EXELIXIS, INC.
Form 10-K
February 20, 2014
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UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
Washington, D.C. 20549
FORM 10-K
(Mark One)
ý ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934
For the fiscal year ended: December 27, 2013 or
.. TRANSITION REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934 For the transition period from to
Commission File Number: 0-30235
EXELIXIS, INC.
(Exact name of registrant as specified in its charter)

Delaware	04-3257395
(State or other jurisdiction of incorporation or organization)	(I.R.S. Employer Identification Number)

210 East Grand Ave.
South San Francisco, CA 94080
(650) 837-7000
(Address, including zip code, and telephone number, including area code, of registrant's principal executive offices)
Securities Registered Pursuant to Section 12(b) of the Act:

Title of Each Class	Name of Each Exchange on Which Registered
Common Stock $.001 Par Value per Share	The Nasdaq Stock Market LLC

Securities Registered Pursuant to Section 12(g) of the Act:
None
Indicate by check mark if the registrant is a well-known seasoned issuer, as defined in Rule 405 of the Securities Act. Yes ý No ¨
Indicate by check mark if the registrant is not required to file reports pursuant to Section 13 or 15(d) of the Act. Yes ¨ No ý
Indicate by check mark whether the registrant (1) has filed all reports required to be filed by Section 13 or 15(d) of the Securities Exchange Act of 1934 during the preceding 12 months (or for such shorter period that the registrant was required to file such reports), and (2) has been subject to such filing requirements for the past 90 days. Yes ý No ¨
Indicate by check mark whether the registrant has submitted electronically and posted on its corporate Web site, if any, every Interactive Data File required to be submitted and posted pursuant to Rule 405 of Regulation S-T during the preceding 12 months (or for such shorter period that the registrant was required to submit and post such files). Yes ý No ¨
Indicate by check mark if disclosure of delinquent filers pursuant to Item 405 of Regulation S-K is not contained herein, and will not be contained, to the best of registrant's knowledge, in definitive proxy or information statements incorporated by reference in Part III of this Form 10-K or any amendment to this Form 10-K. ý
Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer or a smaller reporting company. See the definitions of "large accelerated filer," "accelerated filer" and "smaller reporting company" in Rule 12b-2 of the Exchange Act. (Check one):
Large accelerated filer ý Accelerated filer ¨ Non-accelerated filer (Do not check if a smaller reporting company) ¨ Smaller reporting company ¨
Indicate by check mark whether the registrant is a shell company (as defined in Rule 12b-2 of the Act). Yes ¨ No ý

State the aggregate market value of the voting and non-voting common equity held by non-affiliates computed by reference to the price at which the common equity was last sold, or the average bid and asked price of such common equity, as of the last business day of the registrant's most recently completed second fiscal quarter: $820,780,802 (Based on the closing sales price of the registrant's common stock on that date. Excludes an aggregate of 3,315,554 shares of the registrant's common stock held by persons who were directors and/or executive officers of the registrant at June 28, 2013 on the basis that such persons may be deemed to have been affiliates of the registrant at such date. Exclusion of such shares should not be construed to indicate that any such person possesses the power, direct or indirect, to direct or cause the direction of the management or policies of the registrant or that such person is controlled by or under common control with the registrant.)

As of February 19, 2014, there were 194,614,305 shares of the registrant's common stock outstanding.

DOCUMENTS INCORPORATED BY REFERENCE

Certain portions of the registrant's definitive proxy statement to be filed with the Securities and Exchange Commission pursuant to Regulation 14A, not later than April 26, 2014, in connection with the registrant's 2014 Annual Meeting of Stockholders are incorporated herein by reference into Part III of this Annual Report on Form 10-K.

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PART I

Some of the statements under the captions “Risk Factors,” “Management’s Discussion and Analysis of Financial Condition and Results of Operations” and “Business” and elsewhere in this Annual Report on Form 10-K are forward-looking statements. 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,” “would,” “could,” “estimate,” “predict,” “potential,” “continue,” “encouraging” or such terms or other similar expressions identify 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 in “Item 1A. Risk Factors” as well as those discussed elsewhere in this Annual Report on Form 10-K. These and many other factors could affect our future financial and operating results. We undertake no obligation to update any forward-looking statement to reflect events after the date of this report.

Exelixis has adopted a 52- or 53-week fiscal year that generally ends on the Friday closest to December 31st. Fiscal year 2011, a 52-week year, ended on December 30, 2011, fiscal year 2012, a 52-week year, ended on December 28, 2012, fiscal year 2013, a 52-week year, ended on December 27, 2013, and fiscal year 2014, a 53-week year, will end on January 2, 2015. For convenience, references in this report as of and for the fiscal years ended December 30, 2011, December 28, 2012 and December 27, 2013, are indicated on a calendar year basis, ended December 31, 2011, 2012 and 2013, respectively.

ITEM 1. BUSINESS

Overview

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

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

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

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

they expect top-line data from this trial in 2014.

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

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

Our Strategy

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

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

COMETRIQ(R) (cabozantinib)

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

The recommended dose of COMETRIQ in progressive, metastatic MTC is 140 mg orally, once daily (one 80 mg capsule and three 20 mg starting capsules) administered without food. This dose may be withheld in response to certain adverse reactions, and upon resolutions of adverse reactions may be reduced stepwise to 100 or 60 mg once daily to appropriately adjust the dose 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. This assessment was performed by an Independent Radiology Review Committee, or IRRC, in 89% of patients and by the treating physicians in 11% of patients. Patients were randomized (2:1) to receive COMETRIQ 140 mg (n = 219) or placebo (n = 111) orally, once daily until disease progression determined by the treating physician or until intolerable toxicity. Randomization was stratified by age (≤ 65 years vs. > 65 years) and prior use of a tyrosine kinase inhibitor, or 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 overall survival. The main efficacy outcome measures of PFS, objective response and response duration were based on IRRC-confirmed events using modified Response Evaluation Criteria in Solid Tumors (RECIST), which is a widely used set of rules that define when cancer patients improve ("respond"), stay the same ("stabilize") or worsen ("progress") during treatments.

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

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Postmarketing Commitments

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

We are also subject to the following postmarketing requirements:

- A phase 2 study comparing a lower dose of COMETRIQ with the labeled dose of 140 mg. This study will evaluate safety and PFS in progressive, metastatic MTC patients.
- Two clinical pharmacology studies assessing the pharmacokinetics of COMETRIQ. One will address the effect of administering COMETRIQ in conjunction with agents that increase gastric pH such as proton pump inhibitors, and the other study will assess the pharmacokinetics of COMETRIQ in patients with hepatic impairment.
- Four non-clinical studies to further assess the carcinogenicity, mutagenicity and teratogenicity of COMETRIQ.

Commercialization

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

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

To help ensure that all eligible progressive, metastatic MTC patients have appropriate access to COMETRIQ, we have established a comprehensive reimbursement and support program called Exelixis Access Services. Through Exelixis Access Services, we: provide co-pay assistance to qualified, commercially insured patients to help minimize out-of-pocket costs; provide free drug to uninsured patients who meet certain clinical and financial criteria; and make contributions to an independent co-pay assistance charity to help patients who don’t qualify for our co-pay assistance program. In addition, Exelixis Access Services is designed to provide comprehensive reimbursement support services, such as prior authorization support, benefits investigation, and if needed, appeals support.

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

To further support appropriate utilization of COMETRIQ, our Medical Affairs department is responsible for responding to physician inquiries with appropriate scientific and medical education and information.

EMA Marketing Authorization Application for COMETRIQ

In December 2013, the CHMP issued a positive opinion on the MAA, submitted to the EMA, for COMETRIQ for the proposed indication of progressive, unresectable, locally advanced, or metastatic MTC. The CHMP’s positive opinion will be reviewed by the European Commission, which has the authority to approve medicines for the European Union. COMETRIQ received orphan drug designation in the European Union from the Committee for Orphan Medicinal Products for the treatment of MTC in February 2009.

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

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Named Patient Use Program

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

Cabozantinib Development Program

We believe that cabozantinib's broad clinical profile is attractive and will allow commercial differentiation, assuming regulatory approval. The cabozantinib clinical development program is currently comprised of a total of a broad array of trials, including five pivotal studies. A portion of these trials are being conducted through our own internal development efforts and are funded by us, and the remainder are being conducted through our CRADA with NCI-CTEP and our IST program. The most advanced clinical program for cabozantinib beyond progressive, metastatic MTC are focused on the treatment of metastatic CRPC, metastatic RCC and advanced HCC. We expect 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. Objective tumor responses have been observed in patients treated with cabozantinib in 15 individual tumor types investigated in phase 1 and 2 clinical trials to date, reflecting the broad potential clinical activity and commercial opportunity of this product candidate. In addition to activity against bone and soft tissue lesions in patients with CRPC, we have also observed resolution of metastatic bone lesions on bone scan in patients with metastatic breast cancer and melanoma in the RDT, in patients with RCC and patients with differentiated thyroid cancer in a phase 1 clinical trial, and in patients with bladder cancer in an NCI-CTEP-sponsored phase 2 clinical trial. To support the future development of cabozantinib, our Medical Affairs department is responsible for responsible for responding to physician inquiries with appropriate scientific and medical education and information, preparing scientific presentations and publications, and overseeing the process for ISTs. It is a priority for us to continue to evaluate cabozantinib across a broad range of tumor types, including non-small cell lung cancer, or NSCLC, ovarian cancer, melanoma, breast cancer, differentiated thyroid cancer and others, to support further prioritization of our clinical and commercial options. In addition, postmarketing requirements in connection with the approval of COMETRIQ in progressive, metastatic MTC dictate that we conduct additional studies related to dosing in progressive, metastatic MTC, pharmacokinetics, carcinogenicity, mutagenicity and teratogenicity of COMETRIQ as more fully described above under "--Postmarketing Commitments."

CRPC

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

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

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

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

COMET-2 is a double-blinded study comparing cabozantinib and mitoxantrone/prednisone designed to enroll 246 patients with CRPC that is metastatic to the bone, who are suffering from moderate to severe bone pain despite optimized narcotic medication, and who have failed prior docetaxel therapy and have also failed prior abiraterone and/or enzalutamide therapies. The trial is being conducted in English-speaking regions, including the United States, Canada, Australia, and the United Kingdom. Patients are being randomized 1:1 to receive either cabozantinib or mitoxantrone/prednisone. Alleviation of bone pain will be determined by comparing the percentage of patients in the two treatment arms who achieve a pain response at Week 6 that is confirmed at Week 12. The trial design assumes that 25% of patients in the cabozantinib arm will have a pain response while 8% of patients in the mitoxantrone/prednisone arm will have a pain response. Prior to randomization, patients will undergo a period during which their pain medication is optimized using one long acting narcotic medication and one immediate release narcotic medication. This optimization follows a standard approach defined in the National Comprehensive Cancer Network guidelines. Patients in the cabozantinib arm will be dosed at 60 mg per day until the patient no longer receives clinical benefit. The definition of a responder with respect to the bone pain endpoint is a greater than or equal to 30% decrease from baseline in the average of the daily worst pain intensity collected over seven days in Week 6 and confirmed in Week 12, with neither a concomitant increase in average daily dose of any narcotic pain medication, nor addition of any new narcotic pain medication. Overall survival will be a secondary endpoint of the COMET-2 trial. The trial will be deemed successful if the primary endpoint of statistically significant pain improvement is met and the overall survival analysis does not show an adverse impact on overall survival in the cabozantinib arm.

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

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

RCC

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

HCC

CELESTIAL (Cabozantinib Phase 3 Controlled Study In Hepatocellular Carcinoma), a phase 3 pivotal trial comparing cabozantinib with placebo in patients with advanced HCC who have previously been treated with sorafenib was

initiated in September 2013. The trial is designed to enroll 760 patients at approximately 200 sites. Patients are being randomized 2:1 to receive 60 mg of cabozantinib daily or placebo. The primary endpoint for CELESTIAL is overall survival, and the secondary endpoints include objective response rate and PFS.

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NSCLC

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

Other Cancer Indications

We are also evaluating the potential initiation of pivotal trials in other tumor types. We believe the potential initiation of pivotal trials in other tumor types may increase the value of the cabozantinib franchise, accelerate potential revenues, and spread the development and commercialization risk for cabozantinib across multiple opportunities. We have launched two initiatives to expand the cabozantinib development program beyond our internal development efforts: our CRADA with NCI-CTEP and our IST program.

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

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

Commencement of each of the proposed trials approved under the CRADA is subject to protocol development and satisfaction of certain other conditions. The proposed trials approved under the CRADA will be conducted under an investigational new drug application held by NCI-CTEP. We believe our CRADA reflects a major commitment by NCI-CTEP to support the broad exploration of cabozantinib's potential in a wide variety of cancers that have substantial unmet medical needs. NCI-CTEP provides funding for as many as 20 active clinical trials each year for a five-year period. We believe the agreement will enable us to broadly expand the cabozantinib development program in a cost-efficient manner.

