securities.

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

Special Situations When a Global Security Will Be Terminated

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

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

- if the depositary notifies us that it is unwilling, unable or no longer qualified to continue as depositary for that global security and we do not appoint another institution to act as depositary within 90 days;

- if we notify any applicable trustee that we wish to terminate that global security; or

- if an event of default has occurred with regard to securities represented by that global security and has not been cured or waived.

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

PLAN OF DISTRIBUTION

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

- at a fixed price or prices, which may be changed;

- at market prices prevailing at the time of sale;
- at prices related to such prevailing market prices; or
- at negotiated prices.

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

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

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

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

We may sell securities directly or through agents we designate from time to time. We will name any agent involved in the offering and sale of securities and we will describe any commissions we will pay the agent in the prospectus

supplement. Unless the prospectus supplement states otherwise, our agent will act on a best-efforts basis for the period of its appointment.

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

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

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

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

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

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

LEGAL MATTERS

Unless otherwise indicated in the applicable prospectus supplement, Cooley LLP, San Francisco, California, will pass upon the validity of the securities offered by this prospectus and any supplement thereto.

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 January 2, 2015, and the effectiveness of our internal control over financial reporting as of January 2, 2015, as set forth in their reports, which are incorporated by reference in this prospectus and elsewhere in the registration statement. Our financial statements are incorporated by reference in reliance on Ernst & Young LLP s reports, given on their authority as experts in accounting and auditing.

WHERE YOU CAN FIND MORE INFORMATION

This prospectus is part of the registration statement on Form S-3 we filed with the SEC under the Securities Act and does not contain all the information set forth in the registration statement. Whenever a reference is made in this prospectus to any of our contracts, agreements or other documents, the reference may not be complete and you should refer to the exhibits that are a part of the registration statement or the exhibits to the reports or other documents

incorporated by reference into this prospectus for a copy of such contract, agreement or other document. Because we are subject to the information and reporting requirements of the Exchange Act, we file annual, quarterly and current reports, proxy statements and other information with the SEC. Our SEC filings are available to the public over the Internet at the SEC s website at http://www.sec.gov. You may also read and copy any document we file at the SEC s Public Reference Room at 100 F Street, N.E., Washington, D.C. 20549. Please call the SEC at 1-800-SEC-0330 for further information on the operation of the Public Reference Room.

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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. Information in this prospectus supersedes information incorporated by reference that we filed with the SEC prior to the date of this prospectus, while information that we file later with the SEC will automatically update and supersede the information in this prospectus. We incorporate by reference into this prospectus and the registration statement of which this prospectus is a part the information or documents listed below that we have filed with the SEC (Commission File No. 30235):

- our Annual Report on Form 10-K for the year ended January 2, 2015, which was filed on March 2, 2015;
- the information specifically incorporated by reference into the Form 10-K from our definitive proxy statement on Schedule 14A which was filed on April 16, 2015;
- our Quarterly Report on Form 10-Q for the quarter ended April 3, 2015, which was filed on April 30, 2015;
- our Current Reports on Form 8-K filed on February 11, 2015, March 9, 2015, and May 28, 2015;
- our Current Report on Form 8-K/A filed on April 30, 2015; 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 and will become a part of this prospectus from the date that such documents are filed with the SEC. Information in such future filings updates and supplements the information provided in this prospectus. Any statements in any such future filings will automatically be deemed to modify and supersede any information in any document we previously filed with the SEC that is incorporated or deemed to be incorporated herein by reference to the extent that statements in the later filed document modify or replace such earlier statements.

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

Exelixis, Inc.

210 East Grand Avenue

South San Francisco, CA 94080

(650) 837-7000

Attn: Secretary

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25,000,000 Shares

Common Stock

PROSPECTUS

Cowen and Company **William Blair** **Stifel**

July 23, 2015