EXELIXIS, INC.
Form 10-K
February 22, 2019
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UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
Washington, D.C. 20549
FORM 10-K
ý ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934
For the fiscal year ended December 28, 2018
or
¨ TRANSITION REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934
Commission File Number: 000-30235
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)

1851 Harbor Bay Parkway
Alameda, CA 94502
(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 every Interactive Data File required to be submitted 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 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. ¨
Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer, a smaller reporting company, or emerging growth company. See the definitions of "large accelerated filer," "accelerated filer," "smaller reporting company," and "emerging growth company" in Rule 12b-2 of the Exchange Act.

Large accelerated filer	ý	Accelerated filer	¨
Non-accelerated filer	¨	Smaller reporting company	¨
Emerging growth company	¨		

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 7(a)(2)(B) of the Securities Act. ¨
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: $5,531.1 million (based on the closing sales price of the registrant's common stock on June 29, 2018. Excludes an aggregate of approximately 40.9 million shares of the registrant's common stock held by persons who were directors and/or executive officers of the registrant at June 29, 2018 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 12, 2019, there were 300,129,630 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 27, 2019, in connection with the registrant's 2018 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. 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.

We have adopted a 52- or 53-week fiscal year policy that generally ends on the Friday closest to December 31st. Fiscal year 2016 ended on December 30, 2016; fiscal year 2017 ended on December 29, 2017; fiscal year 2018 ended on December 28, 2018; and fiscal year 2019 will end on January 3, 2020. For convenience, references in this report as of and for the fiscal years ended (or ending, as applicable) December 30, 2016, December 29, 2017, December 28, 2018 and January 3, 2020 are indicated as being as of and for the years ended (or ending, as applicable) December 31, 2016, 2017, 2018 and 2019, respectively. The annual period and quarterly period ending January 3, 2020 are a 53-week fiscal year and a 14-week fiscal quarter, respectively; all other annual periods presented are 52-week fiscal years and all interim periods presented are 13-week fiscal quarters.

Item 1. Business

Overview

Exelixis, Inc. (Exelixis, we, our or us) is an oncology-focused biotechnology company that aims to accelerate the discovery, development and commercialization of new medicines for difficult-to-treat cancers. Our drug discovery and development capabilities and commercialization platform are the foundations upon which we intend to bring to market novel, effective and tolerable therapies to provide cancer patients with additional treatment options.

Since we were founded in 1994, four products resulting from our discovery efforts have progressed through clinical development and received regulatory approval; three have a growing commercial presence worldwide, and we expect that the fourth will soon enter the marketplace in Japan. Two are derived from cabozantinib, our flagship molecule, an inhibitor of multiple tyrosine kinases including MET, AXL, VEGF receptors and RET. These are: CABOMETYX® (cabozantinib) tablets approved for advanced renal cell carcinoma (RCC) and previously treated hepatocellular carcinoma (HCC); and COMETRIQ® (cabozantinib) capsules approved for progressive, metastatic medullary thyroid cancer (MTC). For these types of cancer, cabozantinib has become or is becoming a standard of care. Beyond its approved indications, cabozantinib is currently the focus of a broad clinical development program, and is being investigated both alone and in combination with other therapies in a wide variety of cancers. The growth that we have experienced in recent years is largely attributable to cabozantinib’s clinical and commercial success; consistent with our values and legal obligations, we are committed to ensuring that all patients who are prescribed cabozantinib are able to access this essential medicine.

The other two products resulting from our discovery efforts are: COTELLIC® (cobimetinib), an inhibitor of MEK approved as part of a combination regimen to treat advanced melanoma and marketed under a collaboration with Genentech, Inc. (a member of the Roche Group) (Genentech); and MINNEBRO™ (esaxerenone), an oral, non-steroidal, selective blocker of the mineralocorticoid receptor (MR) approved for the treatment of hypertension in Japan and licensed to Daiichi Sankyo Company, Limited (Daiichi Sankyo).

Over the course of 2018, revenues from the sales of CABOMETYX and COMETRIQ and from the royalties and milestone payments received pursuant to collaboration agreements with our partners, coupled with disciplined expense management, have fueled the growth of our organization. We believe we can continue to grow in a sustainable manner, supported by a healthy cash position and profitability over the past two fiscal years. We are utilizing our cash and investments to enable future success by expanding the development program for cabozantinib and by building a pipeline of new drug candidates through reinitiated internal drug discovery efforts and the execution

of strategic transactions that align with our oncology drug development and commercialization expertise. The following report details the progress we made executing our growth strategy in 2018.

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Exelixis Marketed Products: CABOMETYX and COMETRIQ

CABOMETYX was first approved by the U.S. Food and Drug Administration (FDA) on April 25, 2016, for the treatment of patients with advanced RCC who have received prior anti-angiogenic therapy and by the European Commission (EC) on September 9, 2016, similarly for the treatment of advanced RCC in adults in the European Union (EU) following prior VEGF-targeted therapy. On December 19, 2017, the FDA approved the expanded indication for CABOMETYX to include previously untreated patients with advanced RCC, and the EC approved CABOMETYX on May 17, 2018 as a first-line treatment for adults with intermediate- or poor-risk advanced RCC. Most recently, CABOMETYX was approved by the FDA on January 14, 2019, for the treatment of patients with HCC who have been previously treated with sorafenib, which followed the EC's earlier approval of CABOMETYX on November 15, 2018, for the treatment of HCC in adults previously treated with sorafenib. COMETRIQ, our first marketed product, was approved by the FDA on November 29, 2012, for the treatment of patients with progressive, metastatic MTC, and in March 2014, the EC granted COMETRIQ a conditional marketing authorization for the treatment of adult patients with progressive, unresectable locally advanced or metastatic MTC. In 2018 and 2017, we generated $619.3 million and $349.0 million, respectively, in net product revenues from sales of CABOMETYX and COMETRIQ in the U.S.

Outside the U.S. and Japan, CABOMETYX and COMETRIQ are marketed by our collaboration partner Ipsen Pharma SAS (Ipsen). Should CABOMETYX and COMETRIQ be approved in Japan, they will be marketed by our collaboration partner Takeda Pharmaceutical Company Limited (Takeda). In 2018 and 2017, we earned $32.3 million and $3.8 million, respectively, of gross royalties for net sales of products incorporating cabozantinib outside of the U.S. For additional information on the terms of our collaboration agreements with Ipsen and Takeda, see "—Collaborations—Cabozantinib Commercial Collaborations."

Renal Cell Carcinoma - CABOMETYX is Now the Leading Tyrosine Kinase Inhibitor (TKI) Treatment Option for Patients with Advanced RCC

Kidney cancer is among the top ten most commonly diagnosed forms of cancer among both men and women in the U.S., with approximately 30,000 patients requiring systemic treatment. Globally, approximately 68,000 patients require systemic treatment for kidney cancer. A growing number of these patients with RCC have been or will be treated with CABOMETYX, which has become a new standard of care for the treatment of patients suffering from this difficult-to-treat disease; in fact, as of December 2018, CABOMETYX was the TKI of choice among physicians treating these patients in terms of new prescriptions.

Since CABOMETYX was first approved, our promotional and medical affairs teams have been focused on educating physicians about CABOMETYX's unique clinical profile. We believe that the success of CABOMETYX is attributable to this clinical profile, derived from the results of our clinical trials, METEOR and CABOSUN. CABOMETYX is the first and only single-agent therapy approved for previously treated advanced RCC to demonstrate statistically significant and clinically meaningful improvements in three key efficacy parameters in a global pivotal trial: overall survival (OS); progression-free survival (PFS); and objective response rate (ORR). In addition, in previously untreated patients with advanced RCC, CABOMETYX is the only approved single-agent therapy to improve PFS and ORR compared with sunitinib, a first-generation TKI that was the previous standard of care. It is also noteworthy that on September 7, 2018, the National Comprehensive Cancer Network (NCCN), the nation's foremost non-profit alliance of leading cancer centers, updated its Clinical Practice Guidelines to recommend CABOMETYX as the only TKI with preferred status for advanced RCC patients who have progressed on prior therapy and for the treatment of advanced RCC regardless of patient risk status (favorable-, intermediate-, and poor risk). These updated recommendations strengthened the differentiation of CABOMETYX from other TKIs approved for this indication, leading many physicians to consider CABOMETYX a preferred therapeutic option, despite numerous competing products approved to treat advanced RCC. For additional information about CABOMETYX's profile as expressed in the METEOR and CABOSUN clinical trial data, see "—Cabozantinib Development Program—Clinical Trials Supporting Regulatory Approvals."

In markets outside the U.S. in 2018, we continued to work closely with our partner Ipsen in support of its regulatory strategy and commercialization efforts for CABOMETYX as a treatment for advanced RCC. As a result of the approvals of CABOMETYX for RCC indications in more than ten territories outside of the U.S., including the EU,

Canada, Brazil, Taiwan, South Korea and Australia, CABOMETYX has continued to grow both in sales revenue and the number of RCC patients benefiting from its clinical effect. Additionally, with respect to the Japanese market, our partner Takeda is advancing its clinical development activities in Japan support of potential future regulatory filings for CABOMETYX in both RCC and HCC.

Hepatocellular Carcinoma - the CABOMETYX Label Expanded to Include Previously Treated HCC

According to published studies, liver cancer is a leading cause of cancer death worldwide, accounting for more than 700,000 deaths and 800,000 new cases each year. In the U.S., the incidence of liver cancer has more than tripled since 1980. Although HCC is the most common form of liver cancer, making up about three-fourths of the estimated nearly 42,000 new

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cases of liver cancer in the U.S. during 2018, this patient population was long underserved. Prior to 2017, there was only one approved systemic therapy for the treatment of HCC. Then, in 2017 and 2018, four new therapies were approved in the U.S. for HCC, one for previously untreated patients and three for patients previously treated with sorafenib. Given the introduction of new and more effective therapies, we believe the second- and later-line HCC market has the potential to grow significantly in coming years, as the new treatment options are expected to result in an increasing number of patients receiving multiple lines of therapy. With the recent approval of CABOMETYX in January 2019 for HCC patients previously treated with sorafenib, we aim to play a key role in the advancement of therapeutic options for these patients.

The FDA's approval of CABOMETYX for this HCC indication was based on our phase 3 pivotal study, CELESTIAL. The CELESTIAL study met its primary endpoint, demonstrating that cabozantinib significantly improved OS, as compared to placebo. For additional information on CELESTIAL, see "—Cabozantinib Development Program—Clinical Trials Supporting Regulatory Approvals—HCC - CELESTIAL." Upon FDA approval, we were immediately prepared to offer CABOMETYX to all eligible HCC patients in the U.S. who may benefit from this treatment option. We were able to take action so quickly due to the strength of our existing commercial and medical affairs organizations, in addition to our well-established distribution network and our ability to leverage our RCC commercialization experience. The NCCN's inclusion of CABOMETYX in its Clinical Practice Guidelines for Hepatobiliary Cancers as a Category 1 option for the treatment of patients with HCC (Child-Pugh Class A only) who have been previously treated with sorafenib further supports CABOMETYX as an important new treatment option for eligible HCC patients.

Outside the U.S., the EC's approval of CABOMETYX provided physicians in the EU with a second approved therapy for the second-line treatment of this aggressive and difficult-to-treat cancer.

Medullary Thyroid Cancer - COMETRIQ, the First Commercial Approval of Cabozantinib

We estimate that there are between 500 and 700 first-line and second-line patients in the U.S. who will be eligible for COMETRIQ. The FDA's approval of COMETRIQ for this MTC indication was based on our phase 3 trial, EXAM. The EXAM trial met its primary endpoint, demonstrating a statistically significant and clinically meaningful prolongation in PFS for cabozantinib, as compared to placebo. For additional information on EXAM, see "—Cabozantinib Development Program—Clinical Trials Supporting Regulatory Approvals—MTC - EXAM." In 2018 and 2017, we generated $19.3 million and $25.0 million, respectively, in net product revenues from sales of COMETRIQ in the U.S.

Cabozantinib Development Program

Cabozantinib inhibits the activity of tyrosine kinases, including MET, AXL, VEGF receptors, and RET. These receptor tyrosine kinases are involved in both normal cellular function and in pathologic processes such as oncogenesis, metastasis, tumor angiogenesis, drug resistance and maintenance of the tumor microenvironment. Objective tumor responses have been observed in patients treated with cabozantinib in more than 20 individual tumor types investigated in phase 1 and 2 clinical trials to date, reflecting the medicine's broad clinical potential. We are currently evaluating cabozantinib, both as a single agent and in combination with immune checkpoint inhibitors (ICIs), in a broad development program comprising over 75 ongoing or planned clinical trials across multiple indications. We, along with our clinical and commercial collaboration partners, sponsor some of those trials, and independent investigators conduct the remaining trials through our Cooperative Research and Development Agreement (CRADA) with the National Cancer Institute's Cancer Therapy Evaluation Program (NCI-CTEP) or our investigator sponsored trial (IST) program. In addition to co-sponsoring trials with us, our commercial collaboration partners Ipsen and Takeda also conduct trials in their territories through similar independently-sponsored programs.

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The following two tables summarize select cabozantinib clinical development activities, one describing studies that evaluate the potential of cabozantinib as a single-agent, and the other describing studies that evaluate the potential of cabozantinib in combination with one or more ICIs:

CLINICAL DEVELOPMENT PROGRAM FOR CABOZANTINIB, SINGLE-AGENT

Indication	Status Update
Thyroid Cancer	
Progressive, metastatic medullary thyroid cancer	Approved in U.S. and EU (EXAM)
Progressive, metastatic medullary thyroid cancer	Post-marketing study (EXAMINER)
Differentiated thyroid cancer (DTC)	Phase 3 (COSMIC-311)
Renal Cell Carcinoma (RCC)	
Advanced RCC	Approved in U.S. and EU (METEOR and CABOSUN)
First- or second-line papillary RCC	Randomized phase 2† (PAPMET)
Hepatocellular Carcinoma (HCC)	
Second- and later-line HCC	Approved in U.S. on January 14, 2019; approved in EU in November 2018 (CELESTIAL)
Non-Small Cell Lung Cancer (NSCLC)	
EGFR wild-type	Phase 2†
Molecular alterations in RET, ROS1, MET, AXL, or NTRK1	Phase 2*
Additional Trials	
Metastatic urothelial carcinoma (UC)	Phase 2* (ATLANTIS)
Colorectal cancer (CRC)	Phase 2*
High-grade uterine sarcomas	Phase 2§
Metastatic gastrointestinal stromal tumor	Phase 2§ (CABOGIST)
Pancreatic neuroendocrine tumors and carcinoid tumors	Phase 2* and Phase 3† (CABINET)
Plexiform neurofibromas (pediatric and adult cohorts)	Phase 2*
Relapsed osteosarcoma or Ewing sarcoma	Phase 2†
Soft-tissue sarcomas	Phase 2†

* Trial conducted through our IST program.

† Trial conducted through collaboration with NCI-CTEP.

§ Trial sponsored by the European Organization for Research and Treatment of Cancer.

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CLINICAL DEVELOPMENT PROGRAM FOR CABOZANTINIB, IN COMBINATION WITH IMMUNE CHECKPOINT INHIBITORS

Indication	Combination Regimen	Status Update
Genitourinary Cancers		
First-line advanced RCC	+ nivolumab	Phase 3 pivotal trial (CheckMate 9ER)
Cisplatin-Ineligible advanced UC	+ pembrolizumab	Phase 2* (PemCab)
Advanced or metastatic non-clear cell RCC	+ nivolumab	Phase 2*
Gastrointestinal Cancers		
First-line advanced HCC	+ atezolizumab	Phase 3 pivotal trial (COSMIC-312), including a single-agent cabozantinib exploratory arm
Second- and later-line advanced HCC	+ nivolumab ± ipilimumab	Phase 1/2 (Checkmate 040)
Neoadjuvant locally advanced HCC	± nivolumab	Phase 1b*
KRAS wild-type metastatic CRC and cMET amplified metastatic CRC	± panitumumab	Phase 1* (CaboMAb)
Lung Cancers		
NSCLC	+ nivolumab ± ipilimumab	Phase 2†
Gynecologic Cancers		
Advanced or metastatic endometrial cancer	+ nivolumab	Phase 2†
Metastatic, triple negative breast cancer	+ nivolumab	Phase 2*
Breast cancer with brain metastases	± trastuzumab	Phase 2*
Head and Neck Cancers		
Recurrent, metastatic squamous cell carcinoma	+ cetuximab	Phase 1*
Recurrent, metastatic squamous cell carcinoma	+ pembrolizumab	Phase 2*
Additional Trials in Multiple Tumor Types		
Advanced solid tumors	+ atezolizumab	Phase 1b with 18 cabozantinib and atezolizumab expansion cohorts, including RCC, UC, castration-resistant prostate cancer (CRPC), HCC, colorectal adenocarcinoma, DTC, NSCLC, endometrial cancer, ovarian cancer, breast cancer, gastric or gastroesophageal junction adenocarcinoma and head and neck cancer (COSMIC-021), and 2 single-agent cabozantinib exploratory cohorts (UC and NSCLC)
Genitourinary tumors	+ nivolumab ± ipilimumab	Phase 1b†
Advanced CRC, HCC, gastric, gastroesophageal or esophageal adenocarcinoma	+ durvalumab	Phase 1* (CAMILLA)

* Trial conducted through our IST program.
† Trial conducted through collaboration with NCI-CTEP.
§ Trial sponsored by the European Organization for Research and Treatment of Cancer.