We launched the IST program in October 2010, and it has already provided important interim data through the dose-ranging study in CRPC patients described above. These data were important for dose selection in the COMET pivotal trial program. Cabozantinib is being evaluated in a variety of ISTs. Currently there is one completed IST, 18 ongoing ISTs, 11 studies undergoing activation, and we expect to continue to consider additional IST proposals for the foreseeable future.

Cobimetinib Collaboration

In December 2006, we entered into a worldwide co-development agreement with Genentech for the development and commercialization of cobimetinib. Cobimetinib is a potent, highly selective inhibitor of MEK, a serine/threonine kinase that is a component of the RAS/RAF/MEK/ERK pathway. This pathway mediates signaling downstream of growth factor receptors, and is prominently activated in a wide variety of human tumors. In preclinical studies, oral dosing of cobimetinib resulted in potent and sustained inhibition of MEK in RAS- or BRAF-mutant tumor models. Exelixis discovered cobimetinib internally and advanced the compound to investigational new drug, or IND, status. Genentech paid upfront and milestone payments of $25.0 million in December 2006 and $15.0 million in January 2007 upon signing of the co-development agreement and with the submission of the IND for cobimetinib. Under the terms of the agreement, we were responsible for developing cobimetinib through the end of a phase 1 clinical trial, and Genentech had the option to co-develop cobimetinib, which Genentech could exercise after receipt of certain phase 1 data from us. In March 2008, Genentech exercised its option, triggering a payment to us of $3.0 million, which we received in April 2008. We were responsible for the phase 1 clinical trial until the point that a maximum

tolerated dose, or MTD, was determined. After MTD was determined, we granted to Genentech an exclusive worldwide revenue-bearing license to cobimetinib in March 2009, at which point Genentech became responsible for completing the phase 1 clinical trial and subsequent clinical development. We received an additional $7.0 million payment in March 2010.

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

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

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

- A Phase 1b, Open-Label, Dose-Escalation Study of the Safety, Tolerability, and Pharmacokinetics of MEHD7945A and Cobimetinib in Patients with Locally Advanced or Metastatic Solid Tumors with Mutant KRAS (NCT01986166);
- A Phase 1b, Open-Label Study Evaluating the Safety, Tolerability, and Pharmacokinetics of Onartuzumab in Combination with Vemurafenib and/or Cobimetinib in Patients with Advanced Solid Malignancies (NCT01974258); and
- A Phase 1b Study of the Safety and Pharmacology of MPDL3280A Administered with Cobimetinib in Patients with Locally Advanced or Metastatic Solid Tumors (NCT01988896).

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

Other Collaborations

We have established collaborations with other leading pharmaceutical and biotechnology companies, including GlaxoSmithKline, Bristol-Myers Squibb Company, or Bristol-Myers Squibb, Sanofi, Merck (known as MSD outside of the United States and Canada) and Daiichi Sankyo Company Limited, or Daiichi Sankyo, for various compounds and programs in our portfolio. Pursuant to these collaborations, we have out-licensed compounds or programs to a partner for further development and commercialization, have no further development cost obligations related to such compounds or programs and may be entitled to receive contingent payments and royalties or a share of profits from commercialization. Several of these out-licensed compounds are in multiple phase 2 studies. These partnered compounds could potentially be of significant value to us if their development progresses successfully.

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

GlaxoSmithKline

In October 2002, we established a collaboration with GlaxoSmithKline to discover and develop novel therapeutics in the areas of vascular biology, inflammatory disease and oncology. The collaboration involved three agreements: (1) a product development and commercialization agreement, (2) a stock purchase and stock issuance agreement and (3) a loan and security agreement. During the term of the collaboration, we received $65.0 million in upfront and milestone payments, $85.0 million in

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research and development funding and loans in the principal amount of $85.0 million. In connection with the collaboration, GlaxoSmithKline purchased a total of three million shares of our common stock.

In October 2008, the development term under the collaboration concluded as scheduled. Under the terms of the collaboration, GlaxoSmithKline had the right to select up to two of the compounds in the collaboration for further development and commercialization. GlaxoSmithKline selected foretinib (XL880), an inhibitor of MET and VEGFR2, and had the right to choose one additional compound from a pool of compounds, which consisted of cabozantinib, XL281, XL228, XL820 and XL844 as of the end of the development term.

In July 2008, we achieved proof-of-concept for cabozantinib and submitted the corresponding data report to GlaxoSmithKline. In October 2008, GlaxoSmithKline notified us in writing that it decided not to select cabozantinib for further development and commercialization and that it waived its right to select XL281, XL228, XL820 and XL844 for further development and commercialization. As a result, we retained the rights to develop, commercialize, and/or license all of the compounds, subject to payment to GlaxoSmithKline of a 3% royalty on net sales of any product incorporating cabozantinib. We have discontinued development of XL820, XL228 and XL844.

GlaxoSmithKline continues to develop foretinib (XL880), and as disclosed on ClinicalTrials.gov, is currently recruiting patients into phase 1/2 trials studying the activity of foretinib in metastatic breast cancer both as a single agent (NCT01147484) and in combination with lapatinib (NCT01138384), and in NSCLC as a single agent and in combination with erlotinib (NCT02034097).

The $85.0 million loan we received from GlaxoSmithKline was repayable in three annual installments. We paid the final installment of principal and accrued interest under the loan in shares of our common stock on October 27, 2011, and GlaxoSmithKline subsequently released its related security interest in certain of our patents.

Bristol-Myers Squibb

ROR Collaboration Agreement

In October 2010, we entered into a worldwide collaboration with Bristol-Myers Squibb pursuant to which each party granted to the other certain intellectual property licenses to enable the parties to discover, optimize and characterize ROR antagonists that may subsequently be developed and commercialized by Bristol-Myers Squibb. In November 2010, we received a nonrefundable upfront cash payment of $5.0 million from Bristol-Myers Squibb. Additionally, for each product developed by Bristol-Myers Squibb under the collaboration, we will be eligible to receive payments upon the achievement by Bristol-Myers Squibb of development and regulatory milestones of up to $255.0 million in the aggregate and commercialization milestones of up to $150.0 million in the aggregate, as well as royalties on commercial sales of any such products. The collaboration agreement was amended and restated in April 2011 in connection with an assignment of patents to a wholly-owned subsidiary.

Under the terms of the collaboration agreement, we were responsible for activities related to the discovery, optimization and characterization of the ROR antagonists during the collaborative research period. In July 2011, we earned a $2.5 million milestone payment for achieving certain lead optimization criteria. The collaborative research period began on October 8, 2010 and ended on July 8, 2013. Since the end of the collaborative research period, Bristol-Myers Squibb has and will continue to have sole responsibility for any further research, development, manufacture and commercialization of products developed under the collaboration and will bear all costs and expenses associated with those activities.

Bristol-Myers Squibb may, at any time, terminate the collaboration agreement upon certain prior notice to us on a product-by-product and country-by-country basis. In addition, either party may terminate the agreement for the other party’s uncured material breach. In the event of termination by Bristol-Myers Squibb at will or by us for Bristol-Myers Squibb’s uncured material breach, the license granted to Bristol-Myers Squibb would terminate, the right to such product would revert to us and we would receive a royalty-bearing license for late-stage reverted compounds and a royalty-free license for early-stage reverted compounds from Bristol-Myers Squibb to develop and commercialize such product in the related country. In the event of termination by Bristol-Myers Squibb for our uncured material breach, Bristol-Myers Squibb would retain the right to such product, subject to continued payment of milestones and royalties.

LXR Collaboration

In December 2005, we entered into a collaboration agreement with Bristol-Myers Squibb for the discovery, development and commercialization of novel therapies targeted against LXR, a nuclear hormone receptor implicated in a variety of cardiovascular and metabolic disorders. This agreement became effective in January 2006, at which time we granted Bristol-Myers Squibb an exclusive worldwide license with respect to certain intellectual property primarily relating to compounds that modulate LXR, including BMS-852927 (XL041). During the research term, we jointly identified drug

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candidates with Bristol-Myers Squibb that were ready for IND-enabling studies. After the selection of a drug candidate for further clinical development by Bristol-Myers Squibb, Bristol-Myers Squibb agreed to be solely responsible for further preclinical development as well as clinical development, regulatory, manufacturing and sales/marketing activities for the selected drug candidate. We do not have rights to reacquire the drug candidates selected by Bristol-Myers Squibb. The research term expired in January 2010 and we transferred the technology to Bristol-Myers Squibb in 2011 to enable it to continue the LXR program. BMS has terminated development of XL041 and we have been advised that BMS is continuing additional preclinical research on the program. The collaboration agreement was amended and restated in April 2011 in connection with an assignment of patents to a wholly-owned subsidiary.

Under the collaboration agreement, Bristol-Myers Squibb paid us a nonrefundable upfront cash payment in the amount of $17.5 million and was obligated to provide research and development funding of $10.0 million per year for an initial research period of two years. In September 2007, the collaboration was extended at Bristol-Myers Squibb's request through January 12, 2009, and in November 2008, the collaboration was further extended at Bristol-Myers Squibb's request through January 12, 2010. Under the collaboration agreement, Bristol-Myers Squibb is required to pay us contingent amounts associated with development and regulatory milestones of up to $138.0 million per product for up to two products from the collaboration. In addition, we are also entitled to receive payments associated with sales milestones of up to $225.0 million and royalties on sales of any products commercialized under the collaboration. In connection with the extension of the collaboration through January 2009 and subsequently through January 2010, Bristol-Myers Squibb paid us additional research funding of approximately $7.7 million and approximately $5.8 million, respectively. In December 2007, we received $5.0 million in connection with the achievement by Bristol-Myers Squibb of a development milestone with respect to BMS-852927 (XL041).

Sanofi

In May 2009, we entered into a global license agreement with Sanofi for SAR245408 (XL147) and SAR245409 (XL765), leading inhibitors of phosphoinositide-3 kinase, or PI3K, and a broad collaboration for the discovery of inhibitors of PI3K for the treatment of cancer. The license agreement and collaboration agreement became effective on July 7, 2009. In connection with the effectiveness of the license and collaboration, on July 20, 2009, we received upfront payments of $140.0 million ($120.0 million for the license and $20.0 million for the collaboration), less applicable withholding taxes of $7.0 million, for a net receipt of $133.0 million. We received a refund payment in December 2011 with respect to the withholding taxes previously withheld.

Under the license agreement, Sanofi received a worldwide exclusive license to SAR245408 (XL147) and SAR245409 (XL765), which are in phase 1, phase 1b/2 and phase 2 clinical trials, and has sole responsibility for all subsequent clinical, regulatory, commercial and manufacturing activities. Sanofi is responsible for funding all development activities with respect to SAR245408 (XL147) and SAR245409 (XL765), including our activities. Following the effectiveness of the license agreement, we conducted the majority of the clinical trials for SAR245408 (XL147) and SAR245409 (XL765) at the expense of Sanofi. As provided for under the license agreement, however, the parties transitioned all development activities for these compounds to Sanofi in 2011. As disclosed on ClinicalTrials.gov, SAR245408 (XL147) is currently being studied in a clinical trial evaluating pharmacokinetics of a tablet formulation in patients with solid tumors or lymphoma (NCT01943838). As disclosed on ClinicalTrials.gov, SAR245409 (XL765) is currently being studied in clinical trials in patients with lymphoma either as a single agent (NCT01403636) or in combination with bendamustine and/or rituximab (NCT01410513). In addition SAR245409 (XL765) is being studied in combination with a MEK inhibitor in patients with locally advanced or metastatic solid tumors (NCT01390818). We will be eligible to receive contingent payments associated with development, regulatory and commercial milestones under the license agreement of $745.0 million in the aggregate, as well as royalties on sales of any products commercialized under the license.

Sanofi may, upon certain prior notice to us, terminate the license as to products containing SAR245408 (XL147) and SAR245409 (XL765). In the event of such termination election, Sanofi's license relating to such product would terminate and revert to us, and we would receive, subject to certain terms, conditions and potential payment obligations, licenses from Sanofi to research, develop and commercialize such products.

In December 2011, we and Sanofi entered into an agreement pursuant to which the parties terminated the discovery collaboration agreement and released each other from any potential liabilities arising under the collaboration agreement prior to effectiveness of the termination in December 2011. Each party retains ownership of the intellectual property that it generated under the collaboration agreement, and we granted Sanofi covenants not-to-enforce with respect to certain of our intellectual property rights. The termination agreement also provided that Sanofi would make a payment to us of $15.3 million, which we received in January 2012. If either party or its affiliate or licensee develops and commercializes a therapeutic product containing an isoform-selective PI3K inhibitor that arose from such party’s work (or was derived from such work) under the

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collaboration agreement, then such party will be obligated to pay royalties to the other party based upon the net sales of such products. The termination agreement provides that Sanofi will make a one-time payment to us upon the first receipt by Sanofi or its affiliate or licensee of marketing approval for the first therapeutic product containing an isoform-selective PI3K inhibitor that arose from Sanofi's work (or was derived from such work) under the collaboration agreement.