Clinical Trials Supporting Regulatory Approvals

RCC - METEOR

In July 2015, we announced positive results of METEOR, a phase 3 pivotal trial comparing CABOMETYX to everolimus in patients with advanced RCC who have experienced disease progression following treatment with at least one prior VEGF receptor inhibitor. METEOR met its primary endpoint, demonstrating a statistically significant and clinically

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meaningful increase in PFS for CABOMETYX. The median PFS was 7.4 months for the CABOMETYX arm versus 3.8 months for the everolimus arm. CABOMETYX also significantly improved ORR, a secondary endpoint, compared with everolimus. In September 2015, The New England Journal of Medicine (NEJM) published the complete, detailed positive results from the primary analysis of METEOR, and these results were also presented at the European Society for Medical Oncology (ESMO) 2015 Congress. After additional follow up, METEOR also met its other secondary endpoint of OS, as presented in June 2016 at the American Society of Clinical Oncology (ASCO) 2016 Annual Meeting and published in Lancet Oncology. The median OS was 21.4 months for patients receiving CABOMETYX versus 16.5 months for those receiving everolimus. The safety profile in the study and in later analyses was consistent with the established profile of cabozantinib and other TKIs.

On the basis of the data from the METEOR trial, the FDA approved CABOMETYX for the treatment of patients with advanced RCC following prior antiangiogenic therapy, and the European Medicines Agency (EMA) approved CABOMETYX for the treatment of advanced RCC in adults following prior VEGF-targeted therapy.

RCC - CABOSUN

In October 2016, we announced positive results from CABOSUN, a randomized, open-label, active-controlled phase 2 trial comparing cabozantinib with sunitinib in patients with previously untreated advanced RCC with intermediate- or poor-risk disease conducted by The Alliance for Clinical Trials in Oncology under our CRADA with NCI-CTEP. These results were presented at the ESMO 2016 Congress in October 2016 and subsequently published in the Journal of Clinical Oncology in November 2016. CABOSUN met its primary endpoint, demonstrating a statistically significant and clinically meaningful improvement in investigator-assessed PFS compared with sunitinib. The median PFS for cabozantinib was 8.2 months versus 5.6 months for sunitinib. Investigator-assessed ORR, a secondary endpoint, was also significantly improved, at 33% for cabozantinib versus 12% for sunitinib, and median OS, another secondary endpoint, showed a trend favoring cabozantinib with 30.3 months versus 21.8 months for sunitinib.

Updated results from CABOSUN were presented at the ESMO 2017 Congress in September 2017 and subsequently published in the European Journal of Cancer in May 2018. The updated results included the analysis from a blinded independent radiology review committee (IRRC), which confirmed the primary efficacy endpoint results of investigator-assessed PFS, as well as an updated investigator-assessed analysis. Per the IRRC analysis, the median PFS for cabozantinib was 8.6 months versus 5.3 months for sunitinib, and both the updated investigator assessment and IRRC analysis demonstrated consistent and statistically significant improvement of PFS with cabozantinib as compared to sunitinib. The updated OS analysis had a data cut-off of July 1, 2017, and showed a favorable trend for patients randomized to cabozantinib compared to sunitinib that was not statistically significant. Median OS was 26.6 months for patients receiving cabozantinib versus 21.2 months for those receiving sunitinib. The safety profile in the study and in later analyses was consistent with the established profile of cabozantinib and other TKIs.

On the basis of the data from the CABOSUN trial, the FDA approved CABOMETYX for the treatment of patients with previously untreated, advanced or metastatic RCC on December 19, 2017, and we commenced our commercial launch of CABOMETYX for this new indication immediately upon such approval. Additionally, on May 17, 2018, the EC approved cabozantinib as a first-line treatment for adults with intermediate- or poor-risk advanced RCC.

RCC - Retrospective Analyses of CABOSUN and METEOR

As the advanced RCC treatment landscape continues to evolve and include multiple ICI treatment options, biomarker analyses are of increasing importance to help select for advanced RCC patients who would potentially derive the most clinical benefit from CABOMETYX. Two relevant retrospective analyses were presented at the ESMO 2018 Congress in October 2018 that described the potential utility of CABOMETYX in patients with advanced RCC regardless of their PD-L1 status, as well as in those patients with advanced RCC who progressed on previous ICI monotherapy or combination treatment.

The first analysis of data from the CABOSUN and METEOR trials evaluated the effect of PD-L1 expression on clinical outcomes with cabozantinib in advanced RCC and demonstrated that cabozantinib improved clinical outcomes regardless of PD-L1 status, relative to sunitinib or everolimus, the respective comparator arms for each trial. The findings showed that PD-L1 expression was associated with shorter median PFS and OS in both METEOR and CABOSUN. Treatment with cabozantinib, however, improved PFS and OS compared with everolimus (METEOR) and sunitinib (CABOSUN) in both PD-L1 positive and PD-L1 negative patients. An additional retrospective analysis

found that cabozantinib was active in patients previously treated with ICIs, either alone or in combination with anti-VEGF or other therapies. At a median follow-up of 12 months, ORR was 33%, disease control rate (DCR) was 79% and the one-year OS rate was 53%. Together, these analyses evaluating data from the CABOSUN and METEOR clinical trials contribute to cabozantinib's unique product profile, as well as its value as a treatment option for patients with advanced RCC within an evolving and competitive treatment landscape that includes multiple ICI treatment options.

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HCC - CELESTIAL

In October 2017, we announced positive results of CELESTIAL, our phase 3 pivotal trial comparing cabozantinib to placebo in patients with HCC who had received previous treatment with sorafenib. The CELESTIAL trial, which we initiated in September 2013, was designed to enroll 760 patients who had received prior systemic therapy with sorafenib, could have received up to two prior systemic therapies for HCC, and must have progressed following at least one prior therapy. The CELESTIAL trial was conducted at more than 100 sites globally in 19 countries and enrollment was completed in September 2017. Patients were randomized 2:1 to receive 60 mg of cabozantinib daily or placebo and were stratified based on etiology of the disease (hepatitis C, hepatitis B or other), geographic region (Asia or other regions) and presence of extrahepatic spread and/or macrovascular invasion (yes or no). No cross-over was allowed between the study arms.

In October 16, 2017, we announced that CELESTIAL had met its primary endpoint, with cabozantinib providing a statistically significant and clinically meaningful improvement versus placebo in OS, and that the independent data monitoring committee (IDMC), recommended CELESTIAL be stopped for efficacy. In January 2018, statistically significant and clinically meaningful positive results from the second interim analysis of CELESTIAL were presented during an oral session at the 2018 ASCO's Gastrointestinal Cancers Symposium. In July 2018, the NEJM also published the complete, detailed positive results from CELESTIAL. In the total population of second- and third-line patients, median OS was 10.2 months with cabozantinib versus 8.0 months with placebo (hazard ratio (HR) 0.76; 95% confidence interval (CI) 0.63-0.92; p=0.0049). Median PFS was more than doubled, at 5.2 months with cabozantinib and 1.9 months with placebo (HR 0.44; 95% CI 0.36-0.52; p<0.0001). ORR was 4% with cabozantinib and 0.4% with placebo (p=0.0086). Disease control (partial response (PR) or stable disease (SD)) was achieved by 64% of patients in the cabozantinib group compared with 33% in the placebo group. In a subgroup analysis of patients whose only prior therapy for HCC was sorafenib (70% of patients in the study), median OS was 11.3 months with cabozantinib versus 7.2 months with placebo (HR 0.70; 95% CI 0.55-0.88). PFS in the subgroup was 5.5 months with cabozantinib versus 1.9 months with placebo (HR 0.40; 95% CI 0.32-0.50). The safety profile of cabozantinib observed in the study was consistent with the established profile of cabozantinib and other TKIs.

On the basis of the data from the CELESTIAL trial, the FDA approved CABOMETYX on January 14, 2019 for the treatment of patients with HCC who have been previously treated with sorafenib, and we commenced our commercial launch of CABOMETYX for this new indication immediately upon such approval. Additionally, on November 15, 2018, our partner Ipsen received EC approval of CABOMETYX as a monotherapy for HCC in adults who have previously been treated with sorafenib.

MTC - EXAM

In October 2011, we announced positive results from EXAM, a phase 3 international, multi-center, randomized double-blinded controlled trial of COMETRIQ in patients with progressive, metastatic MTC. EXAM met its primary endpoint, demonstrating a statistically significant and clinically meaningful prolongation in PFS for COMETRIQ-treated patients compared to those receiving placebo, with median PFS of 11.2 months in the COMETRIQ arm versus 4.0 months in the placebo arm. In addition, the ORR was 27% with PRs observed only among patients in the COMETRIQ arm, and the median duration of objective response was 14.7 months for patients treated with COMETRIQ. These primary results were presented at the ASCO 2012 Annual Meeting in June 2012 and subsequently published in the Journal of Clinical Oncology in October 2013. In November 2014, we announced completion of the OS analysis, a secondary endpoint of the study. Consistent with an earlier interim analysis, there was no statistically significant difference in OS between the treatment arms. The median OS was 26.6 months for the COMETRIQ arm and 21.1 months for the placebo arm. We presented the final results at the ASCO 2015 Annual Meeting and submitted the results to regulatory authorities to satisfy post-marketing commitments. The safety profile in the study was consistent with the established profile of cabozantinib and other TKIs.

On the basis of the data from the EXAM trial, the FDA approved COMETRIQ on November 29, 2012, for the treatment of patients with progressive, metastatic MTC. In March 2014, the EC granted COMETRIQ a conditional marketing authorization for the treatment of adult patients with progressive, unresectable locally advanced or metastatic MTC. COMETRIQ is marketed and commercialized in the EU by Ipsen. In connection with the approval of COMETRIQ for the treatment of progressive, metastatic MTC, we were subject to post-marketing requirements, all of

which have been satisfied, other than a requirement to conduct the EXAMINER clinical study, comparing a lower dose of cabozantinib with the labeled dose of 140 mg. EXAMINER is evaluating safety and PFS in progressive, metastatic MTC patients and is ongoing.

Late-Stage Exelixis Sponsored Trials Evaluating Cabozantinib as a Monotherapy

DTC - COSMIC-311

Published studies indicate that approximately 54,000 new cases of thyroid cancer will be diagnosed in the U.S. in 2019. With the incidence of thyroid cancer increasing more rapidly than any other type of cancer in the U.S., and limited

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options available to patients whose disease has progressed following treatment with radioiodine (RAI) and anti-VEGFR therapy, we believe there is an urgent need for new treatment options.

Informed by cabozantinib's encouraging clinical activity in phase 1 and 2 studies in patients with RAI-refractory differentiated thyroid cancer (DTC), in October 2018 we initiated COSMIC-311, a multicenter, randomized, double-blind, placebo-controlled phase 3 pivotal trial evaluating cabozantinib in patients with RAI-refractory DTC who have progressed after up to two prior VEGFR-targeted therapies. The co-primary endpoints for the trial are PFS and ORR. The trial aims to enroll approximately 300 patients at approximately 150 sites globally. Patients will be randomized in a 2:1 ratio to receive either cabozantinib 60 mg or placebo once daily.

Trials Conducted Under our Clinical Collaboration Agreements

Cabozantinib has shown clinical anti-tumor activity with objective responses observed in more than 20 forms of cancer in phase 1 and 2 evaluation; we are, therefore, focused on advancing a broad cabozantinib clinical development program to fully investigate its therapeutic potential, both alone and in combination with other therapies. In particular, given that clinical observations from early-stage clinical trials evaluating cabozantinib in combination with ICIs have shown preliminary promising activity across a diverse range of tumors, and that patients have been able to tolerate these drug combinations, we are focused on exploring the potential of cabozantinib in combination with ICI's in later-stage settings.

Combination Studies with Bristol-Myers Squibb Company (BMS)

Preclinical data and clinical observations from an ongoing phase 1 trial evaluating cabozantinib in combination with nivolumab, with or without ipilimumab, in patients with previously treated genitourinary tumors suggest that cabozantinib may result in a more immune-permissive tumor environment. In consideration of those results, in February 2017, we entered into a clinical collaboration agreement with BMS for the purpose of conducting clinical studies combining cabozantinib with BMS' PD-1 ICI, nivolumab, both with or without BMS' CTLA-4 ICI, ipilimumab. As part of the collaboration, we are evaluating these combinations in a phase 3 pivotal trial in previously untreated or metastatic advanced RCC and in a phase 1/2 trial in both previously treated and previously untreated advanced HCC. We also intend to evaluate these combinations in other phase 3 pivotal trials in various other tumor types, including UC. Pursuant to our agreements with BMS, each party will be responsible for supplying finished drug product for the applicable clinical trial, and responsibility for the payment of costs for each trial will be determined on a trial-by-trial basis. For additional information on the terms of the clinical trial collaboration agreement, see "—Collaborations—Cabozantinib Development Collaborations—BMS."

RCC - CheckMate 9ER

CheckMate 9ER is an open-label, randomized, multi-national phase 3 pivotal trial evaluating nivolumab in combination with cabozantinib versus sunitinib in patients with previously untreated, advanced or metastatic RCC. The original trial protocol required patients to be randomized 1:1:1 to one of three arms: cabozantinib and nivolumab; cabozantinib, nivolumab and ipilimumab; or sunitinib. However, following the positive results of CheckMate 214, BMS's phase 3 trial evaluating nivolumab combined with ipilimumab versus sunitinib monotherapy in patients with previously untreated metastatic RCC and in an effort to accelerate the development of the cabozantinib and nivolumab combination, the trial protocol was amended to remove the triplet combination. The modified protocol for the trial aims to enroll approximately 580 patients with previously untreated, advanced or metastatic RCC of all risk groups. Patients are being randomized 1:1 to receive either 40 mg of cabozantinib daily and 240 mg of nivolumab every 2 weeks, or 50 mg of sunitinib daily on a 4-weeks-on/2-weeks-off schedule. The primary endpoint for the trial is PFS and the secondary endpoint is OS. The triplet combination continues to be evaluated in an ongoing phase 1b trial in patients with advanced genitourinary malignancies and a separate phase 3 trial evaluating the triplet combination versus nivolumab and ipilimumab is in preparation.

HCC - Checkmate 040

CheckMate 040 is a large, multi-cohort phase 1/2 trial in patients with previously treated and previously untreated advanced HCC, including a cohort evaluating treatment regimens that include cabozantinib in combination with nivolumab or in combination with both nivolumab and ipilimumab. This cohort containing the cabozantinib combination treatment regimens enrolled approximately 30 patients into each of two groups in accordance with the trial protocol, with one group receiving 40 mg of cabozantinib daily and 3 mg of nivolumab every two weeks, and the

other group receiving 40 mg of cabozantinib daily, 3 mg of nivolumab every two weeks and 1 mg ipilimumab every six weeks. The primary objectives for the cohorts are safety and tolerability, ORR and duration of response (DOR) and the secondary objectives include time to progression (TTP), PFS and OS.

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Combination Studies with the Roche Group (Roche)

Diversifying our exploration of cabozantinib combinations with ICIs, in February 2017, we entered into a master clinical supply agreement with Roche for the purpose of evaluating cabozantinib and Roche's anti-PD-L1 ICI, atezolizumab, in locally advanced or metastatic solid tumors. As part of the collaboration, we are evaluating this combination in a phase 1b trial in locally advanced or metastatic tumors and a phase 3 pivotal trial in previously untreated advanced HCC. Depending on results from the phase 1b trial, COSMIC-021, we may also evaluate this combination in various other tumor types, including NSCLC. For additional information on the terms of the master clinical supply agreement, see "—Collaborations—Cabozantinib Development Collaborations—Roche."

Locally Advanced or Metastatic Solid Tumors - COSMIC-021

In June 2017, we initiated COSMIC-021, a phase 1b dose escalation study that is evaluating the safety and tolerability of cabozantinib in combination with Roche's atezolizumab in patients with locally advanced or metastatic solid tumors. We are the trial sponsor of COSMIC-021, and Roche is providing atezolizumab free of charge.

The study is divided into two parts: a dose-escalation phase, which was completed in 2018; and an expansion cohort phase, which is ongoing. The dose-escalation phase of the trial enrolled 12 patients with advanced RCC, and results were presented at the ESMO 2018 Congress. The primary objective was to determine the optimal dose and schedule of daily oral administration of cabozantinib when given in combination with atezolizumab to inform the trial's subsequent expansion stage. Cabozantinib doses of 40 mg daily and 60 mg daily were evaluated. All patients received the standard atezolizumab dosing regimen of 1200 mg infusion once every 3 weeks. The dose-escalation phase of the study determined the optimal dose of cabozantinib as 40 mg daily when given in combination with the standard atezolizumab dosing regimen of 1200 mg infusion once every 3 weeks. No dose-limiting toxicities or serious adverse events (AEs) were noted. Dose reductions and higher grade AEs were less frequent with the 40 mg cabozantinib dosing cohort. Encouraging clinical activity was also observed. The safety profile for the combination in the dose-escalation phase of the trial was consistent with the established profile of each combination agent, and no new safety signals have emerged.

Enrollment in the expansion stage of this study, which is currently ongoing, includes the following eighteen combination tumor expansion cohorts:

- patients with advanced non-squamous NSCLC without a defined tumor genetic alteration (EGFR, ALK, ROS1, or BRAF) who have not received prior therapy with an ICI;
- patients with NSCLC without a defined tumor genetic alteration who have progressed following treatment with an ICI;
- patients with NSCLC with an EGFR mutation who have progressed following treatment with an EGFR-targeting TKI for metastatic disease;
- patients with UC who have progressed following treatment with an ICI;
- patients with CRPC who have previously received enzalutamide and/or abiraterone acetate and experienced radiographic disease progression in soft tissue;
- patients with RCC with clear cell histology who have not had prior systemic anticancer therapy;
- patients with RCC with non-clear cell histology who have not had prior systemic anticancer therapy for inoperable, locally advanced, recurrent or metastatic disease;
- patients with UC who have progressed on or after platinum-containing chemotherapy;
- patients with UC who are ineligible for cisplatin-based chemotherapy and have not received prior systemic chemotherapy for inoperable, locally advanced or metastatic disease;
- patients with UC who are eligible for cisplatin-based chemotherapy and have not received prior systemic chemotherapy for inoperable, locally advanced or metastatic disease;
- patients with triple-negative breast cancer (TNBC) who have progressed following treatment with at least one prior systemic therapy for inoperable, locally advanced, recurrent or metastatic disease;
- patients with epithelial ovarian cancer (EOC) who have platinum-resistant or refractory disease;
- patients with endometrial cancer who have progressed following treatment with at least one prior systemic therapy for inoperable, locally advanced, recurrent or metastatic disease;

- patients with advanced HCC who have a Child-Pugh score of A and have not had prior systemic anticancer therapy for inoperable, locally advanced, recurrent or metastatic disease;

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- patients with gastric or gastroesophageal junction adenocarcinoma who have progressed following treatment with platinum-containing or fluoropyrimidine-containing chemotherapy for inoperable locally advanced, recurrent or metastatic disease;
- patients with colorectal adenocarcinoma who have progressed following treatment with systemic chemotherapy that contained fluoropyrimidine in combination with oxaliplatin or irinotecan for metastatic disease;
- patients with head and neck cancer of squamous cell histology who have progressed following treatment with platinum-containing chemotherapy for inoperable locally advanced, recurrent or metastatic disease; and
- patients with DTC who are radio-refractory or deemed ineligible for treatment with iodine-131.

Each expansion cohort will initially enroll approximately 30 patients, and cohorts may be further expanded, including the cohorts of patients with UC or NSCLC who have been previously treated with an ICI, for a total of up to 1,000 patients. In addition, there are two exploratory cohorts that will evaluate cabozantinib as a single-agent therapy in patients with NSCLC without a defined tumor genetic alteration and in patients with UC, in each case who have progressed following treatment with an ICI.

HCC - COSMIC-312

In December 2018, we initiated COSMIC-312, a multicenter, randomized, controlled phase 3 pivotal trial evaluating cabozantinib in combination with atezolizumab versus sorafenib in previously untreated advanced HCC. The co-primary endpoints of the trial are PFS and OS. An exploratory arm will also evaluate cabozantinib monotherapy in this first-line setting. The study aims to enroll approximately 640 patients at up to 200 sites globally. Patients will be randomized to one of three arms: cabozantinib and atezolizumab (40 mg); sorafenib; or cabozantinib (60 mg). The co-primary endpoints for the trial are PFS and OS.

We are sponsoring COSMIC-312, and Ipsen will co-fund the trial. Ipsen will have access to the results to support potential future regulatory submissions outside of the U.S. and Japan. Roche is providing atezolizumab free of charge.

Trials Conducted through our CRADA with NCI-CTEP and our IST Program

In October 2011, we entered into a CRADA with NCI-CTEP for the clinical development of cabozantinib. Through our CRADA with NCI-CTEP and our IST program we have been able to expand the cabozantinib development program while avoiding over-burdening our internal development resources. Our CRADA reflects a major commitment by NCI-CTEP to support the broad exploration of cabozantinib's potential in a wide variety of cancers, each representing a substantial unmet medical need. Through this mechanism, NCI-CTEP provides funding for as many as 20 active clinical trials of cabozantinib each year for a five-year period. The term of the CRADA was extended in October 2016 for an additional five-year period through October 2021, provided that both parties maintain the right to terminate the CRADA for any reason upon sixty days' notice, for an uncured material breach upon thirty days' notice and immediately for safety concerns. Investigational New Drug (IND) applications for trials under the CRADA are held by NCI-CTEP. NCI-CTEP also retains rights to any inventions made in whole or in part by NCI-CTEP investigators. However, for inventions that claim the use and/or the composition of cabozantinib, we have an automatic option to elect a worldwide, non-exclusive license to cabozantinib inventions for commercial purposes, with the right to sublicense to affiliates or collaborators working on our behalf, as well as an additional, separate option to negotiate an exclusive license to cabozantinib inventions. Further, before any trial proposed under the CRADA may commence, the protocol is subject to our review and approval, and the satisfaction of certain other conditions. We believe our CRADA with NCI-CTEP has and will enable us to continue to expand the cabozantinib development program broadly in a cost-efficient manner.

Advanced Genitourinary Tumors

Results from a phase 1 trial evaluating cabozantinib in combination with nivolumab in patients with previously treated genitourinary tumors being conducted under our CRADA with NCI-CTEP were first presented at the ESMO 2016 Congress in October 2016 and most recently updated at the 2018 ASCO Genitourinary Cancers Symposium in February 2018. The updated data reported results from 78 patients treated with either cabozantinib and nivolumab with or without ipilimumab. Forty-nine patients were treated with the doublet combination of cabozantinib and nivolumab and 29 patients were treated with the triplet combination of cabozantinib, nivolumab and ipilimumab. Among the nineteen patients with metastatic UC who were evaluable for response, the ORR across all treatment groups was 42% (2 complete responses (CRs) and 6 PRs of 19 patients) and the DCR (DCR = CR, PR and SD) was

84%. Seven of eight (88%) metastatic UC patients with an objective response had not progressed at the time of the data cut-off. Median PFS in this patient population was 12.8 months and the OS rate at 12 months was 77%. Among the 13 patients with metastatic RCC who were evaluable for response, ORR was 54 percent (7 PRs of 13 patients) and the DCR was 100%. In the overall study the ORR in 64 evaluable patients was 36% (3 CRs and 20 PRs) with a median DOR of 24 months. 78 patients were included in the safety analysis. No dose-limiting

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toxicity was observed in the study. Based on general tolerability, the recommended cabozantinib dose for the expanded dose cohorts and for future late stage evaluation was determined as cabozantinib at 40 mg daily oral dose combined with nivolumab at 3 mg/kg every 2 weeks and ipilimumab at 1 mg/kg every 3 weeks for 4 doses. The safety profile for the combination in the trial was consistent with the established profile of each combination agent, and no new safety signals have emerged. This phase 1b study supported the choice of dose for the ongoing CheckMate 9ER trial in previously untreated advanced RCC.

DTC

Results from a phase 2 single-arm, open-label trial evaluating cabozantinib for the first-line treatment of metastatic RAI-refractory DTC, an IST conducted by the Center for Rare Cancers and Personalized Therapy at the Abramson Cancer Center of the University of Pennsylvania, were presented at the 2018 Multidisciplinary Head and Neck Cancers Symposium in February 2018. The primary endpoint of the trial was ORR. Patients were administered oral cabozantinib 60 mg once daily. Among the 35 patients who were evaluable for response, PR was achieved by 54% of patients (n=19), and SD was reported in 43 percent of patients (n=15) per RECIST 1.1. All but one evaluated patient experienced a decrease in tumor target lesions. Secondary endpoints of the trial included PFS, TTP, DOR and clinical benefit rate (CBR), defined as the number of patients achieving an objective response or stable disease for at least 6 months. The CBR at six months was 80% (n=28). With a median follow up for the study of 35 weeks, the median PFS had not been reached. The median TTP among those patients who progressed was 35 weeks. The safety profile in the study was consistent with the established profile of cabozantinib and other TKIs. It was on the basis of these encouraging trial results and results from earlier phase 1 and 2 trials in RAI-refractory DTC patients who had received prior systemic therapies that we initiated COSMIC-311.

NSCLC

In November 2014, we announced positive top-line results from a randomized phase 2 trial of cabozantinib and erlotinib alone or in combination as second- or third-line therapy in patients with stage IV EGFR wild-type NSCLC. This trial (Study E1512) was sponsored through our CRADA with NCI-CTEP and was conducted by the ECOG-ACRIN Cancer Research Group. The positive results from this trial were reported at the ASCO 2015 Annual Meeting in May 2015 and subsequently published online in Lancet Oncology in November 2016. The study met its primary endpoint, demonstrating significant increases in PFS for cabozantinib and the combination of cabozantinib plus erlotinib when individually compared to the erlotinib arm. The safety profile for the combination in the trial was consistent with the established profile of other TKI/TKI combination therapies. Informed by these clinical results, we are working with clinical collaborators to explore cabozantinib's further development in NSCLC, including potential combination approaches with ICIs, such as within one of the expansion cohorts of COSMIC-021, our phase 1b study with Roche evaluating the combination of cabozantinib and atezolizumab.

Other Cancer Indications

There are 46 ongoing and 30 planned externally sponsored trials evaluating the clinical and therapeutic potential of cabozantinib, including those administered through our CRADA with NCI-CTEP and our IST program. Like our CRADA with NCI-CTEP, our IST program helps us to continue to evaluate cabozantinib across a broad range of tumor types.

These externally sponsored trials include signal seeking studies of single-agent cabozantinib, novel combinations, and randomized trials. The monotherapy trials are focused on solid tumors including genitourinary neoplasms, gastrointestinal malignancies, lung cancer and a variety of less common tumor types. The combination studies include trials combining cabozantinib with several different ICIs, as well as studies adding cabozantinib to monoclonal antibodies and small molecules which target specific cellular pathways. Randomized trials within the CRADA include a phase 3 study in neuroendocrine tumors and phase 2 trials in both endometrial cancer in combination with checkpoint inhibitors and in prostate cancer in combination with docetaxel.

A complete listing of all ongoing cabozantinib trials can be found at www.ClinicalTrials.gov.

XL092 Development Program

XL092 is the first internally-discovered Exelixis compound to enter the clinic following the company's reinitiation of drug discovery activities. XL092 is a next-generation oral TKI that targets VEGF receptors, MET, and other kinases implicated in cancer's growth and spread. The molecule is the subject of an active IND that we submitted to the FDA

in December 2018, and that the FDA accepted in January 2019. XL092 will initially be studied in a multi-center phase 1 clinical trial designed to evaluate its pharmacokinetics, safety and tolerability. The trial is divided into dose-escalation and expansion phases. The dose-escalation phase of the trial will enroll patients with advanced solid tumors, with the primary objective of determining a dose for daily oral administration of XL092 suitable for further evaluation. Assuming positive data from the initial phase of

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the trial, the expansion phase is designed to further explore the selected dose of XL092 in individual tumor cohorts, where safety, tolerability, and initial clinical activity would be evaluated.

Expansion of the Exelixis Pipeline: Drug Discovery and Business Development Programs

We are actively focused on expanding our pipeline through internal drug discovery and targeted business development activities.

Drug Discovery

As we continue to work to maximize the clinical, therapeutic and commercial potential of cabozantinib, we are also working to rebuild our product pipeline by discovering and developing new cancer therapies for patients. From 2000 until 2012, we had an active discovery group that advanced 22 compounds to the IND stage, either independently or with collaboration partners, including cabozantinib and cobimetinib. We built significant infrastructure, including a library of 4.6 million compounds, and gained extensive experience in the identification and optimization of drug candidates against multiple target classes for oncology, inflammation and metabolic diseases.

In 2016, we resumed internal drug discovery efforts with the goal of identifying novel and promising therapeutic candidates to advance into clinical trials. Furthest along in these efforts is XL092. For additional information on XL092, see "—XL092 Development Program."

Our new discovery organization is leveraging that history in a focused and measured manner. We are concentrating our in-house work on the most demanding and time-sensitive aspects of lead optimization and use contract research organizations to support more routine activities, thereby minimizing our internal footprint while still maintaining an agile, competitive approach. We are and will continue to be judicious in the selection of targets, focusing on those with robust preclinical validation datasets. We remain focused on oncology as a therapeutic area, and prioritize those targets that we believe, for example, are key components of signaling pathways frequently deregulated in human cancers or are components of mechanisms that contribute to tumor-mediated immune suppression. We anticipate that our experience identifying high quality lead compounds against a variety of target classes through use of our propriety compound library, coupled with our expertise in medicinal chemistry, tumor biology and pharmacology, will permit us to prosecute competitive and productive discovery programs in areas of high potential.

Business Development

We are also focused on augmenting our pipeline by entering into collaborative relationships or in-licensing agreements for attractive, early-stage oncology assets and then further developing them utilizing our established and validated clinical development infrastructure. As part of this strategy, in January 2018, we entered into an exclusive collaboration and license agreement with StemSynergy Therapeutics, Inc. (StemSynergy) for the discovery and development of novel oncology compounds aimed to inhibit tumor growth by targeting Casein Kinase 1 alpha (CK1), a component of the Wnt signaling pathway implicated in key oncogenic processes. Additionally, in May 2018, we entered into a collaboration and license agreement with Invenra, Inc. (Invenra) which is focused on developing next-generation biologics, to discover and develop multispecific antibodies for the treatment of cancer. We have already made considerable progress under our collaborations with both StemSynergy and Invenra and believe we will continue to do so in 2019. For additional information on our collaboration with StemSynergy, see "—Collaborations—StemSynergy Collaboration," and for additional information on our collaboration with Invenra, see "—Collaborations—Invenra Collaboration."

We are seeking additional, external collaborative relationships around assets and technologies that complement our in-house drug discovery and development efforts. These collaborative relationships are aimed at expanding our ability to discover, develop and commercialize novel therapies with the goal of providing new treatment options for cancer patients and their physicians.

Collaborations

We have established multiple collaborations with leading pharmaceutical companies for the commercialization and further development of cabozantinib, as well as with smaller, discovery-focused biotechnology companies to expand our product pipeline. Additionally, in line with our business strategy prior to the commercialization of our first product, COMETRIQ, we entered into other collaborations with leading pharmaceutical companies including Genentech, Daiichi Sankyo and BMS for other compounds and programs in our portfolio. Under each of our collaborations, we are entitled to receive milestones and royalties or, in the case of cobimetinib, royalties from sales

outside the U.S. and a share of profits (or losses) from commercialization in the U.S.