Merck

In December 2011, we entered into an agreement with Merck pursuant to which we granted Merck an exclusive worldwide license to our PI3K-delta, or PI3K-d, program, including XL499 and other related compounds. Pursuant to the terms of the agreement, Merck has sole responsibility to research, develop, and commercialize compounds from our PI3K-d program. The agreement became effective in December 2011.

Merck paid us an upfront cash payment of $12.0 million in January 2012 in connection with the agreement. We will be eligible to receive payments associated with the successful achievement of potential development and regulatory milestones for multiple indications of up to $239.0 million. We will also be eligible to receive payments for combined sales performance milestones and royalties on net-sales of products emerging from the agreement. Contingent payments associated with milestones achieved by Merck and royalties are payable on compounds emerging from our PI3K-d program or from certain compounds that arise from Merck's internal discovery efforts targeting PI3K-d during a certain period.

Merck may at any time, upon specified prior notice to us, terminate the license. In addition, either party may terminate the agreement for the other party's uncured material breach. In the event of termination by Merck at will or by us for Merck's uncured material breach, the license granted to Merck would terminate. In the event of a termination by us for Merck's uncured material breach, we would receive a royalty-free license from Merck to develop and commercialize certain joint products. In the event of termination by Merck for our uncured material breach, Merck would retain the licenses from us, and we would receive reduced royalties from Merck on commercial sales of products.

Daiichi Sankyo

In March 2006, we entered into a collaboration agreement with Daiichi Sankyo for the discovery, development and commercialization of novel therapies targeted against the mineralocorticoid receptor, or MR, a nuclear hormone receptor implicated in a variety of cardiovascular and metabolic diseases. Under the terms of the agreement, we granted to Daiichi Sankyo an exclusive, worldwide license to certain intellectual property primarily relating to compounds that modulate MR, including CS-3150 (XL550). Daiichi Sankyo is responsible for all further preclinical and clinical development, regulatory, manufacturing and commercialization activities for the compounds and we do not have rights to reacquire such compounds, except as described below.

Daiichi Sankyo paid us a nonrefundable upfront payment in the amount of $20.0 million and was obligated to provide research and development funding of $3.8 million over a 15-month research term. In June 2007, our collaboration agreement with Daiichi Sankyo was amended to extend the research term by six months over which Daiichi Sankyo was required to provide $1.5 million in research and development funding. In November 2007, the parties decided not to further extend the research term. For each product from the collaboration, we are also entitled to receive payments upon attainment of pre-specified development, regulatory and commercialization milestones. In December 2010, we received a milestone payment of $5.0 million in connection with an IND filing made by Daiichi Sankyo for CS-3150 (XL550) and, in August 2012, we received a milestone of $5.5 million in connection with the initiation of a phase 2 clinical trial for CS-3150 (XL550). We are eligible to receive additional development, regulatory and commercialization milestones of up to $145.0 million. In addition, we are also entitled to receive royalties on any sales of certain products commercialized under the collaboration. Daiichi Sankyo may terminate the agreement upon 90 days' written notice in which case Daiichi Sankyo's payment obligations would cease, its license relating to compounds that modulate MR would terminate and revert to us and we would receive, subject to certain terms and conditions, licenses from Daiichi Sankyo to research, develop and commercialize compounds, that were discovered under the collaboration.

Manufacturing and Distribution

We contract with third parties to manufacture the raw materials, the active pharmaceutical ingredient, or API, and finished solid dose COMETRIQ products for clinical and commercial uses. We currently do not operate

manufacturing facilities for clinical or commercial production of COMETRIQ. In addition, we expect for the foreseeable future to continue to rely on third parties for the manufacture of the raw materials, API and finished drug product for COMETRIQ. In this manner, we continue to build and maintain our supply chain.

Our multi-step supply chain for the manufacture and distribution of COMETRIQ consists of several suppliers located in multiple countries. Raw materials required for the production of the API are generally sourced from multiple third-party

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suppliers. Contract manufacturers in Europe and North America convert these raw materials into API for clinical and commercial purposes, respectively. We use a single third party to manufacture drug product for clinical purposes. We use a different third party to manufacture drug product and package and to label the finished product for commercial purposes. We use a single third party logistics provider to handle shipping and warehousing of our commercial supply of COMETRIQ in the United States and a single specialty pharmacy to dispense COMETRIQ to patients in fulfillment of prescriptions. We will also rely on a third party, Sobi, to distribute and commercialize COMETRIQ for the treatment of metastatic MTC in the European Union in the event that COMETRIQ is approved for commercial sale in such jurisdictions. Sobi is currently supporting access to cabozantinib under an NPU program in the European Union and other regions outside of the United States.

We may not be able to obtain sufficient quantities of COMETRIQ if our designated manufacturers do not have the capacity or capability to manufacture the product according to our schedule and specifications. If any of these suppliers were to become unable or unwilling to supply us with API or finished product that complies with applicable regulatory requirements, we could incur significant delays in our clinical trials or interruption of commercial supply which could have a material adverse effect on our business.

Our third-party manufacturers are independent entities, under contract with us, who are subject to their own unique operational and financial risks which are out of our control. If we or any of our third-party manufacturers fail to perform as required, this could impair our ability to deliver COMETRIQ on a timely basis or cause delays in our clinical trials and commercial activities. To the extent these risks materialize and affect their performance obligations to us, our financial results may be adversely affected.

We believe the processes used to manufacture our products are proprietary. For products manufactured by our third-party contract manufacturers, we have licensed the necessary aspects of these processes that we believe are proprietary to us to enable them to manufacture the products for us. We have agreements with these third-party manufacturers that are intended to restrict these manufacturers from using or revealing our processes, but we cannot be certain that these third-party manufacturers will comply with these restrictions.

While we believe there are multiple third parties capable of providing most of the materials and services we need to manufacture and distribute COMETRIQ, and that supply of materials that cannot be second-sourced can be managed with inventory planning, there is always a risk that we may underestimate demand, and that our manufacturing capacity through third-party manufacturers may not be sufficient. In addition, because of the significant lead times involved in our supply chain for COMETRIQ, we may have less flexibility to adjust our supply in response to changes in demand than if we had shorter lead times.

Government Regulation

The following section contains some general background information regarding the regulatory environment and processes affecting our industry and is designed to illustrate in general terms the nature of our business and the potential impact of government regulations on our business. It is not intended to be comprehensive or complete. Depending on specific circumstances, the information below may or may not apply to us or any of our product candidates. In addition, the information is not necessarily a description of activities that we have undertaken in the past or will undertake in the future. The regulatory context in which we operate is complex and constantly changing.

The FDA and comparable regulatory agencies in state and local jurisdictions and in foreign countries impose substantial requirements upon the clinical development, manufacture and marketing of pharmaceutical products. These agencies and other federal, state and local entities regulate research and development activities and the testing, manufacture, quality control, safety, effectiveness, labeling, storage, record keeping, approval, advertising and promotion of our products.

The process required by the FDA before product candidates may be marketed in the United States generally involves the following:

- preclinical laboratory and animal tests that must be conducted in accordance with Good Laboratory Practices;
- submission of an IND, which must become effective before clinical trials may begin;
- adequate and well-controlled human clinical trials to establish the safety and efficacy of the proposed drug candidate for its intended use;
-

pre-approval inspection of manufacturing facilities and selected clinical investigators for their compliance with Good Manufacturing Practices, or GMP, and Good Clinical Practices; and

- FDA approval of a New Drug Application, or NDA, for commercial marketing, or NDA supplement, for an approval of a new indication if the product is already approved for another indication.

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The testing and approval process requires substantial time, effort and financial resources. Prior to commencing the first clinical trial with a product candidate, we must submit an IND to the FDA. The IND automatically becomes effective 30 days after receipt by the FDA, unless the FDA, within the 30-day time period, raises concerns or questions about the conduct of the clinical trial. In such a case, the IND sponsor and the FDA must resolve any outstanding concerns before the clinical trial can begin. Submission of an IND may not result in FDA authorization to commence a clinical trial. A separate submission to the existing IND must be made for each successive clinical trial conducted during product development. Further, an independent institutional review board for each medical center proposing to conduct the clinical trial must review and approve the plan for any clinical trial and its informed consent form before the trial commences at that center. Regulatory authorities or an institutional review board or the sponsor may suspend a clinical trial at any time on various grounds, including a finding that the subjects or patients are being exposed to an unacceptable health risk.

For purposes of NDA approval, human clinical trials are typically conducted in three sequential phases that may overlap.

- Phase 1 – Studies are initially conducted in a limited patient population to test the product candidate for safety, dosage tolerance, absorption, metabolism, distribution and excretion in healthy humans or patients.
- Phase 2 – Studies are conducted with groups of patients afflicted with a specified disease in order to provide enough data to evaluate the preliminary efficacy, optimal dosages and expanded evidence of safety. Multiple phase 2 clinical trials may be conducted by the sponsor to obtain information prior to beginning larger and more expensive phase 3 clinical trials. In some cases, a sponsor may decide to run what is referred to as a “phase 2b” evaluation, which is a second, confirmatory phase 2 trial that could, if positive, serve as a pivotal trial in the approval of a product candidate.
- Phase 3 – When phase 2 evaluations demonstrate that a dosage range of the product is effective and has an acceptable safety profile, phase 3 trials are undertaken in large patient populations to further evaluate dosage, to provide replicate statistically significant evidence of clinical efficacy and to further test for safety in an expanded patient population at multiple clinical trial sites.

The FDA may require, or companies may pursue, additional clinical trials after a product is approved. These so-called phase 4 studies may be made a condition to be satisfied after a drug receives approval. Failure to satisfy such postmarketing commitments can result in FDA enforcement action, up and to including withdrawal of NDA approval. The results of phase 4 studies can confirm the effectiveness of a product candidate and can provide important safety information to augment the FDA’s adverse drug reaction reporting system. The results of product development, preclinical studies and clinical trials are submitted to the FDA as part of an NDA, or as part of an NDA supplement. The submission of an NDA or NDA supplement requires payment of a substantial User Fee to FDA. The FDA may convene an advisory committee to provide clinical insight on NDA review questions. The FDA may deny approval of an NDA or NDA supplement by way of a Complete Response letter if the applicable regulatory criteria are not satisfied, or it may require additional clinical data and/or an additional pivotal phase 3 clinical trial. Even if such data are submitted, the FDA may ultimately decide that the NDA or NDA supplement does not satisfy the criteria for approval. An NDA may be approved with significant restrictions on its labeling, marketing and distribution under a Risk Evaluation and Mitigation Strategy. Once issued, the FDA may withdraw product approval if ongoing regulatory standards are not met or if safety problems occur after the product reaches the market. In addition, the FDA may require testing and surveillance programs to monitor the effect of approved products that have been commercialized, and the FDA has the power to prevent or limit further marketing of a product based on the results of these postmarketing programs.

Satisfaction of FDA requirements or similar requirements of state, local and foreign regulatory agencies typically takes several years and the actual time required may vary substantially based upon the type, complexity and novelty of the product or disease. Government regulation may delay or prevent marketing of product candidates or new diseases for a considerable period of time and impose costly procedures upon our activities. The FDA or any other regulatory agency may not grant approvals for new indications for our product candidates on a timely basis, if at all. Success in early stage clinical trials does not ensure success in later stage clinical trials. Targets and pathways identified in vitro may be determined to be less relevant in clinical studies and results in animal model studies may not be predictive of human clinical results. Data obtained from clinical activities is not always conclusive and may be susceptible to

varying interpretations, which could delay, limit or prevent regulatory approval. Even if a product candidate receives regulatory approval, the approval may be significantly limited to specific disease states, patient populations and dosages. Further, even after regulatory approval is obtained, later discovery of previously unknown problems with a product may result in restrictions on the product or even complete withdrawal of the product from the market.

Any products manufactured or distributed by us pursuant to FDA approvals are subject to continuing regulation by the FDA, including record-keeping requirements and reporting of adverse experiences with the drug. Drug manufacturers and their subcontractors are required to register their establishments with the FDA and certain state agencies, and are subject to periodic unannounced inspections by the FDA and certain state agencies for compliance with GMP, which impose certain procedural

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and documentation requirements upon us and our third-party manufacturers. We cannot be certain that we or our present or future suppliers will be able to comply with the GMP regulations and other FDA regulatory requirements. If our present or future suppliers are not able to comply with these requirements, the FDA may halt our clinical trials, require us to recall a drug from distribution, or withdraw approval of the NDA for that drug.