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Cabozantinib Commercial Collaborations

Ipsen Collaboration

In February 2016, we entered into a collaboration and license agreement with Ipsen for the commercialization and further development of cabozantinib. Pursuant to the terms of the collaboration agreement, Ipsen received exclusive commercialization rights for current and potential future cabozantinib indications outside of the U.S., Canada and Japan. The collaboration agreement was subsequently amended in December 2016 to include commercialization rights in Canada. We have also agreed to collaborate with Ipsen on the development of cabozantinib for current and potential future indications. The parties' efforts are governed through a joint steering committee and appropriate subcommittees established to guide and oversee the collaboration's operation and strategic direction; provided, however, that we retain final decision-making authority with respect to cabozantinib's ongoing development.

In consideration for the exclusive license and other rights contained in the collaboration agreement, including commercialization rights in Canada, Ipsen paid us aggregate upfront payments of $210.0 million. As of December 31, 2018, we achieved aggregate milestone payments of $275.0 million related to regulatory and commercial progress by Ipsen since the inception of the collaboration agreement, including milestone payments during 2018 of (i) $50.0 million upon the EMA filing and the approval of cabozantinib as a treatment for patients with previously untreated RCC, (ii) $25.0 million upon Ipsen's achievement of $100.0 million of net sales cumulatively over four consecutive fiscal quarters, (iii) $50.0 million upon EMA filing and the approval of cabozantinib as a treatment for patients with previously treated HCC, (iv) $5.0 million upon the approval by Health Canada of cabozantinib for the treatment of adults with advanced RCC who have received prior VEGF-targeted therapy and (v) $20.0 million upon the initiation of COSMIC-312.

We are also eligible to receive future development and regulatory milestone payments from Ipsen, totaling an aggregate of $84.0 million upon additional approvals of cabozantinib in future indications and/or jurisdictions, as well as contingent payments of up to $519.5 million associated with future sales volume milestones. We will further receive royalties on net sales of cabozantinib by Ipsen outside of the U.S. and Japan. We were initially entitled to receive a tiered royalty of 2% to 12% on the initial $150.0 million of net sales; this amount was reached in the second quarter of 2018. As of December 31, 2018 and going forward, we are entitled to receive a tiered royalty of 22% to 26% on annual net sales (with separate tiers for Canada); these 22% to 26% royalty tiers reset each calendar year. In Canada, we are entitled to receive a tiered royalty of 22% on the first CAD$30.0 million of annual net sales and a tiered royalty thereafter to 26% on annual net sales; these 22% to 26% royalty tiers for Canada will also reset each calendar year. As of December 31, 2018, we have earned royalties of $36.3 million on net sales of cabozantinib by Ipsen since the inception of the collaboration agreement.

Consistent with our historical agreement with GlaxoSmithKline (GSK), we are required to pay a 3% royalty to GSK on all net sales of any product incorporating cabozantinib, including net sales by Ipsen.

We are responsible for funding cabozantinib-related development costs for those trials in existence at the time we entered into the collaboration agreement with Ipsen; global development costs for additional trials are shared between the parties, with Ipsen reimbursing us for 35% of such costs, provided Ipsen chooses to opt into such trials. In accordance with the collaboration agreement, Ipsen has opted into and is co-funding: CheckMate 9ER; CheckMate 040 (though Ipsen will not be co-funding the triplet arm of the study evaluating cabozantinib with nivolumab and ipilimumab); the dose escalation phase and first eight expansion cohorts of COSMIC-021; and COSMIC-312.

We remain responsible for manufacturing and supply of cabozantinib for all development and commercialization activities under the collaboration agreement. In connection with the collaboration agreement, we entered into a supply agreement with Ipsen to supply finished and labeled drug product to Ipsen for distribution in the territories outside of the U.S. and Japan for the term of the collaboration agreement, as well as a quality agreement that provides respective quality responsibilities for the aforementioned supply. Furthermore, at the time we entered into the collaboration agreement, the parties also entered into a pharmacovigilance agreement, which defines each partner's responsibilities for safety reporting. The pharmacovigilance agreement also requires us to maintain the global safety database for cabozantinib. To meet our obligations to regulatory authorities for the reporting of safety data from territories outside of the U.S. and Japan from sources other than our sponsored global clinical development trials, we rely on data collected and reported to us by Ipsen.

Unless terminated earlier, the collaboration agreement has a term that continues, on a product-by-product and country-by-country basis, until the latter of (i) the expiration of patent claims related to cabozantinib, (ii) the expiration of regulatory exclusivity covering cabozantinib or (iii) ten years after the first commercial sale of cabozantinib, other than COMETRIQ. The supply agreement will continue in effect until expiration or termination of the collaboration agreement. The collaboration agreement may be terminated for cause by either party based on uncured material breach of either the collaboration agreement or the supply agreement by the other party, bankruptcy of the other party or for safety reasons. We may terminate the collaboration agreement if Ipsen challenges or opposes any patent covered by the collaboration

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agreement. Ipsen may terminate the collaboration agreement if the FDA or EMA orders or requires substantially all cabozantinib clinical trials to be terminated. Ipsen also has the right to terminate the collaboration agreement on a region-by-region basis after the first commercial sale of cabozantinib in advanced RCC in the given region. Upon termination by either party, all licenses granted by us to Ipsen will automatically terminate, and, except in the event of a termination by Ipsen for our material breach, the licenses granted by Ipsen to us shall survive such termination and shall automatically become worldwide, or, if Ipsen were to terminate only for a particular region, then for the terminated region. Following termination by us for Ipsen's material breach, or termination by Ipsen without cause or because we undergo a change of control by a party engaged in a competing program, Ipsen is prohibited from competing with us for a period of time.

Takeda Collaboration

In January 2017, we entered into a collaboration and license agreement with Takeda. Pursuant to this collaboration agreement, Takeda has exclusive commercialization rights for current and potential future cabozantinib indications in Japan, and the parties have agreed to collaborate on the clinical development of cabozantinib in Japan. The operation and strategic direction of the parties' collaboration is governed through a joint executive committee and appropriate subcommittees.

In consideration for the exclusive license and other rights contained in the collaboration agreement, we received a $50.0 million upfront nonrefundable payment from Takeda. Effective March 2018, we amended the collaboration agreement to modify the milestones we are eligible to receive under this agreement, and as of December 31, 2018, we are eligible to receive development, regulatory and first-sale milestone payments of up to $90.0 million related to both previously treated and previously untreated RCC and previously treated HCC, as well as additional development, regulatory and first-sale milestone payments for potential future indications. The collaboration agreement also provides that we are eligible to receive pre-specified payments of up to $83.0 million associated with sales volume milestones and royalties on net sales of cabozantinib in Japan. We are entitled to receive a tiered royalty of 15% to 24% on the initial $300.0 million of net sales, and following this initial $300.0 million of net sales, we are then entitled to receive a tiered royalty of 20% to 30% on annual net sales thereafter; these 20% to 30% royalty tiers will reset each calendar year.

Consistent with our historical agreement with GSK, we are required to pay a 3% royalty to GSK on all net sales of any product incorporating cabozantinib, including net sales by Takeda.

Takeda is responsible for 20% of the costs associated with the global cabozantinib development plan's current and future trials, provided Takeda opts into such trials, and 100% of costs associated with the cabozantinib development activities that are exclusively for the benefit of Japan. In accordance with the collaboration agreement, Takeda has opted into and is co-funding CheckMate 9ER.

Pursuant to the terms of the collaboration agreement, we are responsible for the manufacturing and supply of cabozantinib for all development and commercialization activities under the collaboration agreement. In connection with the collaboration agreement, we entered into a clinical supply agreement covering the supply of cabozantinib to Takeda for the term of the collaboration agreement, as well as a quality agreement that provides respective quality responsibilities for the aforementioned supply. Furthermore, at the time we entered into the collaboration agreement, the parties also entered into a safety data exchange agreement, which defines each partner's responsibility for safety reporting. This agreement also requires us to maintain the global safety database for cabozantinib. To meet our obligations to regulatory authorities for the reporting of safety data from Japan from sources other than our sponsored global clinical development trials, we rely on data collected and reported to us by Takeda.

Unless earlier terminated, the collaboration agreement has a term that continues, on a product-by-product basis, until the earlier of (i) two years after first generic entry with respect to such product in Japan or (ii) the later of (A) the expiration of patent claims related to cabozantinib and (B) the expiration of regulatory exclusivity covering cabozantinib in Japan. The collaboration agreement may be terminated for cause by either party based on uncured material breach by the other party, bankruptcy of the other party or for safety reasons. For clarity, Takeda's failure to achieve specified levels of commercial performance, based upon sales volume and/or promotional effort, during the first six years of the collaboration will constitute a material breach of the collaboration agreement. We may terminate the agreement if Takeda challenges or opposes any patent covered by the collaboration agreement. At any time prior

to August 1, 2023, the parties may mutually agree to terminate the collaboration agreement if Japan's Pharmaceuticals and Medical Devices Agency is unlikely to grant any approval of the marketing authorization application (MAA) in any cancer indication in Japan. After the commercial launch of cabozantinib in Japan, Takeda may terminate the collaboration agreement upon twelve months' prior written notice following the third anniversary of the first commercial sale of cabozantinib in Japan. Upon termination by either party, all licenses granted by us to Takeda will automatically terminate, and the licenses granted by Takeda to us shall survive such termination and shall automatically become worldwide.

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Cabozantinib Development Collaborations

BMS

In February 2017, we entered into a clinical trial collaboration agreement with BMS for the purpose of exploring the therapeutic potential of cabozantinib in combination with BMS's ICIs, nivolumab and/or ipilimumab, to treat a variety of types of cancer. As part of the collaboration, we are evaluating these combinations as treatment options for RCC and HCC in the CheckMate 9ER and CheckMate 040 trials, respectively. We also intend to evaluate these combinations in other phase 3 pivotal trials in various other tumor types, including UC. For descriptions of the Checkmate 9ER and Checkmate 040 trials, see "—Cabozantinib Development Program—Trials Conducted Under our Clinical Collaboration Agreements—Combination Studies with BMS."

Pursuant to the terms of the collaboration agreement with BMS, each party granted to the other a non-exclusive, worldwide (within the collaboration territory as defined in the collaboration agreement and its supplemental agreements), non-transferable, royalty-free license to use the other party's compounds in the conduct of each clinical trial. The parties' efforts are governed through a joint development committee established to guide and oversee the collaboration's operation. Each trial will be conducted under a combination IND application, unless otherwise required by a regulatory authority. Each party will be responsible for supplying finished drug product for the applicable clinical trial and unless otherwise agreed between the parties, costs for each such trial will be shared equally between the parties, unless two BMS compounds will be utilized in such trial, in which case BMS will bear two-thirds of the costs for such study treatment arms and we will bear one-third of the costs. Unless earlier terminated, the collaboration agreement will remain in effect until the completion of all clinical trials under the collaboration, all related trial data has been delivered to both parties and the completion of any then agreed upon analysis. The collaboration agreement may be terminated for cause by either party based on uncured material breach by the other party, bankruptcy of the other party or for safety reasons. Upon termination by either party, the licenses granted to each party to conduct a combined therapy trial will terminate.

Roche

In February 2017, we entered into a master clinical supply agreement with Roche for the purpose of evaluating cabozantinib and Roche's ICI, atezolizumab, in locally advanced or metastatic solid tumors. Pursuant to the terms of this agreement with Roche, in June 2017, we initiated COSMIC-021 and in December 2018, we initiated COSMIC-312. We are the trial sponsor, and Roche is providing atezolizumab free of charge. For descriptions of the COSMIC-021 and COSMIC-312 trials, see "—Cabozantinib Development Program—Trials Conducted Under our Clinical Collaboration Agreements—Combination Studies with Roche."

StemSynergy Collaboration

In January 2018, we entered into an exclusive collaboration and license agreement with StemSynergy for the discovery and development of novel oncology compounds targeting CK1 , a component of the Wnt signaling pathway implicated in key oncogenic processes. Activation of -catenin, a key downstream component of the pathway, is increased in multiple tumors, including a majority of colorectal cancers, where mutations in the APC gene that result in -catenin stabilization are prevalent. Compounds targeting CK1 have also been shown to induce degradation of -catenin and pygopus, another member of the pathway, in preclinical CRC models, and to inhibit the growth of tumors. Importantly, their GI-sparing qualities may help overcome limitations of other approaches targeting the Wnt pathway. Under the terms of the agreement, we will partner with StemSynergy to conduct preclinical and clinical studies with compounds targeting CK1 . We paid StemSynergy an upfront payment of $3.0 million in initial research and development funding, and we plan to provide StemSynergy with additional research and development funding of up to $1.2 million during 2019 on an as needed basis. StemSynergy will also be eligible for up to $56.5 million in milestones for the first product to emerge from the collaboration, including preclinical and clinical development and regulatory milestone payments, commercial milestones, as well as single-digit royalties on worldwide sales. We will be solely responsible for the commercialization of products that arise from the collaboration.

Invenra Collaboration

In May 2018, we entered into a collaboration and license agreement with Invenra, which is focused on developing next-generation biologics, to discover and develop multispecific antibodies for the treatment of cancer. Invenra is responsible for antibody lead discovery and generation while we will lead IND-enabling studies, manufacturing,

clinical development in single-agent and combination therapy regimens, and future regulatory and commercialization activities. The collaboration agreement also provides that we will receive an exclusive, worldwide license to one preclinical asset, and that we will pursue up to six additional discovery projects during the term of the collaboration, which in total are directed to three discovery programs.

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In consideration for the exclusive worldwide license and other rights contained in the collaboration agreement, we paid Invenra an upfront payment of $2.0 million and a project initiation fee of $2.0 million. In January 2019, we initiated our second discovery project, for which we paid an additional project initiation fee of $2.0 million. Invenra is eligible to receive payments of up to $131.5 million based on the achievement of specific development and regulatory milestones for a product containing the lead preclinical asset in the first indication. Upon successful commercialization of a product, Invenra is eligible to receive global milestone payments up to $325.0 million if certain sales thresholds are achieved as well as single-digit tiered royalties on net sales of the approved product. We also have the right to initiate four additional discovery projects for development subject to an upfront payment of $2.0 million for each project, as well as additional global milestone payments and royalties for any products that arise from these discovery efforts.

Unless earlier terminated, the collaboration agreement has a term that continues, on a product-by-product and country-by-country basis, until the later of (i) ten years after the first commercial sale of such product in such country or (ii) expiration of patent claims covering the product in such country. We may terminate the collaboration agreement in its entirety or on a project-by-project basis at any time prior to commercialization, for any or no reason, upon thirty days' written notice to Invenra. The collaboration agreement also may be terminated by either party for a material breach by the other, subject to notice and cure provisions.

Other Collaborations

Prior to the commercialization of our first product, COMETRIQ, our primary business strategy was focused on the development and out-license of compounds to pharmaceutical and biotechnology companies under collaboration agreements that allowed us to retain economic participation in compounds and support additional development of our proprietary products. Our collaboration agreements with Genentech, Daiichi Sankyo and BMS described below are representative of this historical strategy. We have since evolved and are now a fully-integrated biopharmaceutical company focused on driving the expansion and depth of our product offerings through the continued development of cabozantinib, internal drug discovery and execution of strategic transactions that align with our oncology drug development and commercialization expertise, all to improve care and outcomes for people with cancer around the world. While the historical collaboration agreements described below have the potential to provide future revenue, and while we have already received some collaboration revenues from these arrangements, we do not expect to receive significant revenues from these historical collaboration agreements unless and until our partnered compounds generate substantial sales in the territories and indications where they are approved, or if not yet approved, enter late-stage clinical development. If these events occur, then the milestone payments, royalties or other rights and benefits under our historical collaboration agreements could become substantial.

Genentech - Cobimetinib

In December 2006, we out-licensed the further development and commercialization of cobimetinib to Genentech pursuant to a worldwide collaboration agreement. Cobimetinib is a reversible inhibitor of MEK, a 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. Under the terms of the collaboration agreement, we developed cobimetinib through the determination of the maximum tolerated dose in a phase 1 clinical trial, and Genentech had the option to co-develop cobimetinib, an option that Genentech exercised, and in March 2009, we granted to Genentech an exclusive worldwide revenue-bearing license to cobimetinib, at which point Genentech became responsible for completing the phase 1 clinical trial and subsequent clinical development. We received aggregate upfront and milestone payments of $50.0 million under our collaboration agreement with Genentech and are not eligible for any additional milestone payments.

On November 10, 2015, the FDA approved cobimetinib, under the brand name COTELLIC, in combination with Genentech's Zelboraf (vemurafenib) as a treatment for patients with BRAF V600E or V600K mutation-positive advanced melanoma. COTELLIC in combination with Zelboraf has also been approved in Switzerland, the EU, Canada, Australia, Brazil and multiple additional countries for use in the same indication. Prior to the FDA's approval of COTELLIC, in November 2013, we exercised an option under the collaboration agreement to co-promote COTELLIC in the U.S., which allows for us to provide up to 25% of the total sales force for approved cobimetinib indications in the U.S. Between November 2015 and December 2017, we fielded 25% of the sales force promoting

COTELLIC in combination with Zelboraf as a treatment for patients with BRAF mutation-positive advanced melanoma in the U.S. However, following a review of the commercial landscape, commencing in January 2018, we and Genentech scaled back the personal promotion of COTELLIC in this indication in the U.S. This decision is not indicative of any change in our intention to promote COTELLIC for other therapeutic indications for which it may be approved in the future.

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Cobimetinib Profit Sharing and Royalty Revenues

Under the terms of our collaboration agreement, as amended in July 2017, we share in the profits and losses received or incurred in connection with COTELLIC's commercialization in the U.S. This profit and loss share has multiple tiers: we receive 50% of profits and losses from the first $200.0 million of U.S. actual sales, decreasing to 30% of profits and losses from U.S. actual sales in excess of $400.0 million. These tiers will reset each calendar year. The revenue for each sale of COTELLIC applied to the profit and loss statement for the collaboration agreement (Genentech Collaboration P&L) is calculated using the average of the quarterly net selling prices of COTELLIC and any additional branded Genentech product(s) prescribed with COTELLIC in such sale. U.S. commercialization costs for COTELLIC are then applied to the Genentech Collaboration P&L, subject to reduction based on the number of Genentech products in any given combination including COTELLIC. In addition to our profit share in the U.S., under the terms of the collaboration agreement, we are entitled to low double-digit royalties on net sales of COTELLIC outside the U.S. During 2018, we earned royalties of $5.6 million on net sales of COTELLIC outside the U.S. and a $8.1 million profit on the profit and loss sharing of U.S. actual sales which are recorded in Collaboration revenues. Unless earlier terminated, the collaboration agreement has a term that continues until the expiration of the last payment obligation with respect to the licensed products under the collaboration. Genentech has the right to terminate the collaboration agreement without cause at any time. If Genentech terminates the collaboration agreement without cause, all licenses that were granted to Genentech under the agreement terminate and revert to us. Additionally, if Genentech terminates the collaboration agreement without cause, or we terminate the collaboration agreement for cause, we would receive, subject to certain conditions, licenses from Genentech to research, develop and commercialize reverted product candidates. The collaboration agreement may be terminated for cause by either party based on uncured material breach by the other party.

Cobimetinib Clinical Development Program

In addition to its established commercialization of COTELLIC, Genentech continues to make significant progress with respect to the clinical development, regulatory status and commercial potential of cobimetinib. Cobimetinib is being evaluated in a broad development program consisting of more than 50 clinical trials by Genentech or through Genentech's investigator sponsored trial program, including two phase 3 pivotal trials currently underway exploring the combination of cobimetinib with atezolizumab or atezolizumab alone in BRAF wild type melanoma (IMspire170) and the combination of cobimetinib with atezolizumab and vemurafenib in BRAF V600 mutant melanoma (IMspire150). Additionally, although IMblaze370, a third phase 3 pivotal trial conducted by Genentech evaluating the combination of cobimetinib with atezolizumab in CRC did not meet its primary endpoint as announced in May 2018, Genentech continues to pursue the cobimetinib development program and is conducting a series of early-stage clinical trials investigating the combination of cobimetinib and atezolizumab in multiple tumor settings. Should these trials prove positive and Genentech obtain regulatory approvals based on such positive results, we believe that cobimetinib could provide us with a potentially meaningful source of revenue in the future.

Melanoma - coBRIM. In July 2014, we announced positive top-line results from coBRIM, the phase 3 pivotal trial conducted by Genentech evaluating cobimetinib in combination with vemurafenib in previously untreated patients with unresectable locally advanced or metastatic melanoma harboring a BRAF V600E or V600K mutation. The primary endpoint was investigator-determined PFS, and secondary endpoints included OS, ORR, IRRC-determined PFS and DOR. coBRIM met its primary endpoint, demonstrating a statistically significant increase in investigator-determined PFS. The median PFS was 9.9 months for the combination of cobimetinib and vemurafenib versus 6.2 months for vemurafenib alone. The median PFS as established by an IRRC, a secondary endpoint, was 11.3 months for the combination arm compared to 6.0 months for the control arm. ORR, another secondary endpoint, was 68% for the combination versus 45% for vemurafenib alone. Data were published in the NEJM and presented at the ESMO 2014 Congress in September 2014. Updated results for PFS and ORR from coBRIM were then presented at the ASCO 2015 Annual Meeting in June 2015 and showed a median PFS of 12.3 months for the combination of cobimetinib and vemurafenib versus 7.2 months for vemurafenib alone, and an ORR of 70% for the combination of vemurafenib and cobimetinib versus 50% for vemurafenib alone. In November 2015, we announced that the coBRIM trial also met its OS secondary endpoint, demonstrating a statistically significant increase in OS for the combination of cobimetinib and vemurafenib compared to vemurafenib monotherapy. The median OS was 22.3 months for the

combination of cobimetinib and vemurafenib versus 17.4 months for vemurafenib alone. The safety profile of the combination was consistent with that observed in a previous study.

CoBRIM served as the basis for the regulatory approval of COTELLIC in combination with Zelboraf as a treatment for patients with BRAF V600E or V600K mutation-positive advanced melanoma in the U.S., Switzerland, the EU, Canada, Australia, Brazil and other countries.

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Melanoma - IMspire150. In January 2017, Genentech initiated IMspire150, a phase 3 pivotal trial evaluating the combination of cobimetinib, vemurafenib and atezolizumab vs. cobimetinib plus vemurafenib in previously untreated BRAF V600 mutation positive patients with metastatic or unresectable locally advanced melanoma. This trial, which has a primary endpoint of PFS, was based on the results of Genentech's ongoing phase 1b trial in the same patient population. The trial completed enrollment of approximately 500 patients in April 2018. Genentech has announced that top-line results are expected during 2019, and should the results prove positive, Genentech also intends to submit regulatory filings for this combination in 2019.

Melanoma - IMspire170. In October 2017, Genentech initiated IMspire170, a phase 3 trial comparing cobimetinib plus atezolizumab to pembrolizumab in previously untreated BRAF WT patients with metastatic or unresectable locally advanced melanoma. IMspire170 was based on the results of Genentech's ongoing phase 1b trial in the same patient population. This trial, which has a primary endpoint of PFS, is designed to enroll 450 patients; the first patient was enrolled in December 2017. Genentech has announced that top-line results for the trials are expected during 2019, and should the results prove positive, Genentech also intends to submit regulatory filings for this combination in 2019.

Other Cancer Indications. In addition to IMspire150 and IMspire170, additional earlier-stage clinical trials are ongoing studying the combination of cobimetinib with a variety of agents in multiple tumor types. These include:

- the combination of cobimetinib and vemurafenib in additional melanoma patient populations and settings;
- a phase 2 trial of cobimetinib in combination with taxanes, with or without atezolizumab in first-line TNBC (COLET);
- Phase 2 studies of cobimetinib in combination with atezolizumab in RCC, head and neck squamous cell carcinoma, UC and hormone receptor positive, HER2 negative breast cancer;
- Phase 1/2 studies of cobimetinib in combination with atezolizumab in melanoma and NSCLC, in combination with vemurafenib and atezolizumab in melanoma, and in combination with venetoclax in relapsed or refractory acute myeloid leukemia and multiple myeloma;
- a phase 1b study evaluating the safety, tolerability and pharmacokinetics of cobimetinib in combination with atezolizumab and bevacizumab in patients with metastatic CRC; and
- a phase 1b/2 study of cobimetinib in combination with atezolizumab (one arm of a randomized umbrella study) in metastatic pancreatic ductal adenocarcinoma.

A complete listing of all ongoing cobimetinib trials can be found at www.ClinicalTrials.gov.

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 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 esaxerenone, an oral, non-steroidal, selective MR antagonist. 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. During the research term, which concluded in November 2007, we jointly identified drug candidates with Daiichi Sankyo for further development. Esaxerenone is the only remaining drug candidate identified under the collaboration that continues to be developed by Daiichi Sankyo, and we are entitled to receive payments upon attainment of pre-specified development, regulatory and commercialization milestones for esaxerenone

In September 2017, Daiichi Sankyo reported positive top-line results from ESAX-HTN, a phase 3 pivotal trial of esaxerenone, and submitted a Japanese regulatory application for esaxerenone for an essential hypertension indication in February 2018, for which we received a $20.0 million milestone payment, which we recorded in the first quarter of 2018. Data from ESAX-HTN were published in the Journal of Hypertension in June 2018. Daiichi Sankyo's application was then approved by the Japanese Ministry of Health, Labour and Welfare (MHLW) in January 2019, and the first commercial sale of the branded esaxerenone product MINNEBRO in Japan will trigger the payment of a $20.0 million milestone payment to us. As of December 31, 2018, and after giving effect to the milestone payment associated with the Japanese regulatory application for esaxerenone, we have achieved an aggregate of $45.5 million in development, regulatory and commercialization milestone payments related to MINNEBRO over the life of the

collaboration agreement. We are eligible to receive additional commercialization milestone payments of up to $110.0 million, including the $20.0 million milestone payment associated with the first commercial sale of MINNEBRO in Japan. In addition, we are entitled to receive low double-digit royalties on sales of MINNEBRO. 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,

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develop and commercialize compounds that were discovered under the collaboration. In addition, pursuant to a license agreement we entered into with Ligand Pharmaceuticals, Inc. (Ligand), we are required to pay a royalty of 0.5% to Ligand on net sales of MINNEBRO.

Daiichi Sankyo also continues to advance the development program for esaxerenone, with an ongoing phase 3 pivotal trial evaluating esaxerenone as a treatment option for patients in Japan with diabetic nephropathy. Should this trial prove positive and Daiichi Sankyo obtain regulatory approval based on such positive results, and taking into account the approval of MINNEBRO by the MHLW in January 2019 for the treatment of hypertension, we believe that esaxerenone will provide an additional source of revenue in the future.

BMS - ROR Collaboration Agreement

In October 2010, we entered into a worldwide collaboration with BMS 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 BMS. 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 which began on October 8, 2010 and ended on July 8, 2013. Since the end of the collaborative research period, BMS 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.

For each product developed by BMS under the collaboration, we will be eligible to receive payments upon the achievement by BMS of development and regulatory milestones. As of December 31, 2017, we have earned aggregate development and regulatory milestones of $12.5 million, including a $2.5 million development milestone payment in February 2017 in connection with the achievement of certain preclinical milestones set forth in the collaboration agreement and a $10.0 million regulatory milestone payment in October 2017 in connection with BMS's filing of a Clinical Trial Authorization in Europe for a first in-human study of an ROR inverse agonist. We are eligible for additional development and regulatory milestone payment of up to $240.0 million in the aggregate and commercialization milestones of up to $150.0 million in the aggregate, as well as royalties on commercial net sales, depending on the advancement of the product candidate and eventual product.

The collaboration agreement was amended and restated in April 2011 in connection with an assignment of patents to a wholly-owned subsidiary. BMS 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 BMS at will or by us for BMS's uncured material breach, the license granted to BMS 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 BMS to develop and commercialize such product in the related country. In the event of termination by BMS for our uncured material breach, BMS would retain the right to such product, subject to continued payment of milestones and royalties.

Manufacturing and Product Supply

We do not own or operate manufacturing facilities, distribution facilities or resources for clinical or commercial production and distribution of our products. Instead, we have multiple contractual agreements in place with third-party contract manufacturing organizations who, on our behalf, manufacture clinical and commercial supplies of CABOMETYX and COMETRIQ. As our operations expand due to our development and commercial progress, we expect to enter into new agreements with additional third-party contract manufacturers and suppliers as needed. This will continue for the foreseeable future for all of our product candidates and all of our current and future commercial products. We have selected well-established and reputable global third-party contract manufacturers for our drug substance and drug product manufacturing that have good regulatory standing, large manufacturing capacities and multiple manufacturing sites within their business footprint. These third parties must comply with applicable regulatory requirements, including the FDA's Current Good Manufacturing Practices, the EC's Guidelines on Good Distribution Practice (GDP), as well as other stringent regulatory requirements enforced by the FDA or foreign regulatory agencies, as applicable, and are subject to routine inspections by such regulatory agencies.

Through our third-party manufacturers and data service providers, we have implemented product serialization designed to comply with the Drug Supply Chain Security Act (DSCSA), pursuant to which all prescription pharmaceutical products manufactured and distributed in the U.S. were required to be serialized as of November 27, 2018.

We monitor and evaluate the performance of our third-party contract manufacturers on an ongoing basis to ensure compliance with these requirements and to affirm their continuing capabilities to meet both our commercial and clinical

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needs. We also have contracted with a third-party logistics provider, with multiple distribution locations, to provide shipping and warehousing services for our commercial supply of both CABOMETYX and COMETRIQ in the U.S. We employ highly skilled personnel with both technical and manufacturing experience to diligently manage the activities at our third-party contract manufacturers, and our quality department audits them on a periodic basis.

We source raw materials that are used to manufacture our drug substance from multiple third-party suppliers in Asia and Europe. We stock sufficient quantities of these materials and provide them to our third-party drug substance contract manufacturers to ensure they can manufacture adequate drug substance quantities per our requirements, for both clinical and commercial purposes. We then store drug substance at third-party facilities and provide appropriate amounts to our third-party drug product contract manufacturers, who then manufacture, package and label our specified quantities of finished goods for COMETRIQ and CABOMETYX, respectively. In addition, we rely on our third-party contract manufacturers to source materials such as excipients, components and reagents, which are required to manufacture our drug substance and finished drug product.

Within our supply chain, we have established safety stock amounts for both our drug substance and drug products, and store these quantities in multiple locations. The quantities that we store are based on our business needs and take into account scenarios for market demand, production lead times, potential supply interruptions and shelf life for our drug substance and drug products. In parallel, for business continuity reasons, we expect to establish additional suppliers for our drug substance and drug product manufacturers soon. We believe that our current manufacturing network has the appropriate capacity to produce sufficient commercial quantities of CABOMETYX to support the currently approved advanced RCC and HCC indications, as well as potential additional indications if trials evaluating CABOMETYX in those indications prove to be successful and gain regulatory approval in the future. Our manufacturing footprint also enables us to fulfill our supply obligations for CABOMETYX and COMETRIQ to our collaboration partners, Ipsen and Takeda, for global development and commercial purposes.

Marketing, Sales and Distribution

We have a fully integrated commercial team consisting of sales, marketing, market access, and commercial operations functions. Our sales team promotes CABOMETYX and COMETRIQ in the U.S. In addition, although we currently do not co-promote COTELLIC alongside Genentech, we have the right to do so and will do so if we, in consultation with Genentech, deem it useful and appropriate to realize COTELLIC's commercial objectives. We use customary pharmaceutical company practices to market our products in the U.S. and concentrate our efforts on oncologists, oncology nurses and pharmacists. Our commercial products, CABOMETYX and COMETRIQ, are sold initially through wholesale distribution and specialty pharmacy channels and then, if applicable, resold to hospitals and other organizations that provide CABOMETYX and COMETRIQ to end-user patients. To facilitate our commercial activities in the U.S., we also employ various third-party vendors, such as advertising agencies, market research firms and other sales-support related services as needed. We believe that our commercial team and distribution practices are sufficient to ensure our marketing efforts reach our target audience and deliver our products to patients in a timely and compliant fashion.