The FDA closely regulates the marketing and promotion of drugs. A company can make only those claims relating to safety and efficacy that are approved by the FDA. Failure to comply with these requirements can result in adverse publicity, warning letters, corrective advertising and potential civil and criminal penalties. Physicians may prescribe legally available drugs for uses that are not described in the product's labeling and that differ from those tested by us and approved by the FDA. Such off-label uses are common across medical specialties. Physicians may believe that such off-label uses are the best treatment for many patients in varied circumstances. The FDA does not regulate the behavior of physicians in their choice of treatments. The FDA does, however, restrict manufacturer's communications on the subject of off-label use.

The FDA's policies may change and additional government regulations may be enacted which could prevent or delay regulatory approval of our product candidates or approval of new diseases for our product candidates. We cannot predict the likelihood, nature or extent of adverse governmental regulation that might arise from future legislative or administrative action, either in the United States or abroad.

The United States Orphan Drug Act promotes the development of products that demonstrate promise for the diagnosis and treatment of diseases or conditions that affect fewer than 200,000 people in the United States. Upon FDA receipt of Orphan Drug Designation, the sponsor is eligible for tax credits of up to 50% for qualified clinical trial expenses, the ability to apply for annual grant funding, waiver of Prescription Drug User Fee Act application fee, and upon approval, the potential for seven years of market exclusivity for the orphan-designated product for the orphan-designated indication.

Regulation Outside of the United States

In addition to regulations in the United States, we will be subject to regulations of other countries governing clinical trials and commercial sales and distribution of our products. Whether or not we obtain FDA approval for a product, we must obtain approval by the comparable regulatory authorities of countries outside of the United States before we can commence clinical trials in such countries and approval of the regulators of such countries or economic areas, such as the European Union, before we may market products in those countries or areas. The approval process and requirements governing the conduct of clinical trials, product licensing, pricing and reimbursement vary greatly from place to place, and the time may be longer or shorter than that required for FDA approval.

Under European Union regulatory systems, a company may submit marketing authorization applications either under a centralized or decentralized procedure. The centralized procedure provides for the grant of a single marketing authorization that is valid for all European Union member states. The decentralized procedure provides for mutual recognition of national approval decisions. Under this procedure, the holder of a national marketing authorization may submit an application to the remaining member states. Within 90 days of receiving the applications and assessments report, each member state must decide whether to recognize approval. If a member state does not recognize the marketing authorization, the disputed points are eventually referred to the European Commission, whose decision is binding on all member states.

As in the United States, we may apply for designation of a product as an Orphan Drug for the treatment of a specific indication in the European Union before the application for marketing authorization is made. Orphan Drugs in Europe enjoy economic and marketing benefits, including up to ten years of market exclusivity for the approved indication unless another applicant can show that its product is safer, more effective or otherwise clinically superior to the orphan-designated product.

Healthcare Regulation

Federal and state healthcare laws, including fraud and abuse and health information privacy and security laws, are also applicable to our business. If we fail to comply with those laws, we could face substantial penalties and our business, results of operations, financial condition and prospects could be adversely affected. The laws that may affect our ability to operate include: the federal Anti Kickback Statute, which prohibits soliciting, receiving, offering or paying remuneration, directly or indirectly, to induce, or in return for, the purchase or recommendation of an item or service

reimbursable under a federal healthcare program, such as the Medicare and Medicaid programs; and 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. State law equivalents of each of the above federal laws, many of which differ from each other in significant ways and may not have the same effect, further complicate compliance efforts.

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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 the Health Insurance Portability and Accountability Act of 1996, as amended by the Health Information Technology and Clinical Health Act, or HIPPA. Although we are not directly subject to HIPPA, 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.

There are also an increasing number of state laws that require manufacturers to make reports to states on pricing and marketing information. In addition, beginning in 2014, a similar federal requirement will require manufacturers to track and report to the federal government certain payments made to physicians and teaching hospitals made in the previous calendar year. These laws may affect our sales, marketing, and other promotional activities by imposing administrative and compliance burdens on us. In addition, given the lack of clarity with respect to these laws and their implementation, our reporting actions could be subject to the penalty provisions of the pertinent state, and soon federal, authorities.

Reimbursement

Sales of COMETRIQ and any future products of ours will depend, in part, on the extent to which their costs will be covered by third-party payors, such as government health programs, commercial insurance and managed healthcare organizations. These third-party payors are increasingly challenging the prices charged for medical products and services. Additionally, the containment of healthcare costs has become a priority of federal and state governments and the prices of drugs have been a focus in this effort. The U.S. government, state legislatures and foreign governments have shown significant interest in implementing cost-containment programs, including price controls, restrictions on reimbursement and requirements for substitution of generic products, when available. Adoption of price controls and cost-containment measures, and adoption of more restrictive policies in jurisdictions with existing controls and measures, could further limit our product revenue and results. If these third-party payors do not consider our products to be cost-effective compared to other therapies, they may not cover our products or, if they do, the level of payment may not be sufficient to allow us to sell our products on a profitable basis.

The Medicare Prescription Drug, Improvement, and Modernization Act of 2003, or the MMA, imposed new requirements for the distribution and pricing of prescription drugs for Medicare beneficiaries. Under Part D, Medicare beneficiaries may enroll in prescription drug plans offered by private entities which will provide coverage of outpatient prescription drugs. Part D plans include both stand-alone prescription drug benefit plans and prescription drug coverage as a supplement to Medicare Advantage plans. Unlike Medicare Part A and B, Part D coverage is not standardized. Part D prescription drug plan sponsors are not required to pay for all covered Part D drugs, and each drug plan can develop its own drug formulary that identifies which drugs it will cover and at what tier or level. However, Part D prescription drug formularies must include drugs within each therapeutic category and class of covered Part D drugs, though not necessarily all the drugs in each category or class. Any formulary used by a Part D prescription drug plan must be developed and reviewed by a pharmacy and therapeutic committee. Government payment for some of the costs of prescription drugs may increase demand for our products for which we receive marketing approval. However, any negotiated prices for our products covered by a Part D prescription drug plan will likely be lower than the prices we might otherwise obtain. Moreover, while the MMA applies only to drug benefits for Medicare beneficiaries, private payors often follow Medicare coverage policy and payment limitations in setting their

own payment rates. Any reduction in payment that results from the MMA may result in a similar reduction in payments from non-governmental payors.

The Patient Protection and Affordable Care Act, as amended by the Health Care and Education Affordability Reconciliation Act of 2010, collectively referred to as the PPACA, enacted in March 2010, is expected to have a significant impact on the health care industry. The PPACA is expected to expand coverage for the uninsured while at the same time containing overall healthcare costs. With regard to pharmaceutical products, the PPACA is expected to, among other things, expand and increase industry rebates for drugs covered under Medicaid programs and make changes to the coverage requirements under the Medicare Part D program. We cannot predict the full impact of the PPACA on our operations, as many of PPACA's reforms require the promulgation of detailed regulations implementing the statutory provisions, which has not yet

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occurred. In June 2012, the U.S. Supreme Court upheld the constitutionality of the PPACA, except that the Court held unconstitutional the provision of PPACA authorizing the Secretary of the U.S. Department of Health and Human Services to withdraw all of a state's Medicaid funding if the state declines to participate in the PPACA's expansion of Medicaid eligibility. Yet, some states have indicated that they intend to not implement certain sections of the PPACA, and some members of the U.S. Congress are still working to repeal the PPACA. As a result, the PPACA and/or certain of its provisions may be modified or eliminated by future legislation or litigation.

In addition, in some non-U.S. jurisdictions, the proposed pricing for a drug must be approved before it may be lawfully marketed. The requirements governing drug pricing vary widely from country to country. For example, the European Union provides options for its member states to restrict the range of medicinal products for which their national health insurance systems provide reimbursement and to control the prices of medicinal products for human use. A member state may approve a specific price for the medicinal product or it may instead adopt a system of direct or indirect controls on the profitability of the company placing the medicinal product on the market. There can be no assurance that any country that has price controls or reimbursement limitations for pharmaceutical products will allow favorable reimbursement and pricing arrangements for any of our products. Historically, products launched in the European Union do not follow the price structures of the United States and generally tend to be priced significantly lower.

Competition

There are many companies focused on the development of small molecules and antibodies for cancer. Our competitors and potential competitors include major pharmaceutical and biotechnology companies, as well as academic research institutions, clinical reference laboratories and government agencies that are pursuing research activities similar to ours. Many of our competitors and potential competitors have significantly more financial, technical and other resources than we do, which may allow them to have a competitive advantage.

We believe that our ability to successfully compete will depend on, among other things:

- efficacy, safety and reliability of COMETRIQ (cabozantinib);
- timing and scope of regulatory approval;
- the speed at which we develop cabozantinib for the treatment of additional tumor types beyond progressive, metastatic MTC;
- our ability to complete preclinical testing and clinical development and obtain regulatory approvals for cabozantinib;
- our ability to manufacture and sell commercial quantities of COMETRIQ (cabozantinib) to the market;
- our ability to successfully commercialize COMETRIQ (cabozantinib) and secure reimbursement in approved indications;
- product acceptance by physicians and other health care providers;
- quality and breadth of our technology;
- skills of our employees and our ability to recruit and retain skilled employees;
- protection of our intellectual property; and
- the availability of substantial capital resources to fund development and commercialization activities.

We believe that the quality and breadth of activity observed with cabozantinib, the skill of our employees and our ability to recruit and retain skilled employees, our patent portfolio and our capabilities for research and drug development are competitive strengths. However, many large pharmaceutical and biotechnology companies have significantly larger intellectual property estates than we do, more substantial capital resources than we have, and greater capabilities and experience than we do in preclinical and clinical development, sales, marketing, manufacturing and regulatory affairs.

The markets for which we intend to pursue regulatory approval of cabozantinib are highly competitive. We are aware of products in research or development by our competitors that are intended to treat all of the tumor types we are targeting, and any of these products may compete with cabozantinib. Our competitors may succeed in developing their products before we do, obtaining approvals from the FDA or other regulatory agencies for their products more rapidly than we do, or developing products that are more effective than cabozantinib. These products or technologies might render our technology obsolete or noncompetitive. There may also be drug candidates of which we are not aware at an earlier stage of development that may compete with cabozantinib. In addition, cabozantinib may compete with

existing therapies that have long histories of use, such as chemotherapy and radiation treatments in cancer indications. 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

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treatment of symptomatic or progressive MTC in patients with unresectable, locally advanced, or metastatic disease. In addition, we believe that COMETRIQ also faces competition as a treatment for progressive, metastatic MTC from off-label use of Bayer's and Onyx Pharmaceuticals' (a wholly-owned subsidiary of Amgen) multikinase inhibitor sorafenib, Pfizer's multikinase inhibitor sunitinib, and Ariad Pharmaceutical's multikinase inhibitor ponatinib.
We believe that if cabozantinib is approved for the treatment of the indications for which we currently have ongoing phase 3 pivotal trials, its potential principal competition in such indications may include the following:

- CRPC: Bayer's alpha-pharmaceutical (radium 223); Janssen Biotech's CYP17 inhibitor abiraterone; Medivation's androgen receptor inhibitor enzalutamide; and chemotherapeutic agents, including Sanofi's cabazitaxel and generic docetaxel;
- RCC: Pfizer's axitinib, sunitinib and temsirolimus; Novartis' everolimus; Bayer's and Onyx Pharmaceuticals' sorafenib; GlaxoSmithKline's pazopanib; and Genentech's bevacizumab; and
- HCC: Bayer's and Onyx Pharmaceuticals' sorafenib; Bayer's regorafenib; ImClone System's ramucirumab; and ArQule's tivantinib.

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

Research and Development Expenses

Research and development expenses consist primarily of personnel expenses, laboratory supplies, consulting and facilities costs. Research and development expenses were $178.8 million for the year ended December 31, 2013, compared to $128.9 million for the year ended December 31, 2012 and $156.8 million for the year ended December 31, 2011.

Revenues

In 2013, we derived 52% and 45% of our revenues from Bristol-Myers Squibb and Diplomat Specialty Pharmacy, respectively. We operate as a single business segment and have operations solely in the United States. Information regarding total revenues, net loss and total assets is set forth in our financial statements included in Item 8 of this Form 10-K.

Patents and Proprietary Rights

We actively seek patent protection in the United States, the European Union, and selected other foreign countries to cover our drug candidates and related technologies. Patents extend for varying periods according to the date of patent filing or grant and the legal term of patents in the various countries where patent protection is obtained. The actual protection afforded by a patent, which can vary from country to country, depends on the type of patent, the scope of its coverage and the availability of legal remedies in the country. We have numerous patents and pending patent applications that relate to methods of screening drug targets, compounds that modulate drug targets, as well as methods of making and using such compounds. While many patent applications have been filed relating to the drug candidates that we have developed, the majority of these are not yet issued or allowed.