In addition, we rely on Ipsen and Takeda for ongoing and further commercialization and distribution of CABOMETYX in territories outside of the U.S., as well as for access and distribution activities for the approved products under named patient use programs or similar programs with the effect of introducing earlier patient access to CABOMETYX, and we also rely on Ipsen for these same activities with respect to the commercialization and distribution of COMETRIQ outside of the U.S. For COTELLIC, we rely on Genentech, as our collaboration partner, for all current and future commercialization and marketing activities, with the exception of the limited co-promotion activities highlighted above.

To help ensure that all eligible patients in the U.S. have appropriate access to CABOMETYX and COMETRIQ, we have established a comprehensive reimbursement and patient support program called Exelixis Access Services (EASE). Through EASE, we provide co-pay assistance to qualified, commercially insured patients to help minimize out-of-pocket costs and provide free drug to uninsured or under-insured patients who meet certain clinical and financial criteria. In addition, EASE provides comprehensive reimbursement support services, such as prior authorization support, benefits investigation and, if needed, appeals support.

Seasonal Operations and Backlog

Sales of our marketed products do not reflect any significant degree of seasonality.

The markets in which we operate are characterized by short lead times and the absence of significant backlogs. We do not believe that backlog information is material to our business as a whole.

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Environment, Health and Safety

In support of the development and expansion of our product pipeline, we have resumed discovery activities. Our research and development processes involve the controlled use of certain hazardous materials and chemicals. We are subject to federal, state and local environmental, health and workplace safety laws and regulations governing the use, manufacture, storage, handling and disposal of hazardous materials. While we have incurred, and may continue to incur, expenditures to ensure we are in compliance with these laws and regulations, we do not expect the cost of complying with these laws and regulations to be material.

Government Regulation

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, among other things, research and development activities and the testing, marketing approval, manufacture, quality control, safety, effectiveness, labeling, storage, distribution, post-marketing safety reporting, export, import, record keeping, advertising and promotion of our products.

The process required by the FDA before product candidates may be marketed in the U.S. generally involves the following:

- nonclinical laboratory and animal tests, some of which must be conducted in accordance with Good Laboratory Practices;
- submission of an IND, which must become effective before human clinical trials may begin;
- adequate and well-controlled human clinical trials to establish the safety and efficacy of the investigational drug candidate for its proposed intended use;
- for drug products, submission of an New Drug Application (NDA) to the FDA for commercial marketing, or generally of a supplemental New Drug Application (sNDA), for approval of a new indication if the product is already approved for another indication;
- for biological products, submission of a Biologics License Application (BLA) to FDA for commercial marketing, or generally a supplemental Biologics License Application (sBLA) for approval of a new indication if the product is already approved for another indication;
- pre-approval inspection of manufacturing facilities and selected clinical investigators for their compliance with Good Manufacturing Practices (GMP) and Good Clinical Practices (GCP);
- if FDA convenes an advisory committee, satisfactory completion of the advisory committee review; and
- FDA approval of the NDA or sNDA, or BLA or sBLA.

The testing and approval process requires substantial time, effort and financial resources. Prior to commencing the first human 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 provide 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, which involve the initial introduction of a new drug product candidate into humans, are initially conducted in a limited number of subjects to test the product candidate for safety, tolerability, 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 dosage, and common short-term side effect and risks associated with

the drug. 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. Phase 2 studies are typically well controlled, closely monitored, and conducted in a relatively small number of patients, usually involving no more than several hundred subjects. In some cases, a sponsor may decide to run what is referred to as a “phase 2b”

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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 earlier phase evaluations provide preliminary evidence suggesting that a dosage range of the product is effective and has an acceptable safety profile, phase 3 trials are performed to gather the additional information about effectiveness and safety that is needed to evaluate the overall benefit-risk relationship of the drug and to provide an adequate basis for physician labeling. Phase 3 trials are undertaken in large patient populations to further evaluate dosage, to provide 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 post-marketing commitments can result in FDA enforcement action, up to and 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 sNDA. The submission of an NDA requires payment of a substantial user fee to the FDA. The FDA may convene an advisory committee to provide clinical insight on NDA review questions. Although the FDA is not required to follow the recommendations of an advisory committee, the agency usually does so. The FDA may deny approval of an NDA or sNDA 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 phase 3 pivotal clinical trial. Even if such data are submitted, the FDA may ultimately decide that the NDA or sNDA 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 post-marketing programs.

Satisfaction of FDA development and approval 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 for 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 are 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, including withdrawal of the NDA approval.

Any products manufactured or distributed by us pursuant to FDA approvals are subject to continuing regulation by the FDA, including obtaining prior FDA approval of certain changes to the approved NDA, 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 manufacturing requirements, including procedural and documentation requirements, upon us and our third-party manufacturers.

The FDA closely regulates the marketing and promotion of drugs, including restricting the promotion of uses for which a drug is not approved by the agency. Not only must a company have appropriate substantiation to support claims made about a drug, under the FDA's current interpretation of the relevant laws, a company can make only those claims relating to safety and efficacy that are for indications for which the FDA has approved the drug and that are otherwise consistent with the FDA-approved label for the drug. Failure to comply with these requirements can result

in adverse publicity, warning or untitled letters, corrective advertising and potential civil and criminal penalties. Physicians may, in their independent medical judgment, 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 generally does not regulate the behavior of physicians in their choice of treatments. The FDA does, however, restrict manufacturers' communications on the subject of off-label uses. Additionally, a significant number of pharmaceutical companies have been the target of inquiries and investigations by various U.S. federal and state regulatory, investigative,

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prosecutorial and administrative entities in connection with the promotion of products for off-label uses and other sales practices. These investigations have alleged violations of various U.S. federal and state laws and regulations, including claims asserting antitrust violations, violations of the Federal Food, Drug, and Cosmetic Act (FDCA), false claims laws, the Prescription Drug Marketing Act, anti-kickback laws and other alleged violations in connection with the promotion of products for unapproved uses, pricing and Medicare and/or Medicaid reimbursement.

In the U.S., the Orphan Drug Act of 1983, as amended, is intended to incentivize the development of drugs and biological products for rare diseases or conditions that affect fewer than 200,000 people in the U.S. (or that affects more than 200,000 persons in the U.S. and for which there is no reasonable expectation that the cost of developing and making available the drug in the U.S. for such disease or condition will be recovered from sales of the drug in the U.S.). If a drug is being developed for a rare disease or condition, to be eligible for designation as an orphan drug, the FDA must not have previously approved a drug considered the "same drug," as defined in the FDA's orphan drug regulations, for the same orphan-designated indication. If the FDA has previously approved another same drug for the same indication, to obtain orphan drug designation, the sponsor of the subsequent drug would be required to provide a plausible hypothesis of clinical superiority over the previously approved drug to obtain an orphan designation. 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 grant funding, and waiver of the Prescription Drug User Fee Act (PDUFA) application fee. Following the passage of the Tax Cuts and Jobs Act of 2017, for clinical trial expenses incurred in tax years 2018 and going forward, the tax credit is reduced to 25%. In addition, upon marketing approval, an orphan-designated drug could be eligible for seven years of market exclusivity for the approved orphan-designated indication. Such orphan drug exclusivity, if awarded, would only block the approval of any drug considered the same drug for the same orphan indication. Moreover, a subsequent same drug could break a previously approved drug's orphan exclusivity through a demonstration of clinical superiority over the previously approved drug.

The FDA has various programs, including Fast Track, priority review and accelerated approval, which are intended to expedite or simplify the process for developing and reviewing promising drugs, or to provide for the approval of a drug on the basis of a surrogate endpoint. Generally, drugs that are eligible for these programs are those for serious or life-threatening conditions, those with the potential to address unmet medical needs and those that offer meaningful benefits over existing treatments. For example, Fast Track is a process designed to facilitate the development and expedite the review of drugs intended to treat serious or life-threatening diseases or conditions that demonstrate the potential to fill unmet medical needs. Priority review is designed to shorten the review period for drugs that treat serious conditions and that, if approved, would offer significant advances in safety or effectiveness or would provide a treatment where no adequate therapy exists. Under priority review, the FDA aims to take action on application within six months as compared to a standard review time of 10 months. Certain other types of drug applications are also eligible for priority review. Although Fast Track and priority review do not affect the standards for approval, the FDA will attempt to facilitate early and frequent meetings with a sponsor of a Fast Track designated drug and expedite review of the application for a drug designated for priority review. Accelerated approval provides for an earlier approval for a new drug that is intended to treat a serious or life-threatening disease or condition and that fills an unmet medical need based on a surrogate endpoint, or certain clinical endpoints, reasonably likely to predict clinical benefit. As a condition of approval, the FDA may require that a sponsor of a product candidate receiving accelerated approval perform post-marketing clinical trials to confirm the clinically meaningful outcome as predicted by the surrogate marker trial. In addition to the Fast Track, accelerated approval and priority review programs, the FDA also designates Breakthrough Therapy status to drugs that are intended, alone or in combination with one or more other drugs, to treat a serious or life-threatening disease or condition, and preliminary clinical evidence indicates that the drug may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development. Drugs designated as breakthrough therapies are also eligible for accelerated approval. The FDA will seek to ensure the sponsor of a breakthrough therapy product candidate receives: intensive guidance on an efficient drug development program; intensive involvement of senior managers and experienced staff on a proactive, collaborative and cross-disciplinary review; and rolling review.

The Drug Price Competition and Patent Term Restoration Act of 1984 (The Hatch-Waxman Act)

The Hatch-Waxman Act established two abbreviated approval pathways for drug products in which potential competitors may rely upon the FDA's prior approval of the same or similar drug product.

Abbreviated New Drug Application (ANDA). An ANDA may be approved by the FDA if the applicant demonstrates that the proposed generic product is the same as the approved drug, which is referred to as the Reference Listed Drug (RLD). Generally, an ANDA must contain data and information showing that the proposed generic product and RLD (1) have the same active ingredient, in the same strength and dosage form, to be delivered via the same route of administration, (2) are intended for the same uses, and (3) are bioequivalent. This is instead of independently demonstrating the proposed product's safety and effectiveness, which are inferred from the fact that the product is the same as the RLD, which the FDA

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previously found to be safe and effective. Furthermore, conducting bioequivalence testing is generally less time consuming and costly than conducting a full set of clinical trials in humans. In this regard, the FDA has published draft guidance containing product-specific bioequivalence recommendations for drug products containing cabozantinib, the active pharmaceutical ingredient in CABOMETYX and COMETRIQ, as it does for many FDA-approved therapeutic products.

505(b)(2) NDAs. A 505(b)(2) application is one for which one or more of the investigations relied upon by the applicant for approval were not conducted by or for the applicant and for which the applicant has not obtained a right of reference or use from the person by or for whom the investigations were conducted. Under Section 505(b)(2) of the FDCA, an applicant may rely, in part, on the FDA's previous approval of a similar product, or published literature, in support of its application. If the 505(b)(2) applicant establishes that reliance on FDA's prior findings of safety and efficacy for an approved product is scientifically appropriate, it may eliminate the need to conduct certain preclinical or clinical studies. The FDA may require additional studies or measurements, including comparability studies.

Unlike a full NDA for which the sponsor has conducted or obtained a right of reference to all the data essential to approval, the filing of both an ANDA application and a 505(b)(2) application may be delayed due to patent or exclusivity protections covering an approved product. The Hatch-Waxman Act provides (a) up to five years of exclusivity for the first approval of a new chemical entity (NCE) exclusivity and (b) three years of exclusivity for approval of an NDA or supplemental application for a product that is not an NCE but rather where the application contains new clinical studies considered essential to the approval of the NDA or sNDA (three-year "changes" exclusivity). NCE exclusivity runs from the time of approval of the NDA and bars FDA from accepting for review of any ANDA or 505(b)(2) application for a drug containing the same active moiety for five years (or for four years if the application contains a paragraph IV certification that a reference product patent is invalid or not infringed by the ANDA/505(b)(2) product). The three-year "changes" exclusivity generally bars the FDA from approving any ANDA or 505(b)(2) application that relies on the information supporting the approval of the drug or the change to the drug for which the information was submitted and the exclusivity granted.

Orange Book Listing. An NDA sponsor must identify to the FDA patents that claim the drug substance or drug product or approved method of using the drug. When the drug is approved, those patents are among the information about the product that is listed in the FDA publication, Approved Drug Products with Therapeutic Equivalence Evaluations, which is referred to as the Orange Book. Any applicant who files an ANDA or a 505(b)(2) NDA must certify, for each patent listed in the Orange Book for the RLD that (1) no patent information on the drug product that is the subject of the application has been submitted to the FDA, (2) such patent has expired, (3) the listed patent will expire on a particular date and approval is sought after patent expiration, or (4) such patent is invalid or will not be infringed upon by the manufacture, use or sale of the drug product for which the application is submitted. An ANDA or 505(b)(2) applicant may also submit a statement that it intends to carve-out from the labeling of its product an RLD's use that is protected by exclusivity or a method of use patent. The fourth certification described above is known as a Paragraph IV certification. A notice of the Paragraph IV certification must be provided to each owner of the patent that is the subject of the certification and to the reference NDA holder. The reference NDA holder and patent owners may initiate a patent infringement lawsuit in response to the Paragraph IV notice. Filing such a lawsuit within 45 days of the receipt of the Paragraph IV certification notice prevents the FDA from approving the ANDA or 505(b)(2) NDA until the earlier of 30 months, expiration of the patent, settlement of the lawsuit, or a decision in the infringement case that is favorable to the ANDA or 505(b)(2) applicant. The ANDA or 505(b)(2) application also will not receive final approval until any applicable non-patent exclusivity listed in the Orange Book for the RLD has expired. We intend to defend vigorously any patents for our approved products.

Regulation Outside of the United States

In addition to regulations in the U.S., we are subject to regulations of other countries governing clinical trials and the manufacturing, commercial sales and distribution of our products outside of the U.S. Whether or not we obtain FDA approval for a product, we must obtain approval by the comparable regulatory authorities of countries outside of the U.S. before we can commence clinical trials in such countries and approval of the regulators of such countries or economic areas, such as the EU, 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.

The way clinical trials are conducted in the EU will undergo a major change when Regulation (EU) 536/2014 governing clinical trials in the EU, repealing the existing Directive 2001/20/EC comes into application in 2019. This regulation harmonizes the assessment and supervision processes for clinical trials throughout the EU, via an EU portal and database. The EMA will set up and maintain the portal and database, in collaboration with the Member States and the EC.

Under EU regulatory systems, a company may submit MAAs either under centralized or decentralized procedure. Under the centralized procedure, MAAs are submitted to the EMA for scientific review by the Committee for Medicinal

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Products for Human Use (CHMP) so that an opinion is issued on product approvability. The opinion is considered by the EC which is responsible for granting the centralized marketing authorization in the form of a binding EC decision. If the application is approved, the EC grants a single marketing authorization that is valid for all EU member states as well as Iceland, Liechtenstein and Norway, collectively the European Economic Area (EEA). The decentralized and mutual recognition procedures, as well as national authorization procedure are available for products for which the centralized procedure is not compulsory. The mutual recognition procedure provides for the EU member states selected by the applicant to mutually recognize a national marketing authorization that has already been granted by the competent authority of another member state, referred to as the Reference Member State (RMS). The decentralized procedure is used when the product in question has yet to be granted a marketing authorization in any member state. Under this procedure the applicant can select the member state that will act as the RMS. In both the mutual recognition and decentralized procedures, the RMS reviews the application and submits its assessment of the application to the member states where marketing authorizations are being sought, referred to as Concerned Member States. Within 90 days of receiving the application and assessment report, each Concerned Member State must decide whether to recognize the RMS assessment. If a member state does not agree with the assessment, and the disputed points cannot be resolved the matter is eventually referred to the Coordination Group on Mutual Recognition and Decentralised procedures in the first instance to reach an agreement and failing to reach such an agreement, a referral to the EMA and the CHMP for arbitration that will result in an opinion to form the basis of a decision to be issued by the EC binding on all member states. If the application is successful during the decentralized or mutual recognition procedure, national marketing authorizations will be granted by the competent authorities in each of the member states chosen by the applicant.