Cabozantinib is covered by an issued patent in the United States (U.S. Pat. No. 7,579,473) for the composition-of-matter of cabozantinib and pharmaceutical compositions thereof. Cabozantinib is also covered by an additional issued patent in the United States (covering certain methods of use) and also by an issued patent in Europe (covering cabozantinib's composition-of-matter and certain methods of use). These issued patents will expire in September 2024, subject to any available extensions. Foreign counterparts of the issued U.S. and European patents are pending in Australia, Japan and Canada, which, if issued, are anticipated to expire in 2024. We have patent applications pending in the United States, European Union, Australia, Japan and Canada covering certain synthetic methods related to making cabozantinib, which, if issued, are anticipated to expire in 2024. We have filed patent applications in the United States and other selected countries covering certain salts, polymorphs and formulations of cabozantinib which, if issued, are anticipated to expire in approximately 2030. We have filed several patent applications in the United States and other selected countries relating to combinations of cabozantinib with certain

other anti-cancer agents which, if issued, are anticipated to expire in approximately 2030.
We have pending patent applications in the United States and European Union covering the composition-of-matter of our other drug candidates in clinical or preclinical development which, if issued, are anticipated to expire between 2023 and 2030.

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We have obtained licenses from various parties that give us rights to technologies that we deem to be necessary or desirable for our research and development. These licenses (both exclusive and non-exclusive) may require us to pay royalties as well as upfront and milestone payments.

While trade secret protection is an essential element of our business and we have taken security measures to protect our proprietary information and trade secrets, we cannot give assurance that our unpatented proprietary technology will afford us significant commercial protection. We seek to protect our trade secrets by entering into confidentiality agreements with third parties, employees and consultants. Our employees and consultants are also required to sign agreements obligating them to assign to us their interests in intellectual property arising from their work for us. All employees sign an agreement not to engage in any conflicting employment or activity during their employment with us and not to disclose or misuse our confidential information. However, it is possible that these agreements may be breached or invalidated, and if so, there may not be an adequate corrective remedy available. Accordingly, we cannot ensure that employees, consultants or third parties will not breach the confidentiality provisions in our contracts, infringe or misappropriate our trade secrets and other proprietary rights or that measures we are taking to protect our proprietary rights will be adequate.

In the future, third parties may file claims asserting that our technologies or products infringe on their intellectual property. We cannot predict whether third parties will assert such claims against us or against the licensors of technology licensed to us, or whether those claims will harm our business. If we are forced to defend ourselves against such claims, whether they are with or without merit and whether they are resolved in favor of, or against, our licensors or us, we may face costly litigation and the diversion of management's attention and resources. As a result of such disputes, we may have to develop costly non-infringing technology or enter into licensing agreements. These agreements, if necessary, may be unavailable on terms acceptable to us, or at all.

Employees

As of December 31, 2013, we had 227 full-time employees worldwide, 61 of whom held Ph.D. and/or M.D. degrees, most of whom were engaged in full-time research and development activities. None of our employees are represented by a labor union, and we consider our employee relations to be good.

Available Information

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

We maintain a site on the worldwide web at www.exelixis.com; however, information found on our website is not incorporated by reference into this report. We make available free of charge on or through our website our Securities and Exchange Commission, or SEC, filings, including our annual report on Form 10-K, quarterly reports on Form 10-Q, current reports on Form 8-K and amendments to those reports filed or furnished pursuant to Section 13(a) or 15(d) of the Securities Exchange Act of 1934, as amended, as soon as reasonably practicable after we electronically file such material with, or furnish it to, the SEC. Further, copies of our filings with the SEC are available at the SEC's Public Reference Room at 100 F Street, NE, Washington, D.C. 20549. Information on the operation of the Public Reference Room can be obtained by calling the SEC at 1-800-SEC-0330. The SEC maintains a site on the worldwide web that contains reports, proxy and information statements and other information regarding our filings at www.sec.gov.

ITEM 1A. RISK FACTORS

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

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

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

We may need to raise additional capital to:

- fund our operations and clinical trials;
- continue our research and development efforts; and

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

As of December 31, 2013, we had $415.9 million in cash and investments, which included short- and long-term restricted cash and investments of $12.2 million and $16.9 million, respectively, and short- and long-term unrestricted investments of $138.5 million and $144.3 million, respectively. We are required to maintain on deposit with Silicon Valley Bank or one of its affiliates short- and long-term unrestricted investments of $1.8 million and $81.9 million, respectively, pursuant to covenants in our loan and security agreement with Silicon Valley Bank. We anticipate that our current cash and cash equivalents, short- and long-term investments and product revenues will enable us to maintain our operations for a period of at least 12 months following the end of 2013. However, our future capital requirements will be substantial, and we may need to raise additional capital in the future. Our capital requirements will depend on many factors, and we may need to use available capital resources and raise additional capital significantly earlier than we currently anticipate. These factors include:

- the progress and scope of the development and commercialization activities with respect to COMETRIQ® (cabozantinib);
- repayment of our $287.5 million aggregate principal amount of the 4.25% convertible senior subordinated notes due 2019, or the 2019 Notes, that mature on August 15, 2019, unless earlier converted, redeemed or repurchased;
- repayment of the $104.0 million principal amount outstanding as of the filing date of this report ($114.0 million principal amount was outstanding at December 31, 2013) of our secured convertible notes, or the Deerfield Notes, issued to entities affiliated with Deerfield Management Company, L.P., or Deerfield, for which will be required to make a mandatory prepayment on the Deerfield Notes in 2015 equal to 15% of certain revenues from collaborative arrangements (other than intercompany arrangements) received during the prior fiscal year, subject to a maximum prepayment amount of $27.5 million, and if we exercise our extension option for the Deerfield Notes, for which we may be subject to similar mandatory prepayment obligations in 2016, 2017 and 2018, in each case unless we are able to repay the Deerfield Notes with our common stock, which we are only able to do under specified conditions
- repayment of our term loan and line of credit from Silicon Valley Bank, which had an outstanding balance at December 31, 2013, of $82.1 million;
- the commercial success of COMETRIQ and the revenues we generate;
- the level of payments received under existing collaboration agreements, licensing agreements and other arrangements;
- the degree to which we conduct funded development activity on behalf of partners to whom we have out-licensed compounds or programs;
- whether we enter into new collaboration agreements, licensing agreements or other arrangements (including, in particular, with respect to COMETRIQ (cabozantinib)) that provide additional capital;
- our ability to control costs;
- our ability to remain in compliance with, or amend or cause to be waived, financial covenants contained in agreements with third parties;
- the amount of our cash and cash equivalents, short- and long-term investments that serve as collateral for bank lines of credit;
- future clinical trial results;
- our need to expand our product and clinical development efforts;
- the cost and timing of regulatory approvals;
- the cost of clinical and research supplies of our product candidates;
- our obligation to share U.S. marketing and commercialization costs for cobimetinib under our collaboration with Genentech;
- our ability to share the costs of our clinical development efforts with third parties;
- the effect of competing technological and market developments;
-

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

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

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We may seek to raise funds through the sale of equity or debt securities or through external borrowings. In addition, we may enter into additional strategic partnerships, collaborative arrangements or other strategic transactions. It is unclear whether any such partnership, arrangement or transaction will occur, on satisfactory terms or at all, or what the timing and nature of such a partnership, arrangement or transaction may be. The sale of equity or convertible debt securities in the future may be dilutive to our stockholders, and debt-financing arrangements may require us to pledge certain assets and enter into covenants that would restrict certain business activities or our ability to incur further indebtedness, and may contain other terms that are not favorable to our stockholders or us. If we are unable to obtain adequate funds on reasonable terms, we may be required to curtail operations significantly or obtain funds by entering into financing, supply or collaboration agreements on unattractive terms or we may be required to relinquish rights to technology or product candidates or to grant licenses on terms that are unfavorable to us.

We may need to obtain additional funding in order to stay in compliance with financial covenants contained in 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 annual net losses since inception through the year ended December 31, 2013, with the exception of the fiscal year ended December 31, 2011. In 2011, we had net income primarily as a result of the acceleration of revenue recognized under our 2008 collaboration agreement with Bristol-Myers Squibb that terminated in October 2011 and under our 2009 discovery collaboration agreement with Sanofi that terminated in December 2011. We anticipate net losses and negative operating cash flow for the foreseeable future. For the year ended December 31, 2013, we had a net loss of $244.8 million; as of December 31, 2013, we had an accumulated deficit of $1.5 billion. We commercially launched COMETRIQ for the treatment of progressive, metastatic MTC in the United States in late January 2013. From the commercial launch through December 31, 2013, we have generated $15.0 million in net revenues from the sale of COMETRIQ. We have derived substantially all of our revenues since inception from collaborative research and development agreements. Revenues from research and development collaborations depend on research funding, the achievement of milestones, and royalties we earn from any future products developed from the collaborative research. If we are unable to successfully achieve milestones or our collaborators fail to develop successful products, we will not earn the revenues contemplated under such collaborative agreements. The amount of our net losses will depend, in part, on the rate of growth, if any, in our sales of COMETRIQ for progressive, metastatic MTC, license and contract revenues and on the level of our expenses. These losses have had and will continue to have an adverse effect on our stockholders' equity and working capital. Our research and development expenditures and general and administrative expenses have exceeded our revenues for each year other than 2011, and we expect to spend significant additional amounts to fund the continued development of cabozantinib. As a result, we expect to continue to incur substantial operating expenses, and, consequently, we will need to generate significant additional revenues to achieve future profitability. Because of the numerous risks and uncertainties associated with developing drugs, we are unable to predict the extent of any future losses or whether or when we will become profitable, if at all.

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

We incurred significant additional indebtedness and substantial debt service requirements as a result of our offering of the 2019 Notes in August 2012. As of December 31, 2013, our total consolidated indebtedness through maturity was $483.6 million (excluding trade payables). We may also incur additional indebtedness to meet future financing needs. If we incur additional indebtedness, it would increase our interest expense, leverage and operating and financial costs. Our indebtedness could have significant negative consequences for our business, results of operations and financial condition, including:

- making it more difficult for us to meet our payment and other obligations under the 2019 Notes, the Deerfield Notes, our loan and security agreement with Silicon Valley Bank or our other indebtedness;
- resulting in an event of default if we fail to comply with the financial and other restrictive covenants contained in our debt agreements, which event of default could result in all of our debt becoming immediately due and payable;
- increasing our vulnerability to adverse economic and industry conditions;
- subjecting us to the risk of increased sensitivity to interest rate increases on our indebtedness with variable interest rates, including borrowings under our loan and security agreement with Silicon Valley Bank;

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- 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.

We cannot assure you that we will continue to maintain sufficient cash reserves or that our business will continue to generate cash flow from operations at levels sufficient to permit us to pay principal, premium, if any, and interest on our indebtedness, or that our cash needs will not increase. If we are unable to generate sufficient cash flow or otherwise obtain funds necessary to make required payments, or if we fail to comply with the various requirements of the 2019 Notes, the Deerfield Notes, our loan and security agreement with Silicon Valley Bank, or any indebtedness which we have incurred or may incur in the future, we would be in default, which would permit the holders or the Trustee of the 2019 Notes or other indebtedness to accelerate the maturity of such notes or other indebtedness and could cause defaults under the 2019 Notes, the Deerfield Notes, our loan and security agreement with Silicon Valley Bank or our other indebtedness. Any default under the 2019 Notes, the Deerfield Notes, our loan and security agreement with Silicon Valley Bank, or any indebtedness that we have incurred or may incur in the future could have a material adverse effect on our business, results of operations and financial condition.

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

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

Managing costs is a key element of our business strategy. Consistent with this element of our strategy, and as a consequence of our decision to focus our proprietary resources and development efforts on the late-stage development and commercialization of cabozantinib, between March 2010 and May 2013 we implemented five restructurings, which resulted in an aggregate reduction in headcount of 429 employees. We have recorded aggregate restructuring charges of $53.3 million from inception through December 31, 2013 in connection with the restructurings and anticipate that we will incur additional restructuring charges related to the exit of all or portions of certain of our buildings in South San Francisco, California. These charges will be recorded through the end of the building lease terms, the last of which ends in 2017.

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

If we experience excessive unanticipated inefficiencies or incremental costs in connection with restructuring activities, such as unanticipated inefficiencies caused by reducing headcount, we may be unable to meaningfully realize cost savings and we may incur expenses in excess of what we anticipate. Either of these outcomes could prevent us from

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

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

Most of our foreign expenses incurred are associated with establishing and conducting clinical trials for cabozantinib. The amount of expenses incurred will be impacted by fluctuations in the currencies of those countries in which we conduct

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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 report we are not aware of any downgrades, material losses, or other significant deterioration in the fair value of our cash equivalents, short-term investments or long-term investments since December 31, 2013, no assurance can be given that a deterioration in conditions of the global credit and financial markets would not negatively impact our current portfolio of cash equivalents or investments or our ability to meet our financing objectives.

We may not achieve expected benefits as a result of changes to our corporate structure.

During 2013, we engaged in intercompany transactions with a newly established wholly-owned foreign subsidiary pursuant to which such subsidiary acquired the existing and future intellectual property rights to exploit cabozantinib in jurisdictions outside of the United States, and we may establish additional wholly-owned foreign subsidiaries in the future. We established this structure in anticipation of an increase in the international nature of our business activities and to reduce our overall effective tax rate through changes in how we develop and use our intellectual property and the structure of our international procurement and sales, including by entering into transfer-pricing arrangements that establish transfer prices for our intercompany transactions. One of our objectives is to achieve a reduction in our overall effective tax rate in the future as a result. There can be no assurance that the taxing authorities of the jurisdictions in which we determine to operate or to which we will otherwise be deemed to have sufficient tax nexus will not challenge the tax benefits that we expect to realize as a result of the new structure. In addition, future changes to U.S. or non-U.S. tax laws, including proposed legislation to reform U.S. taxation of international business activities, would negatively impact the anticipated tax benefits of the new structure. Any benefits to our tax rate will also depend on our ability to operate our business in a manner consistent with the new structure of our corporate organization and applicable taxing provisions, including by eliminating the amount of cash distributed to us by our subsidiaries. If the intended tax treatment is not accepted by the applicable taxing authorities, changes in tax law negatively impact the structure or we do not operate our business consistent with the new structure and applicable tax provisions, we may fail to achieve the financial efficiencies that we anticipate as a result of the changes to our corporate structure, and our future operating results and financial condition may be negatively impacted.

Risks Related to COMETRIQ(R) (cabozantinib)

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

The success of our business is dependent upon the successful development and commercialization of COMETRIQ. As part of our strategy, we are dedicating substantially all of our proprietary resources to advance COMETRIQ as aggressively as possible. On November 29, 2012, the FDA approved COMETRIQ for the treatment of progressive, metastatic MTC in the United States and we commercially launched COMETRIQ in late January 2013. In December 2013, CHMP issued a positive opinion of the MAA, submitted to the EMA, for COMETRIQ for the proposed indication of progressive, unresectable, locally advanced, or metastatic MTC. The CHMP's positive opinion will be reviewed by the European Commission, which has the authority to approve medicines for the European Union. We view the approval of COMETRIQ by the FDA for the treatment of progressive, metastatic MTC as a transitional event towards our objective of developing COMETRIQ into a major oncology franchise. Our ability to realize this objective or the value of our investment is contingent on, among other things, successful clinical development, regulatory approval and market acceptance of COMETRIQ. If we encounter difficulties in the development of COMETRIQ in

other indications beyond progressive, metastatic MTC due to any of the factors discussed in this “Risk Factors” section or otherwise, or we do not receive regulatory approval in such indications or are unable to successfully commercialize COMETRIQ in progressive, metastatic MTC or such other indications if approved, we will not have the resources necessary to continue our business in its current form.

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

Our ability to commercialize COMETRIQ for the treatment of progressive, metastatic MTC and potentially other

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

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

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

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

We currently rely on a single third party logistics provider to handle shipping and warehousing of our commercial supply of COMETRIQ and a single specialty pharmacy to dispense COMETRIQ to patients in fulfillment of prescriptions in the United States. We will also rely on a third party, Sobi, to distribute and commercialize COMETRIQ for the treatment of metastatic MTC primarily in the European Union and potentially other countries in the event that COMETRIQ is approved for commercial sale in those jurisdictions. Sobi is currently supporting access to cabozantinib under a NPU program in the European Union and other regions outside of the United States. Our current and anticipated future dependence upon 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:

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

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- federal civil and criminal false claims laws and civil monetary penalty laws, which prohibit, among other things, individuals or entities from knowingly presenting, or causing to be presented, claims for payment from Medicare, Medicaid, or other third-party payors that are false or fraudulent;
- federal criminal laws that prohibit executing a scheme to defraud any healthcare benefit program or making false statements relating to healthcare matters;
- state law equivalents of each of the above federal laws, such as anti-kickback and false claims laws which may apply to items or services reimbursed by any third-party payor, including commercial insurers, and state laws governing the privacy and security of health information in certain circumstances, many of which differ from each other in significant ways and may not have the same effect, thus complicating compliance efforts;
- the Foreign Corrupt Practices Act, a U.S. law which regulates certain financial relationships with foreign government officials (which could include, for example, certain medical professionals);
- federal and state consumer protection and unfair competition laws, which broadly regulate marketplace activities and activities that potentially harm consumers;
- state and federal government price reporting laws that require us to calculate and report complex pricing metrics to government programs, where such reported priced may be used in the calculation of reimbursement and/or discounts on our marketed drugs (participation in these programs and compliance with the applicable requirements may subject us to potentially significant discounts on our products, increased infrastructure costs, and potentially limit our ability to offer certain marketplace discounts); and
- state and federal marketing expenditure tracking and reporting laws, which generally require certain types of expenditures in the United States to be tracked and reported (compliance with such requirements may require investment in infrastructure to ensure that tracking is performed properly, and some of these laws result in the public disclosure of various types of payments and relationships, which could potentially have a negative effect on our business and/or increase enforcement scrutiny of our activities).

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

Numerous federal and state laws, including state security breach notification laws, state health information privacy laws and federal and state consumer protection laws, govern the collection, use and disclosure of personal information. Other countries also have, or are developing, laws governing the collection, use and transmission of personal information. In addition, most healthcare providers who are expected to prescribe our products and from whom we obtain patient health information are subject to privacy and security requirements under the federal Health Insurance Portability and Accountability Act of 1996, or HIPAA. Although we are not directly subject to HIPAA, we could be subject to criminal penalties if we knowingly obtain individually identifiable health information from a HIPAA-covered entity in a manner that is not authorized or permitted by HIPAA. The legislative and regulatory landscape for privacy and data protection continues to evolve, and there has been an increasing amount of focus on privacy and data protection issues with the potential to affect our business, including recently enacted laws in a majority of states requiring security breach notification. These laws could create liability for us or increase our cost of doing business. International laws, such as the EU Data Privacy Directive (95/46/EC) and Swiss Federal Act on Data Protection, regulate the processing of personal data within Europe and between European countries and the United States. Failure to provide adequate privacy protections and maintain compliance with safe harbor mechanisms could jeopardize business transactions across borders and result in significant penalties.

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

Our ability to successfully commercialize COMETRIQ will be highly dependent on the extent to which coverage and reimbursement for it is, and will be, available from third-party payors, including governmental payors, such as Medicare and Medicaid, and private health insurers. Many patients will not be capable of paying for COMETRIQ

themselves and will rely on third-party payors to pay for, or subsidize, their medical needs. If third-party payors do not provide coverage or reimbursement for COMETRIQ, our revenues and prospects for profitability will suffer. In addition, even if third-party payors provide some coverage or reimbursement for COMETRIQ, the availability of such coverage or reimbursement for prescription drugs under private health insurance and managed care plans often varies based on the type of contract or plan purchased.

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

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

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

For example, under the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Affordability Reconciliation Act of 2010, collectively referred to as the PPACA, enacted in March 2010, substantial changes may be made to the way healthcare is financed by both governmental and private insurers, and those changes may significantly affect the pharmaceutical industry. Among other things, the PPACA creates a new system of health insurance “exchanges,” designed to make health policies available to individuals and certain groups though state- or federally-administered marketplaces, beginning in 2014. In connection with such exchanges, certain “essential health benefits” are intended to be made more consistent across plans, setting basically a baseline coverage level. While prescription drugs are broadly considered “essential,” there is some discretion to the plans as to what categories of prescription drug products will be covered (and the scope of coverage in each category). We cannot predict at this time whether COMETRIQ would be covered by the health plans offered in any or all of the exchanges. Failure to be covered by plans offered in the exchanges could have a material adverse impact on our business. We anticipate that the PPACA, as well as other healthcare reform measures that may be adopted in the future, may result in more rigorous coverage criteria and an additional downward pressure on the price that we receive for COMETRIQ and any subsequently approved product, and could seriously harm our business. Under the Budget Control Act of 2011, as amended, federal budget “sequestration” became effective in March 2013, automatically reducing payments under various government programs, including, for example, certain Medicare provider and supplier reimbursement payments. Sequestration may have a material adverse effect on our customers and accordingly, our financial operations. Any reduction in reimbursement from Medicare or other government programs may result in a similar reduction in payments from private payors. Insurers may also refuse to provide any coverage of uses of approved products for medical indications other than those for which the FDA has granted market approvals. As a result, significant uncertainty exists as to whether and how much third-party payors will reimburse for newly-approved drugs, which in turn will put pressure on the pricing of drugs.

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

As a result of the overall trend towards cost-effectiveness criteria and managed healthcare in the United States, third-party payors are increasingly attempting to contain healthcare costs by limiting both coverage and the level of reimbursement of new drugs. They may use tiered reimbursement and may adversely affect demand for COMETRIQ

by placing it in an expensive tier. They may also refuse to provide any coverage of uses of approved products for medical indications other than those for which the FDA has granted market approvals. As a result, significant uncertainty exists as to whether and how much third-party payors will reimburse for newly approved drugs, which in turn will put pressure on the pricing of drugs. Further, we do not have experience in ensuring approval by applicable third-party payors outside of the United States for coverage and reimbursement of COMETRIQ. We also anticipate pricing pressures in connection with the sale of COMETRIQ due to the increasing influence of health maintenance organizations and additional legislative proposals.

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

The biotechnology industry is highly fragmented and is characterized by rapid technological change. In particular, the area of kinase-targeted therapies is a rapidly evolving and competitive field. We face, and will continue to face, intense competition from biotechnology and pharmaceutical companies, as well as academic research institutions, clinical reference laboratories and government agencies that are pursuing research activities similar to ours. Some of our competitors have entered into collaborations with leading companies within our target markets, including some of our existing collaborators. Some of our competitors are further along in the development of their products than we are. In addition, delays in the development of cabozantinib for the treatment of additional tumor types beyond progressive, metastatic MTC could allow our competitors to bring products to market before us, which would impair our ability to commercialize cabozantinib in such tumor types. Our future success will depend upon our ability to maintain a competitive position with respect to technological advances. The markets for which we intend to pursue regulatory approval of cabozantinib are highly competitive. Further, our competitors may be more effective at using their technologies to develop commercial products. Many of the organizations competing with us have greater capital resources, larger research and development staff and facilities, more experience in obtaining regulatory approvals and more extensive product manufacturing and commercial capabilities than we do. As a result, our competitors may be able to more easily develop technologies and products that would render our technologies and products, and those of our collaborators, obsolete and noncompetitive. There may also be drug candidates of which we are not aware at an earlier stage of development that may compete with cabozantinib. In addition, cabozantinib may compete with existing therapies that have long histories of use, such as chemotherapy and radiation treatments in cancer indications. We believe that the principal competing anti-cancer therapy to COMETRIQ in progressive, metastatic MTC is AstraZeneca's RET, VEGFR and EGFR inhibitor vandetanib, which has been approved by the FDA and the EMA for the treatment of symptomatic or progressive MTC in patients with unresectable, locally advanced, or metastatic disease. In addition, we believe that COMETRIQ also faces competition as a treatment for progressive, metastatic MTC from off-label use of Bayer's and Onyx Pharmaceuticals' (a wholly-owned subsidiary of Amgen) multikinase inhibitor sorafenib, Pfizer's multikinase inhibitor sunitinib, and Ariad Pharmaceutical's multikinase inhibitor ponatinib. We believe that if cabozantinib is approved for the treatment of the indications for which we currently have ongoing phase 3 pivotal trials, its potential principal competition in such indications may include the following:

- CRPC (castration-resistant prostate cancer): Bayer's and Algeta's alpha-pharmaceutical alpharadin (radium 223); Janssen Biotech's CYP17 inhibitor abiraterone; Medivation's androgen receptor inhibitor enzalutamide; and chemotherapeutic agents, including Sanofi's cabazitaxel and generic docetaxel;
- RCC (renal cell cancer): Pfizer's axitinib, sunitinib and temsirolimus; Novartis' everolimus; Bayer's and Onyx Pharmaceuticals' sorafenib; GlaxoSmithKline's pazopanib; and Genentech's bevacizumab; and
- HCC (hepatocellular): Bayer's and Onyx Pharmaceuticals' sorafenib; Bayer's regorafenib; ImClone System's ramucirumab; and ArQule's tivantinib.