Conditional marketing authorizations may be granted in the centralized procedure for a limited number of medicinal products for human use referenced in EU law applicable to conditional marketing authorizations where the clinical dataset is not comprehensive, if (1) the risk-benefit balance of the product is positive, (2) it is likely that the applicant will be in a position to provide the required comprehensive clinical trial data, (3) unmet medical needs will be fulfilled and (4) the benefit to public health of the immediate availability on the market of the medicinal product outweighs the risk inherent in the fact that additional data are still required. Specific obligations, such as the completion of ongoing or new studies and obligations relating to the collection of pharmacovigilance data, may be amongst the conditions stipulated in the marketing authorization.

As in the U.S., we may apply for designation of a product as an Orphan drug for the treatment of a specific indication in the EU before the application for marketing authorization is made. In the EU orphan designation is available for products in development which are either: (a) intended for the diagnosis, prevention or treatment of life-threatening or chronically debilitating conditions affecting not more than 5 in 10,000 persons in the EU, or (b) intended for the diagnosis, prevention or treatment of a life-threatening, seriously debilitating or serious and chronic condition in the Community and when, without incentives, it is unlikely that sales of the drug in the EU would be sufficient to justify the necessary investment in developing the medicinal product. Additionally, the sponsor of an application for orphan drug designation must establish that there exists no satisfactory authorized method of diagnosis, prevention, or treatment of the condition or even if such treatment exists, the product will be of significant benefit to those affected by that condition.

Orphan drugs in the EU enjoy economic and marketing benefits, including up to ten years of market exclusivity for the approved indication unless another applicant for a similar medicinal product can show that its product is safer, more effective or otherwise clinically superior to the orphan-designated product. The period of market exclusivity may be reduced to six years if at the end of the fifth year it is established that the criteria for orphan designation are no longer met, including where it is shown that the product is sufficiently profitable not to justify maintenance of market exclusivity.

Healthcare Regulation

Federal and state healthcare laws, including fraud and abuse and health information privacy and security laws, also apply 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, but are not limited to: the federal Anti-Kickback Statute, which prohibits. among other

things, 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. Additionally, we are subject to state law equivalents of each of the above federal laws, which may be broader in scope and apply regardless of whether the payer is a federal healthcare program, and 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. For example, in June 2018, California Governor Jerry Brown signed the California Consumer Privacy Act of 2018 (CCPA), which takes effect on January 1, 2020 and will broadly define personal information, give California residents expanded privacy rights and protections and provide for civil penalties for violations and a private right of action for data breaches. There are similar legislative proposals being advanced in other states, as well as in Congress. 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 (HIPAA). Although we are not directly subject to HIPAA, we could be subject to criminal penalties if we obtain and/or disclose individually identifiable health information from a HIPAA-covered entity, including healthcare providers, 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.
Other countries also have, or are developing, laws governing the collection, use and transmission of personal information. International laws, such as the EU General Data Protection Regulation 2016/679 (GDPR) and Swiss Federal Act on Data Protection, regulate the processing of personal data within the EU and between countries in the EU and countries outside of the EU, including the U.S. On April 27, 2016, the EU legislature adopted the GDPR, which replaced the prior Directive 95/46/EC when it took effect on May 25, 2018, and it is directly applicable in all Member States. The GDPR applies to EU-based organizations engaged in the processing of personal data belonging to EU data subjects. The GDPR has an extra-territorial effect in the sense that it applies to a “controller” or “processor” who is not established in the EU and is engaged in processing of personal data of EU subjects. Furthermore, in October 2015, the Court of Justice of the EU declared the previous framework, the International Safe Harbor Privacy Principles (the Safe Harbor) invalid for data transfer between the U.S. and the EU. The Safe Harbor has now been replaced by the EU-U.S. Privacy Shield, a framework for transatlantic exchanges of personal data for commercial purposes between the EU and the U.S. in accordance with the principles of the GDPR. Accordingly, there may be an immediate impact on companies located in the U.S. as they devote resources to comply with these new obligations. The GDPR establishes a tiered approach to penalties for breach which enables the data protection authorities of the various Member States to impose fines for certain infringements, including the breach of requirements relating to international transfers or the basic principles for processing of personal data (such as conditions for obtaining consent from that individual whose data is being transferred). The severity of these fines may be up to the higher of 4% of annual worldwide revenue or €20 million.
In addition, the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act (the PPACA) created a federal requirement under the federal Open Payments program, that requires certain manufacturers to track and report to the Centers for Medicare and Medicaid Services annually certain payments and other transfers of value provided to physicians and teaching hospitals made in the previous calendar year. In addition, there are also an increasing number of state laws that require manufacturers to make reports to states on pricing and marketing information. 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 federal authorities.
Because our products are covered in the U.S. by the Medicaid programs, we have various obligations, including government price reporting and rebate requirements, which generally require our products be offered at substantial rebates/discounts to Medicaid and certain purchasers (including “covered entities” purchasing under the 340B Drug Discount Program). We are also required to discount such products to authorized users of the Federal Supply Schedule of the General Services Administration, under which additional laws and requirements apply. These programs require submission of pricing data and calculation of discounts and rebates pursuant to complex statutory formulas, as well as the entry into government procurement contracts governed by the Federal Acquisition Regulations, and the guidance

governing such calculations is not always clear. Compliance with such requirements can require significant investment in personnel, systems and resources, but failure to properly calculate prices, or offer required discounts or rebates could subject us to substantial penalties. Subject to the application in the EU of the Transparency Directive 89/105/EEC, which aims to ensure the transparency of measures adopted to control pricing and reimbursement, pricing and reimbursement in the EU/EEA is governed by national rules and policy and may vary from Member State to Member State.

Reimbursement

Sales of our approved products and any future products of ours will depend, in part, on the extent to which their costs will be covered by third-party payers, such as government health programs, commercial insurance and managed healthcare organizations. Patients may be less likely to use our products if coverage is not provided and reimbursement is inadequate to cover a significant portion of the cost of our products. In addition, although to date qualified patients who

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would not otherwise be able to afford our products have been able to receive financial support from us in some cases, and from independent patient support foundations in other cases, these programs have recently been subject to significant government scrutiny, and in the future these patients may no longer be able to use our products.

Third-party payers may limit coverage to specific drug products on an approved list, also known as a formulary, which might not include all of the FDA-approved drugs for a particular indication. Moreover, a third-party payer's decision to provide coverage for a drug product does not imply that an adequate reimbursement rate will be approved. Additionally, a third-party payer's decision to cover a particular drug product does not ensure that other payers will also provide coverage for the drug product, or will provide coverage at an adequate reimbursement rate.

In the U.S. and other potentially significant markets for our products, government authorities and third-party payers are increasingly attempting to limit or regulate the price of medical products and services, particularly for new and innovative products and therapies, which may result in lower average selling prices. In some cases, for example, third-party payers try to encourage the use of less expensive generic products through their prescription benefits coverage and reimbursement and co-pay policies. Further, the increased emphasis on managed healthcare in the U.S. and on country-specific and national pricing and reimbursement controls in the EU will put additional pressure on product pricing, reimbursement and usage, which may adversely affect our future product sales and results of operations. These pressures can arise from rules and practices of managed care groups, judicial decisions and governmental laws and regulations related to Medicare, Medicaid and healthcare reform, pharmaceutical reimbursement policies and pricing in general. Adoption of price controls and cost-containment measures, and adoption of more restrictive policies in jurisdictions with existing coverage and/or reimbursement controls and measures, could have a material adverse impact on our net product revenues and results of operations.

The U.S. and some foreign jurisdictions are considering proposals or have enacted legislative and regulatory changes to the healthcare system that could affect our ability to sell our products profitably. Among policy makers and payers in the U.S. and elsewhere, there is significant interest in promoting changes in healthcare systems with the stated goals of containing healthcare costs, improving quality and/or expanding access. There has been particular and increasing legislative and enforcement interest in the U.S. with respect to drug pricing practices, particularly with respect to drugs that have been subject to relatively large price increases over relatively short time periods. At the federal level, there have been several U.S. Congressional inquiries and proposed bills designed to, among other things, bring more transparency to drug pricing, review the relationship between pricing and manufacturer patient programs, and reform government program reimbursement methodologies for drugs. Also, the Trump administration's budget proposal for fiscal year 2019 contains drug price control measures that could be enacted during the 2019 budget process or in other future legislation, including measures to permit Medicare Part D plans to negotiate the price of certain drugs under Medicare Part B, to allow some states to negotiate drug prices under Medicaid, and to eliminate cost sharing for generic drugs for low-income patients. Further, in October 2018, the Centers for Medicare & Medicaid Services (CMS) proposed a rule that would require drug manufacturers to disclose drug prices in television advertisements. While any proposed measure will require authorization through additional legislation to become effective, Congress and the Trump administration have each indicated that they will continue to seek new legislative and/or administrative measures to control drug costs. At the state level, legislatures have increasingly passed legislation and implemented regulations designed to control pharmaceutical and biological product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, to encourage importation from other countries and bulk purchasing. With respect to drug pricing transparency, for example, in October 2017, California Governor Jerry Brown signed legislation known as SB-17, which requires, among other provisions, pharmaceutical manufacturers to provide notice of price increases above a defined threshold to certain purchasers and related reports to the government. SB-17 is currently subject to challenge, but in the meantime, manufacturers must comply with its requirements.

In the U.S., the pharmaceutical industry has already been significantly affected by major legislative initiatives, including, for example, the PPACA. Since January 2017, President Trump has signed two Executive Orders designed to delay the implementation of certain provisions of the PPACA or otherwise circumvent some of the requirements for health insurance mandated by the PPACA. Concurrently, Congress has considered legislation that would repeal or repeal and replace all or part of the PPACA. While Congress has not passed comprehensive repeal legislation, two

bills affecting the implementation of certain taxes under the PPACA recently have been enacted. The Tax Cuts and Jobs Act of 2017 includes a provision repealing, effective January 1, 2019, the tax-based shared responsibility payment imposed by the PPACA on certain individuals who fail to maintain qualifying health coverage for all or part of a year that is commonly referred to as the “individual mandate.” Additionally, on January 23, 2018, President Trump signed a continuing resolution on appropriations for fiscal year 2018 that delayed the implementation of certain PPACA-mandated fees, including the so-called “Cadillac” tax on certain high cost employer-sponsored insurance plans, the annual fee imposed on certain health insurance providers based on market share, and the medical device excise tax on non-exempt medical devices. Congress may continue to consider legislation to repeal and replace some or all elements of the PPACA, and in December 2018, a Texas U.S. District

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Court Judge ruled that the PPACA is unconstitutional in its entirety because of the repeal of the "individual mandate" that was part of the Tax Cuts and Jobs Act. Although that ruling is being appealed, we cannot predict the outcome of this litigation, including a possible decision by the United States Supreme Court, or whether other healthcare reform initiatives will continue to be pursued or adopted in the future. Further federal, state and foreign legislative and regulatory developments are likely, and we expect ongoing initiatives to increase pressure on drug pricing, which could have a negative impact on our revenue or sales of any products or future approved products.

Other legislative changes have also been proposed and adopted since the PPACA was enacted. For example, the Budget Control Act of 2011 resulted in aggregate reductions in Medicare payments to providers of up to 2% per fiscal year, starting in 2013, and the American Taxpayer Relief Act of 2012, among other things, reduced Medicare payments to several types of providers and increased the statute of limitations period for the government to recover overpayments to providers from three to five years. Further, in November 2018, CMS proposed a rule that would allow Medicare Part D and Medicare Advantage plans to limit coverage under certain defined circumstances for certain drugs, including cancer medicines, pursuant to exceptions to the existing "protected classes" policy. Such laws or regulations, and others that may affect our business that have been recently enacted or may in the future be enacted, may result in additional reductions in Medicare and other healthcare funding for our products. In the future, there will likely continue to be additional proposals relating to the reform of the U.S. healthcare system, some of which could further limit coverage and reimbursement of drug products, including our approved products and any future approved products. Any reduction in reimbursement from Medicare or other government programs may result in a similar reduction in payments from private payers. The implementation of cost containment measures or other healthcare reforms may prevent us from being able to generate revenue, attain profitability or commercialize our products.

In addition, in some non-U.S. jurisdictions, the proposed pricing for a drug must be approved before its cost may be funded within the respective national healthcare system. The requirements governing drug pricing vary widely from country to country. For example, EU member states may restrict the range of medicinal products for which their national healthcare systems provide reimbursement and may 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 profits the medicinal product generates for the company placing it 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 on cost-effectiveness grounds. Historically, products launched in countries in the EU do not follow the price structures of the U.S. and they 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 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, which may allow them to have a competitive advantage.

Competition for Cabozantinib

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

- efficacy, safety and reliability of cabozantinib;
- timing and scope of regulatory approval;
- the speed at which we develop cabozantinib for the treatment of additional tumor types beyond its approved indications;
- our ability to complete clinical development and obtain regulatory approvals for cabozantinib;
- our ability to manufacture and sell commercial quantities of cabozantinib product to the market;
- our ability to successfully commercialize cabozantinib and secure coverage and adequate reimbursement in approved indications;
- product acceptance by physicians and other health care providers;
-

the level of our collaboration partners' investments in the resources necessary to successfully commercialize cabozantinib in territories where it is approved outside of the U.S.;
- skills of our employees and our ability to recruit and retain skilled employees;
- protection of our intellectual property; and

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- 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 should they demonstrate suitable clinical evidence, any of these products may compete with cabozantinib. We believe our future success will depend upon our ability to maintain a competitive position with respect to technological advances and the shifting landscape of therapeutic strategy following the advent of immunotherapy. While we have adapted our development strategy for cabozantinib to address the fact that this approach to treating cancer with ICIs, or ICIs in combination with other therapeutic agents, has become highly prevalent in indications for which our products are approved, CABOMETYX may become less marketable if our clinical trials fail to show efficacy in comparison to competing ICI products or ICI product combinations. Furthermore, the complexities of such a strategy has and may continue to require collaboration with some of our competitors.

CABOMETYX - RCC: We believe the principal competition for CABOMETYX in advanced RCC includes: BMS' nivolumab; the combination of BMS's ipilimumab and nivolumab; Pfizer's axitinib, sunitinib and temsirolimus, each as single-agent therapies; Novartis' everolimus and pazopanib, each as single-agent therapies; Bayer's and Onyx Pharmaceuticals' (a wholly-owned subsidiary of Amgen) (Onyx's) sorafenib; Roche's bevacizumab; the combination of Eisai's lenvatinib and Novartis' everolimus; and Prometheus' aldesleukin. Additionally, there are a variety of therapies being developed for advanced RCC, including: the combination of Roche's bevacizumab and atezolizumab; the combination of Merck's pembrolizumab and Eisai's lenvatinib; the combination of Merck's pembrolizumab and Pfizer's axitinib; the combination of Pfizer's avelumab and axitinib; the combination of Calithera's CB-938 and Novartis' everolimus; AVEO Pharmaceutical's tivozanib; and generic versions of sorafenib, everolimus and sunitinib.

The competitive landscape for RCC is evolving rapidly, especially given the entrance of ICI combination therapies and potential entrance of ICI-TKI combination therapies into the RCC treatment landscape, particularly in the first-line setting. This will lead to new trends in prescribing and sequencing of certain drugs and combinations across different lines of therapy. It is therefore difficult to predict how these changes will affect sales of CABOMETYX during 2019 and going forward.

CABOMETYX - HCC: We believe the principal competition for CABOMETYX in previously treated HCC includes: Bayer's regorafenib; Bayer's and Onyx's sorafenib; BMS' nivolumab; Eisai's levantinib; and Merck's pembrolizumab. Additionally, there are a variety of therapies being developed for previously treated HCC, including: Eli Lilly's ramucirumab; and generic versions of sorafenib.

COMETRIQ: We believe that the principal competing anti-cancer therapy to COMETRIQ in progressive, metastatic MTC is Genzyme's vandetanib, which has been approved by the FDA and the EC for the treatment of symptomatic or progressive MTC in patients with unresectable, locally advanced, or metastatic disease. We believe that COMETRIQ also faces competition as a treatment for progressive, metastatic MTC from off-label use of certain treatments, including: Bayer's and Onyx's sorafenib; Pfizer's sunitinib; Takeda's ponatinib; Novartis' pazopanib; and Eisai's lenvatinib. Additionally, there are a variety of compounds being developed for MTC with early-stage clinical trials in progress, including: Blueprint Medicine Corporation's BLU-667 (for certain subsets of MTC patients); and Loxo Oncology, Inc.'s LOXO-292 (which was recently granted Breakthrough Therapy Designation by the FDA for the treatment of patients with RET-mutant MTC who require systemic therapy, have progressed following prior treatment and have no acceptable alternative treatment options).