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

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

We do not have the manufacturing capabilities or experience necessary to enable us to produce materials for our clinical trials or for commercial sale of COMETRIQ and rely on third party contractors to do so. These third parties must comply with applicable regulatory requirements, including the FDA's current GMP. Our current and anticipated future dependence upon these third parties may adversely affect our future profit margins and our ability to develop and commercialize COMETRIQ on a timely and competitive basis. These third parties may not be able to produce material on a timely basis or manufacture material at the quality or in the quantity required to meet our development and commercial timelines and applicable regulatory requirements. We may not be able to maintain or renew our existing third party manufacturing and supply arrangements, or enter into new arrangements, on acceptable terms, or

at all. Our third party manufacturers and suppliers could terminate or decline to renew our manufacturing and supply arrangements based on their own business priorities, at a time that is costly or inconvenient for us. If we are unable to contract for the production of materials in sufficient quantity and of sufficient quality on acceptable terms, our clinical trials and commercialization efforts may be delayed or otherwise adversely affected.

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Our third-party manufacturers may not be able to comply with the GMP regulations, other applicable FDA regulatory requirements or similar regulations applicable outside of the United States. Additionally, if we are required to enter into new manufacturing or supply arrangements, we may not be able to obtain approval from the FDA of any alternate manufacturer or supplier in a timely manner, or at all, which could delay or prevent the clinical development and commercialization of COMETRIQ. Failure of our third party manufacturers or suppliers or us to obtain approval from the FDA or to comply with applicable regulations could result in sanctions being imposed on us, including fines, civil penalties, delays in or failure to grant marketing approval of COMETRIQ, injunctions, delays, suspension or withdrawal of approvals, license revocation, seizures or recalls of products and compounds, operating restrictions and criminal prosecutions, any of which could have a significant adverse effect on our business. In addition, COMETRIQ requires precise, high-quality manufacturing. The failure to achieve and maintain these high manufacturing standards, including the incidence of manufacturing errors, could result in patient injury or death, product recalls or withdrawals, delays or failures in product testing or delivery, cost overruns or other problems that could have also a significant adverse effect on our business.

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

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

The results of preliminary studies do not necessarily predict clinical or commercial success, and later-stage clinical trials may fail to confirm the results observed in earlier-stage trials or preliminary studies. Although we have established timelines for manufacturing and clinical development of cabozantinib based on existing knowledge of our compounds in development and industry metrics, we may not be able to meet those timelines.

We may experience numerous unforeseen events during, or as a result of, clinical testing that could delay or prevent commercialization of cabozantinib for the treatment of CRPC, RCC, HCC and other indications, including:

- cabozantinib may not prove to be efficacious or may cause, or potentially cause, harmful side effects;
- negative or inconclusive clinical trial results may require us to conduct further testing or to abandon projects that we had expected to be promising;
- our competitors may discover or commercialize other compounds or therapies that show significantly improved safety or efficacy compared to cabozantinib;
- patient registration or enrollment in our clinical testing may be lower than we anticipate, resulting in the delay or cancellation of clinical testing; and
- regulators or institutional review boards may withhold authorization of cabozantinib, or delay, suspend or terminate clinical research for various reasons, including noncompliance with regulatory requirements or their determination that participating patients are being exposed to unacceptable health risks.

If we were to have significant delays in or termination of our clinical testing of cabozantinib as a result of any of the events described above or otherwise, our expenses could increase and our ability to generate revenues could be impaired, either of which could adversely impact our financial results.

We have limited experience in conducting clinical trials and may not be able to rapidly or effectively continue the further development of cabozantinib or meet current or future requirements of the FDA or regulatory authorities in other jurisdictions, including those identified based on our discussions with the FDA or such other regulatory authorities. Our planned clinical trials may not begin on time, or at all, may not be completed on schedule, or at all, may not be sufficient for registration of cabozantinib or may not result in an approvable product.

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

- the number of patients who ultimately participate in the clinical trial;
- the duration of patient follow-up that is appropriate in view of the results or required by regulatory authorities;

- the number of clinical sites included in the trials; and
- the length of time required to enroll suitable patient subjects.

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

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with respect to the compounds we have out-licensed to them. If any of the events described above were to occur with such programs or compounds, the likelihood of receipt of milestones and royalties under such collaboration agreements could decrease.

If third parties upon which we rely do not perform as contractually required or expected, we may not be able to obtain regulatory approval for or commercialize cabozantinib for the treatment of additional indications beyond progressive, metastatic MTC.

We do not have the ability to independently conduct clinical trials for cabozantinib, including our postmarketing commitments for COMETRIQ for the treatment of progressive, metastatic MTC, and we rely on third parties we do not control such as the federal government (including NCI-CTEP, with whom we have our CRADA), third-party contract research organizations, or CROs, medical institutions, clinical investigators and contract laboratories to conduct our clinical trials. If these third parties do not successfully carry out their contractual duties or regulatory obligations or meet expected deadlines, if the third parties need to be replaced or if the quality or accuracy of the data they obtain is compromised due to the failure to adhere to our clinical protocols or regulatory requirements or for other reasons, our preclinical development activities or clinical trials may be extended, delayed, suspended or terminated, and we may not be able to obtain regulatory approval for or commercialize cabozantinib for additional indications beyond progressive, metastatic MTC.

Cabozantinib is subject to a lengthy and uncertain regulatory process that may not result in the necessary regulatory approvals, which could adversely affect our ability to commercialize cabozantinib.

Cabozantinib, as well as the activities associated with its research, development and commercialization, are subject to extensive regulation by the FDA and other regulatory agencies in the United States and by comparable authorities in other countries. Failure to obtain regulatory approval for cabozantinib would prevent us from promoting its use. We have only limited experience in preparing and filing the applications necessary to gain regulatory approvals. The process of obtaining regulatory approvals in the United States and other foreign jurisdictions is expensive, and often takes many years, if approval is obtained at all, and can vary substantially based upon the type, complexity and novelty of the product candidates involved. For example, before 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.

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

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

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

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Any clinical trial may fail to produce results satisfactory to the FDA or regulatory authorities in other jurisdictions. For example, the FDA could determine that the design of a clinical trial is inadequate to produce reliable results. The regulatory process also requires preclinical testing, and data obtained from preclinical and clinical activities are susceptible to varying interpretations. The FDA has substantial discretion in the approval process and may refuse to approve any NDA (regardless of prior receipt of a SPA) or decide that our data is insufficient for approval and require additional preclinical, clinical or other studies. For example, varying interpretations of the data obtained from preclinical and clinical testing could delay, limit or prevent regulatory approval of cabozantinib.

In addition, delays or rejections may be encountered based upon changes in regulatory policy for product approval during the period of product development and regulatory agency review. Changes in regulatory approval policy, regulations or statutes or the process for regulatory review during the development or approval periods of cabozantinib may cause delays in the approval or rejection of an application.

Even if the FDA or a comparable authority in another jurisdiction approves cabozantinib, the approval may impose significant restrictions on the indicated uses, conditions for use, labeling, distribution, advertising, promotion, marketing and/or production of cabozantinib and may impose ongoing requirements for post-approval studies, including additional research and development and clinical trials. For example, in connection with the FDA's approval of COMETRIQ for the treatment of progressive, metastatic MTC, we are subject to the various postmarketing requirements, including a requirement to conduct a phase 2 clinical trial comparing a lower dose of COMETRIQ to the approved dose of 140 mg daily COMETRIQ in progressive, metastatic MTC and to conduct other clinical pharmacology and preclinical studies. These agencies also may impose various civil or criminal sanctions for failure to comply with regulatory requirements, including withdrawal of product approval.

Risks Related to Our Relationships with Third Parties

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

We have established collaborations with leading pharmaceutical and biotechnology companies, including Genentech, GlaxoSmithKline, 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. We may pursue collaborations for selected unpartnered preclinical and clinical programs and compounds. Our dependence on our relationships with existing collaborators for the development and commercialization of 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 result in costly litigation or arbitration that diverts management's attention and resources;
- collaborators may experience financial difficulties;
- collaborators may not be successful in their efforts to obtain regulatory approvals in a timely manner, or at all;
- collaborators may not properly maintain or defend our intellectual property rights or may use our proprietary information in such a way as to invite litigation that could jeopardize or invalidate our proprietary information or expose us to potential litigation;
- business combinations or significant changes in a collaborator's business strategy may adversely affect a collaborator's willingness or ability to complete its obligations under any arrangement;
- a collaborator could independently move forward with a competing drug candidate developed either independently or in collaboration with others, including our competitors;

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

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- future collaborators may require us to relinquish some important rights, such as marketing and distribution rights; and
- collaborations may be terminated or allowed to expire, which would delay, and may increase the cost of development of, our drug candidates.

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

We may not receive revenue from our collaborations.

Historically, we have derived substantially all of our revenues since inception from collaborative research and development agreements. Revenues from research and development collaborations depend on the achievement of milestones, and royalties we earn from any future products developed by our collaborators. If our collaborators fail to develop successful products, or if any of these agreements is terminated early, whether unilaterally or by mutual agreement, we will not earn the revenues contemplated under such collaborative agreements.

Most of our collaboration agreements contain early termination provisions. In addition, from time to time we review and assess certain aspects of our collaborations, partnerships and agreements and may amend or terminate, either by mutual agreement or pursuant to any applicable early termination provisions, such collaborations, partnerships or agreements if we deem them to be no longer in our economic or strategic interests.

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

We may 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. 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

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

Our success will depend in part upon our ability to obtain patents and maintain adequate protection of the intellectual property related to our technologies and products. The patent positions of biotechnology companies, including our patent position, are generally uncertain and involve complex legal and factual questions. We will be able to protect our intellectual property rights from unauthorized use by third parties only to the extent that our technologies are covered by valid and enforceable patents or are effectively maintained as trade secrets. We will continue to apply for patents covering our technologies and products as, where and when we deem appropriate. However, these applications may be challenged or may fail to result in issued patents. In addition, because patent applications can take many years to issue, there may be pending applications, unknown to us, which may later result in issued patents that cover the production, manufacture, commercialization or use of our product candidates. Our existing patents and any future patents we obtain may not be sufficiently broad to prevent others from practicing our technologies or from developing competing products. Furthermore, others may independently develop similar or alternative technologies or design around our patents. In addition, our patents may be challenged or invalidated or may fail to provide us with any competitive advantages, if, for example, others were the first to invent or to file patent applications for closely related inventions.

The laws of some foreign countries do not protect intellectual property rights to the same extent as the laws of the United States, and many companies have encountered significant problems in protecting and defending such rights in foreign jurisdictions. Many countries, including certain countries in Europe, have compulsory licensing laws under which a patent owner may be compelled to grant licenses to third parties (for example, the patent owner has failed to "work" the invention in that country or the third party has patented improvements). In addition, many countries limit the enforceability of patents against government agencies or government contractors. In these countries, the patent owner may have limited remedies, which could materially diminish the value of the patent. Compulsory licensing of life-saving drugs is also becoming increasingly popular in developing countries either through direct legislation or international initiatives. Such compulsory licenses could be extended to include our products or product candidates,

which could limit our potential revenue opportunities. Moreover, the legal systems of certain countries, particularly certain developing countries, do not favor the aggressive enforcement of patent and other intellectual property protection, which makes it difficult to stop infringement. We rely on trade secret protection for some of our confidential and proprietary information. We have taken security measures to protect our proprietary information and trade secrets, but these measures may not provide adequate protection. While we seek to protect our proprietary

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

Risks Related to Employees and Location

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

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

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

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collaborators sign agreements not to disclose our confidential information, it is possible that valuable proprietary knowledge may become publicly known through them.

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

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

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

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

Risks Related to Environmental and Product Liability

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

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

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

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

We may be held liable if any product we or our collaborators develop causes injury or is found otherwise unsuitable during product testing, manufacturing, marketing or sale. Regardless of merit or eventual outcome, product liability claims could result in decreased demand for our product candidates, injury to our reputation, withdrawal of patients from our clinical trials, substantial monetary awards to third parties and the inability to commercialize any products that we may develop. These claims might be made directly by consumers, health care providers, pharmaceutical companies or others selling or testing our products. We have obtained limited product liability insurance coverage for our clinical trials and commercial activities for cabozantinib in the amount of $15.0 million per occurrence and $15.0 million in the aggregate. However, our insurance may not reimburse us or may not be sufficient to reimburse us for expenses or losses we may suffer. Moreover, if insurance coverage becomes more expensive, we may not be able to maintain insurance coverage at a reasonable cost or in sufficient amounts to protect us against losses due to liability.

On occasion, juries have awarded large judgments in class action lawsuits for claims based on drugs that had unanticipated side effects. In addition, the pharmaceutical and biotechnology industries, in general, have been subject to significant medical malpractice litigation. A successful product liability claim or series of claims brought against us could harm our reputation and business and would decrease our cash reserves.

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Risks Related to Our Common Stock and the 2019 Notes

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

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

- the progress and scope of our development and commercialization activities;
- the commercial success of COMETRIQ and the revenues we generate;
- recognition of upfront licensing or other fees or revenues;
- payments of non-refundable upfront or licensing fees, or payment for cost-sharing expenses, to third parties;
- acceptance of our technologies and platforms;
- the success rate of our efforts leading to milestone payments and royalties;
- the introduction of new technologies or products by our competitors;
- the timing and willingness of collaborators to further develop or, if approved, commercialize our product candidates out-licensed to them;
- our ability to enter into new collaborative relationships;
- the termination or non-renewal of existing collaborations;
- the timing and amount of expenses incurred for clinical development and manufacturing of cabozantinib;
- adjustments to expenses accrued in prior periods based on management's estimates after the actual level of activity relating to such expenses becomes more certain;
- the impairment of acquired goodwill and other assets;
- the impact of our restructuring activities; and
- general and industry-specific economic conditions that may affect our collaborators' research and development expenditures.

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

Due to the possibility of fluctuations in our revenues and expenses, we believe that quarter-to-quarter comparisons of our operating results are not a good indication of our future performance. As a result, in some future quarters, our operating results may not meet the expectations of securities analysts and investors, which could result in a decline in the price of our common stock.

Our stock price may be extremely volatile.

The trading price of our common stock has been highly volatile, and we believe the trading price of our common stock will remain highly volatile and may fluctuate substantially due to factors such as the following, many of which we cannot control:

- adverse results or delays in our or our collaborators' clinical trials;
- announcement of FDA approval or non-approval, or delays in the FDA review process, of cabozantinib or our collaborators' product candidates or those of our competitors or actions taken by regulatory agencies with respect to our, our collaborators' or our competitors' clinical trials;
- the commercial success of COMETRIQ and the revenues we generate;
- the timing of achievement of our clinical, regulatory, partnering and other milestones, such as the commencement of clinical development, the completion of a clinical trial, the filing for regulatory approval or the establishment of collaborative arrangements for one or more of our out-licensed programs and compounds;
- actions taken by regulatory agencies with respect to cabozantinib or our clinical trials for cabozantinib;
- the announcement of new products by our competitors;
- quarterly variations in our or our competitors' results of operations;

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- developments in our relationships with our collaborators, including the termination or modification of our agreements;
- conflicts or litigation with our collaborators;
- litigation, including intellectual property infringement and product liability lawsuits, involving us;
- failure to achieve operating results projected by securities analysts;
- changes in earnings estimates or recommendations by securities analysts;
- financing transactions;
- developments in the biotechnology or pharmaceutical industry;
- sales of large blocks of our common stock or sales of our common stock by our executive officers, directors and significant stockholders;
- departures of key personnel or board members;
- developments concerning current or future collaborations;
- FDA or international regulatory actions;
- third-party reimbursement policies;
- disposition of any of our subsidiaries, technologies or compounds; and
- general market, economic and political conditions and other factors, including factors unrelated to our operating performance or the operating performance of our competitors.

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 report.

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

Future sales of our common stock or conversion of our convertible notes, or the perception that such sales or conversions may occur, may depress our stock price.

A substantial number of shares of our common stock is reserved for issuance upon conversion of the 2019 Notes, upon the exercise of stock options, upon vesting of restricted stock unit awards, upon sales under our employee stock purchase program, upon exercise of certain warrants issued to Deerfield and upon conversion of the Deerfield Notes. The issuance and sale of substantial amounts of our common stock, including upon conversion of the 2019 Notes or the Deerfield Notes, or the perception that such issuances and sales may occur, could adversely affect the market price of our common stock and impair our ability to raise capital through the sale of additional equity or equity-related securities in the future at a time and price that we deem appropriate. Trading of the 2019 Notes is likely to influence and be influenced by the market for our common stock. For example, the price of our common stock could be affected by possible sales of common stock by investors who view the 2019 Notes as a more attractive means of equity participation in our company and by hedging or arbitrage trading activity that we expect to occur involving our common stock.

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

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

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

Certain provisions applicable to the 2019 Notes and the indenture pursuant to which the 2019 Notes were issued, and the Deerfield Notes and the note purchase agreement governing the Deerfield Notes, could make it more difficult or more

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expensive for a third party to acquire us. For example, if an acquisition event constitutes a Fundamental Change under the indenture for the 2019 Notes or a Major Transaction under the note purchase agreement governing the Deerfield Notes, holders of the 2019 Notes or the Deerfield Notes, applicable, will have the right to require us to purchase their notes in cash. In addition, if an acquisition event constitutes a Make-Whole Fundamental Change under the indenture for the 2019 Notes, we may be required to increase the conversion rate for holders who convert their 2019 Notes in connection with such Make-Whole Fundamental Change. In any of these cases, and in other cases, our obligations under the 2019 Notes and the indenture pursuant to which such notes were issued and the Deerfield Notes and the note purchase agreement governing the Deerfield Notes, as well as provisions of our organizational documents and other agreements, could increase the cost of acquiring us or otherwise discourage a third party from acquiring us or removing incumbent management.

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

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

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

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

ITEM 1B. UNRESOLVED STAFF COMMENTS

Not applicable.

ITEM 2. PROPERTIES

We lease a total of 367,773 square feet of office and laboratory facilities in South San Francisco, California. The leased premises comprise six buildings and are covered by four lease agreements, as follows:

- The first two leases cover three buildings for a total of 179,964 square feet and expires in 2017, with two five-year options to extend their respective terms prior to expiration. We have subleased a total of 76,120 square feet of portions of these buildings to four different subtenants. The terms of the subleases covering 74,163 square feet expire at the end of our lease term and the sublease for the balance is for a term of one year with annual options to extend through the end of our lease term.
- The third lease covers two buildings for a total of 116,063 square feet and expire in 2018.
- The fourth lease covering a portion of one building containing 71,746 square feet and expire in 2015. We have subleased approximately 68,738 square feet of the building covered by the fourth lease to a single subtenant. The term of the sublease will expire at the end of our lease term.

We believe that our leased facilities have sufficient space to accommodate our current needs.

ITEM 3. LEGAL PROCEEDINGS

We are not a party to any material legal proceedings. We may from time to time become a party to various legal proceedings arising in the ordinary course of business.

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ITEM 4. MINE SAFETY DISCLOSURES

Not applicable.

PART II

ITEM 5. MARKET FOR REGISTRANT'S COMMON EQUITY, RELATED STOCKHOLDER MATTERS AND ISSUER PURCHASES OF EQUITY SECURITIES

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

	Common Stock Price	
	High	Low
Year ended December 28, 2012:		
Quarter ended March 30, 2012	$6.57	$4.47
Quarter ended June 29, 2012	$5.59	$4.37
Quarter ended September 28, 2012	$6.95	$4.19
Quarter ended December 28, 2012	$5.39	$4.29
Year ended December 27, 2013:		
Quarter ended March 29, 2013	$5.06	$4.32
Quarter ended June 28, 2013	$5.30	$4.33
Quarter ended September 27, 2013	$5.88	$4.58
Quarter ended December 27, 2013	$6.14	$4.66

On February 19, 2014, the last reported sale price on the NASDAQ Global Select Market for our common stock was $7.18 per share.

Holders

On February 19, 2014, there were approximately 506 holders of record of our common stock.

Dividends

Since inception, we have not paid dividends on our common stock. We currently intend to retain all future earnings, if any, for use in our business and currently do not plan to pay any cash dividends in the foreseeable future. Any future determination to pay dividends will be at the discretion of our Board of Directors. Our loan and security agreement with Silicon Valley Bank restricts our ability to pay dividends and make distributions. In addition, our note purchase agreement with Deerfield restricts our ability to make distributions.

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Performance Graph

This performance graph shall not be deemed "filed" for purposes of Section 18 of the Securities Exchange Act of 1934, as amended, or otherwise subject to the liabilities under that Section and shall not be deemed to be incorporated by reference into any filing of ours under the Securities Act of 1933, as amended.

The following graph compares, for the five year period ended December 31, 2013, the cumulative total stockholder return for our common stock, the NASDAQ Stock Market (U.S. companies) Index, or the NASDAQ Market Index, and the NASDAQ Biotechnology Index. The graph assumes that $100 was invested on December 31, 2008 in each of our common stock, the NASDAQ Market Index and the NASDAQ Biotechnology Index and assumes reinvestment of any dividends. The stock price performance on the following graph is not necessarily indicative of future stock price performance.

	12/31/2008	12/31/2009	12/31/2010	12/31/2011	12/31/2012	12/31/2013
Exelixis, Inc.	100	141	157	91	86	114
NASDAQ Market Index	100	139	163	160	181	255
NASDAQ Biotechnology Index	100	114	131	146	190	318

ITEM 6. SELECTED FINANCIAL DATA

The following selected consolidated financial information has been derived from our audited consolidated financial statements. The financial information as of December 31, 2013 and 2012 and for each of the three years in the period ended December 31, 2013, are derived from audited consolidated financial statements included elsewhere in this Annual Report on Form 10-K. The following Selected Financial Data should be read in conjunction with "Item 7. Management's Discussion and Analysis of Financial Condition and Results of Operations" and "Item 8. Financial Statements and Supplementary Data" included elsewhere in this Annual Report on Form 10-K. The historical results are not necessarily indicative of the results of operations to be expected in the future.

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	Year Ended December 31,				
	2013	2012	2011	2010	2009
	(In thousands, except per share data)				
Consolidated Statements of Operations Data:					
Revenues	$31,338	$47,450	$289,636	$185,045	$151,759
Operating expenses:					
Cost of goods sold	1,118	—	—	—	—
Research and development	178,763	128,878	156,836	210,678	234,702
Selling, general and administrative	50,958	31,837	33,129	33,020	34,382
Collaboration cost sharing	—	—	—	—	4,582
Restructuring charge	1,231	9,171	10,136	32,744	—
Total operating expenses	232,070	169,886	200,101	276,442	273,666
(Loss) income from operations	(200,732)	(122,436)	89,535	(91,397)	(121,907)
Other income (expense), net (1)	(44,124)	(25,102)	(12,543)	(1,005)	(18,936)
(Loss) income before taxes	(244,856)	(147,538)	76,992	(92,402)	(140,843)
Income tax (benefit) provision	(96)	107	1,295	(72)	(1,286)
Net (loss) income	(244,760)	(147,645)	75,697	(92,330)	(139,557)
Loss attributed to noncontrolling interest	—	—	—	—	4,337
Net (loss) income attributable to Exelixis, Inc.	$(244,760)	$(147,645)	$75,697	$(92,330)	$(135,220)
Net (loss) income per share, basic, attributable to Exelixis, Inc.	$(1.33)	$(0.92)	$0.60	$(0.85)	$(1.26)
Net (loss) income per share, diluted, attributable to Exelixis, Inc.	$(1.33)	$(0.92)	$0.58	$(0.85)	$(1.26)
Shares used in computing basic net (loss) income per share	184,062	160,138	126,018	108,522	107,073
Shares used in computing diluted net (loss) income per share	184,062	160,138	130,479	108,522	107,073

(1) In 2007, we sold 80.1% of our former German subsidiary, Artemis Pharmaceuticals GmbH (now known as TaconicArtemis GmbH), or Artemis, and our plant trait business. We exercised our option to sell our remaining 19.9% ownership in Artemis in 2011 and recognized an additional gain of $2.2 million in other income. In 2009 and 2010, in association with the sale of our plant trait business, we recognized an additional gain on the sale of the business of $2.1 million and $7.2 million, respectively. In June 2009, we recorded a $9.8 million loss upon deconsolidation of Symphony Evolution, Inc. as a result of the expiration of our purchase option. In addition, our credit facility with Deerfield expired in November 2009, resulting in our acceleration of interest expense of $5.2 million relating to the closing fee and outstanding warrants issued in connection with the facility.

	December 31,				
	2013	2012	2011	2010	2009
	(In thousands)				
Consolidated Balance Sheet Data:					
Cash and investments	$415,862	$633,961	$283,720	$256,377	$220,993
Working capital (deficit)	$178,756	$350,837	$136,500	$(16,455)	$22,882
Total assets	$503,287	$721,097	$393,262	$360,790	$343,410
Long-term obligations	$349,196	$342,959	$193,983	$186,702	$57,688
Accumulated deficit	$(1,498,762)	$(1,254,002)	$(1,106,357)	$(1,182,054)	$(1,089,724)
Total stockholders' equity (deficit)	$66,238	$296,434	$90,632		