Potential Cabozantinib Indications Beyond RCC, MTC and previously treated HCC: We have initiated COSMIC-311, a phase 3 pivotal trial evaluating cabozantinib in patients with DTC who have progressed after up to two prior VEGFR-targeted therapies, and COSMIC-312, a phase 3 pivotal trial evaluating the combination of cabozantinib and

atezolizumab in patients with previously untreated HCC. However, we face a rapidly evolving treatment landscape for the treatment of both of these indications, as other therapies have recently received regulatory approval or are in advanced stages of clinical development, which may impair the relative value of CABOMETYX or a combination of CABOMETYX with an ICI in DTC and previously untreated HCC, respectively. Should cabozantinib be approved for this indication of DTC, we believe its principal competition may include: Bayer's and Onyx's sorafenib; and Eisai's lenvatinib. Should the combination of cabozantinib and atezolizumab be approved for the treatment of patients with previously untreated advanced HCC, we believe its principal competition may include: Eisai's levantinib; Bayer's and Onyx's sorafenib; BMS's nivolumab; the combination of Merck's pembrolizumab and Eisai's lenvatinib; BeiGen and Celgene's tislelizumab; the combination of Roche's bevacizumab and atezolizumab;

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AstraZeneca's durvalumab; the combination of AstraZeneca's durvalumab and tremelimumab; and generic versions of sorafenib. Examples of potential competition for cabozantinib in other cancer indications include: other VEGF pathway inhibitors, including Genentech's bevacizumab and Pfizer's axitinib; other RET inhibitors including Eisai's lenvatinib and Takeda's ponatinib; other MET inhibitors, including Astra Zeneca's savolitinib, Pfizer's crizotinib and Mirati's glesatinib; and ICIs such as BMS's ipilimumab and nivolumab, Merck's pembrolizumab and Roche's atezolizumab.

Competition for Cobimetinib

We believe that cobimetinib's principal competition amongst targeted agents includes: the combination of Novartis' trametinib and dabrafenib; and the combination of Array's encorafenib and binimetinib. Within the class of ICIs, we believe that cobimetinib's principal competition includes: the combination of BMS's ipilimumab and nivolumab; and Merck's pembrolizumab. The second category, ICIs, are of particular competitive importance vis-a-vis cobimetinib in advanced melanoma as they are already FDA approved in melanoma patient populations that overlap with those that may be eligible for cobimetinib, they have been rapidly incorporated into the NCCN treatment guidelines, and they are viewed with a high degree of enthusiasm by physicians and key opinion leaders. Ongoing and future trials incorporating ICIs, including combination trials, may further impact usage of cobimetinib in melanoma and potentially in additional tumor types in which cobimetinib may ultimately gain approval.

Competition for Esaxerenone

We believe that esaxerenone's principal competition for the treatment of hypertension in Japan will be Bayer's MR antagonist, finerenone, if and when it is approved by the MHLW. Finerenone is still in development for this indication, and results from ongoing clinical studies are not expected during 2019.

Significant Customers

We operate as a single business segment and have operations solely in the U.S. During the year ended December 31, 2018, we derived 21% of our revenues from Ipsen, 13% of our revenues from Caremark L.L.C. and 12% of our revenues from affiliates of McKesson Corporation.

Patents and Proprietary Rights

We actively seek patent protection in the U.S., Europe 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. We own all global patents associated with cabozantinib, cobimetinib and our other drug candidates referenced below.

Cabozantinib

Cabozantinib is covered by 10 issued patents in the U.S., building from U.S. Pat. No. 7,579,473, for the composition-of-matter of cabozantinib and pharmaceutical compositions thereof. This composition of matter patent would expire in September 2024, but we have been granted a patent term extension to extend the term to August 2026. The following table describes the US patents that cover our marketed cabozantinib products, and which are listed in the Orange Book. Except as otherwise noted, the stated expiration dates include any patent term extensions already granted. In addition to the composition of matter patent referenced above, the table includes patents directed to, among other things, particular salts, polymorphs, formulations, or use of the compound in the treatment of specified diseases or conditions. We continue to pursue additional patents and patent term extensions in the U.S. and other territories covering various aspects of our cabozantinib products that may, if issued, extend exclusivity beyond the expiration of the patents listed in the table.

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Product	Patent No.	General Subject Matter	Patent Expiration
CABOMETYX	7,579,473	Composition of matter	2026
	8,497,284	Methods of treatment	2024
	8,877,776	Salt and polymorphic forms of cabozantinib	2030
	9,724,342	Formulations of cabozantinib	2033
	10,039,757	Methods of treatment	2031
	10,034,873	Methods of treatment	2031[(1)]
COMETRIQ	7,579,473	Composition of matter	2026
	8,877,776	Salt and polymorphic forms of cabozantinib	2030
	9,717,720	Formulations of cabozantinib	2032

(1) Filed for inclusion in the Orange Book for patients with HCC who have been previously treated with sorafenib

In Europe, cabozantinib is protected by issued patents covering the composition-of-matter and methods of use. The issued patent would expire in September 2024, but we have applied for and either have obtained, or expect to obtain Supplementary Protection Certificates in Europe to extend the term to 2029. In addition to the composition of matter patent, the table below includes later-expiring patents directed to the commercial product, including, particular salts, polymorphs, formulations, or use of the compound in the treatment of specified diseases or conditions.

Product	Patent No.	General Subject Matter	Patent Expiration
CABOMETYX	2213661	Composition of matter and methods of treatment	2029
	2387563	Salt and polymorphic forms of cabozantinib and methods of treatment	2030
COMETRIQ	2213661	Composition of matter and methods of treatment	2029
	2387563	Salt and polymorphic forms of cabozantinib and methods of treatment	2030

Similarly in Japan, cabozantinib is protected by an issued patent covering the composition-of-matter, and salts thereof, as well as pharmaceutical compositions and related methods of use. We intend to apply for patent term extension in Japan to extend the term to 2029. Foreign counterparts of the issued U.S. and European composition of matter patents have been issued in Australia and Canada, and are anticipated to expire in 2024. We have other filed patent applications and issued patents in the U.S. and other selected countries covering certain synthetic methods, salts, polymorphs, formulations, and combinations of cabozantinib that, if issued, are anticipated to expire as late as 2035. Outside the U.S. and Japan, cabozantinib is licensed to Ipsen; in Japan cabozantinib is licensed to Takeda, each in accordance with the respective collaboration agreements. A discussion of risks and uncertainties that may affect our patent position and other proprietary rights is set forth in “Risk Factors,” contained in Part I, Item 1A of this Annual Report on Form 10-K.

Cobimetinib

Cobimetinib is covered by three issued patents in the U.S., including U.S. Pat. No 7,803,839 for the composition of matter of cobimetinib and pharmaceutical compositions thereof. U.S. Pat. No 7,803,839 would normally expire in February 2027, but we have applied for a patent term extension to extend the term to November 2029. Cobimetinib is also covered by an issued patent in Europe (covering the composition-of-matter of cobimetinib and certain methods of use), which would normally expire in October 2026, but we have applied for and are obtaining Supplementary Protection Certificates to extend the term to November 2030. Foreign counterparts of the issued U.S. and European patents are issued or pending in Australia, Canada, Japan and selected other foreign countries. We have filed patent applications in the U.S. and other selected countries covering certain salts and polymorphs of cobimetinib that, if issued, are anticipated to expire in approximately 2036. We have filed patent applications in the U.S. and other selected countries covering certain synthetic methods related to making cobimetinib that, if issued, are anticipated to expire in approximately 2033. Cobimetinib is licensed to Genentech in the U.S. and to Roche outside of the U.S.

Other Drug Candidates

We also have pending patent applications, and will continue to file new patent applications, in the U.S., Europe and other selected countries covering the composition-of-matter of our other drug candidates in clinical and/or preclinical

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development. We intend to describe these patents in more detail once it is determined that a particular drug candidate warrants further development.

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.

We require our scientific personnel to maintain laboratory notebooks and other research records in accordance with our policies, which are designed to strengthen and support our intellectual property protection. In addition to our patented intellectual property, we also rely on trade secrets and other proprietary information, especially when we do not believe that patent protection is appropriate or can be obtained. We also require all of our employees and consultants, outside scientific collaborators, sponsored researchers and other advisors who receive proprietary information from us to execute confidentiality agreements upon the commencement of employment or consulting relationships with us. These agreements provide that all proprietary information developed or made known to the individual during the course of the individual's relationship with us is to be kept confidential and not disclosed to third parties except in specific circumstances. Furthermore, our agreements with employees and, in most circumstances, our agreements with consultants, outside scientific collaborators, sponsored researchers and other advisors expressly provide that all inventions, concepts, developments, copyrights, trademarks or other intellectual property developed by an employee during the employment period, or developed by a service provider during the service period or utilizing our proprietary drugs or information, shall be our exclusive property. There can be no assurance, however, that these agreements will provide meaningful protection or adequate remedies for our trade secrets in the event of unauthorized use or disclosure of such information.

Employees

As of December 31, 2018, we had 484 full-time equivalent employees, all of which are located in the U.S. None of our employees are represented by a labor union, and we consider our employee relations to be good.

Corporate Information

We were incorporated in Delaware in November 1994 as Exelixis Pharmaceuticals, Inc. and changed our name to Exelixis, Inc. in February 2000. Our principal executive offices are located at 1851 Harbor Bay Parkway, Alameda, California 94502. Our telephone number is (650) 837-7000. 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 (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. 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, 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 currently 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 occur, our business could be harmed.

Risks Related to Our Business and Industry

Our ability to grow our company is critically dependent upon the commercial success of CABOMETYX in its approved indications and the further clinical development, regulatory approval and commercial success of cabozantinib in additional indications.

Our mission is to maximize the clinical and commercial potential of cabozantinib, and to position us for future growth through our discovery efforts and expansion of our development pipeline. We anticipate that for the foreseeable future our ability to maintain or meaningfully increase unrestricted cash flow to fund our commercial operations and our development and discovery programs is dependent upon the continued successful commercialization of CABOMETYX for the treatment of RCC and HCC, in each case in territories where it has been approved and

according to the terms of such regulatory approvals. The commercial opportunity for CABOMETYX as a treatment for RCC and HCC remains subject to a

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variety of factors, most importantly, CABOMETYX's perceived benefit/risk profile as compared to the benefit/risk profiles of other treatments available or currently in development for these conditions. If revenue from CABOMETYX decreases or remains flat, or if we fail to achieve anticipated product royalties and collaboration milestones, we may need to reduce our operating expenses, access other sources of cash or otherwise modify our business plans, which could have a material adverse impact on our business, financial condition and results of operations. Furthermore, as a consequence of our collaboration agreements with Ipsen and Takeda, we rely heavily upon their regulatory, commercial, medical affairs, market access and other expertise and resources for commercialization of CABOMETYX in their respective territories outside of the U.S. We cannot control the amount and timing of resources that our collaborators dedicate to the commercialization of CABOMETYX, or to its marketing and distribution, and our ability to generate revenues from the commercialization of CABOMETYX by our collaborators depends on their ability to obtain and maintain regulatory approvals for, achieve market acceptance of, and to otherwise effectively market, CABOMETYX in its approved indications in their respective territories. Further, foreign sales of CABOMETYX by our collaborators could be adversely affected by the imposition of governmental controls, political and economic instability, trade restrictions or barriers and changes in tariffs, including as a result of the United Kingdom's (UK) pending withdrawal from the EU (commonly referred to as "Brexit"), escalating global trade and political tensions, or otherwise. If our collaborators are unable to, or do not invest the resources necessary to successfully commercialize CABOMETYX in the EU and other international territories where it has been approved, this could reduce the amount of revenue we are due to receive under these collaboration agreements, thus resulting in harm to our business and operations.

CABOMETYX has been approved for the treatment of advanced RCC in the U.S., the EU and other territories, and for the treatment of previously treated HCC in the U.S. and the EU. Following these approvals, our ability to grow our company remains contingent upon, among other things, further success in the clinical development, regulatory approval and market acceptance of cabozantinib, the active pharmaceutical ingredient in CABOMETYX, in potential additional indications. We cannot be certain that the clinical trials we and our collaboration partners are currently conducting, or may conduct in the future, will demonstrate adequate safety and efficacy in these additional indications to receive regulatory approval. Should we prove unsuccessful in advancing the further clinical development and commercialization of cabozantinib beyond its currently approved indications, we may be unable to execute our business plans, which could have a material adverse impact on our business, financial condition and results of operations. Even if we and our partners receive the required regulatory approvals to market cabozantinib for any additional indications or in additional territories, we and our partners may not be able to effectively commercialize CABOMETYX in these additional indications or territories.

Our ability to grow revenues from sales of CABOMETYX will depend upon the degree of market acceptance among physicians, patients, health care payers, and the medical community.

Our ability to increase revenues from sales of CABOMETYX for its approved indications is, and if approved for additional indications will be, highly dependent upon the extent of market acceptance of CABOMETYX among physicians, patients, government health care payers such as Medicare and Medicaid, commercial health care plans and the medical community. If CABOMETYX does not continue to be prescribed broadly for the treatment of advanced RCC and achieve market acceptance for the treatment of previously treated HCC, we may not be able to grow product revenues. The degree of market acceptance of CABOMETYX will depend upon a number of factors, including:

- the effectiveness, or perceived effectiveness, of CABOMETYX in comparison to competing products;
- the safety of CABOMETYX, including the existence of serious side effects of CABOMETYX and their severity in comparison to those of competing products;
- CABOMETYX's relative convenience and ease of administration;
- potential unexpected results connected with analysis of data from future or ongoing clinical trials of cabozantinib;
- the timing of CABOMETYX label expansions for additional indications, if any, relative to competitive treatments;
- the price of CABOMETYX relative to competitive therapies;
- price increases taken by us and the impact on the net sales price of CABOMETYX as a result of any new laws, regulations or other government initiatives affecting pharmaceutical pricing;
- the strength of CABOMETYX sales efforts, marketing, market access and product distribution support;

- the sufficiency of commercial and government health insurance coverage and adequacy of reimbursement for CABOMETYX; and
- our ability to enforce our intellectual property rights with respect to CABOMETYX.

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Further, in the event that any of these or other factors cause market acceptance of CABOMETYX to decrease, this could negatively impact our revenues, which could have a material adverse impact on our business, financial condition and results of operations.

Our competitors may develop products and technologies that impair the relative value of our marketed products and any future product candidates.

The pharmaceutical, biopharmaceutical and biotechnology industries are competitive, highly diversified and are characterized by rapid technological change, particularly in the area of novel oncology therapies. 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, which may allow them to have a competitive advantage. Further, our competitors may be more effective at using their technologies to develop commercial products. As a result, our competitors may be able to more easily develop products that would render our products, and those of our collaborators, obsolete and noncompetitive. There may also be drug candidates that we are not aware of at an earlier stage of development that may compete with our marketed products and product candidates. We face, and will continue to face, intense competition from biotechnology, biopharmaceutical and pharmaceutical companies, as well as academic research institutions, clinical reference laboratories and government agencies that are pursuing research activities similar to ours. Delays in the development of cabozantinib for the treatment of additional tumor types, for example, could allow our competitors to bring products to market before us.

Specifically, the indications for which CABOMETYX is approved are highly competitive. Several novel therapies and combinations of therapies have been approved, are in advanced stages of clinical development or are under expedited regulatory review in these indications, and these other therapies are currently competing or are expected to compete with CABOMETYX. We believe our future success will depend upon our ability to maintain a competitive position with respect to technological advances and the shifting landscape of therapeutic strategy following the advent of immunotherapy. While we have adapted our development strategy for cabozantinib to address the fact that this approach to treating cancer with ICIs in combination with other therapeutic agents has become highly prevalent in indications for which our products are approved, we cannot ensure that our clinical trials will show efficacy in comparison to competing products or product combinations. Furthermore, the complexities of such a development strategy has and may continue to require collaboration with some of our competitors.

We also may face competition from manufacturers of generic versions of our marketed products, and both Congress and the FDA are seeking to promote generic competition, including through proposals that may limit or reduce the term for patent exclusivity or regulatory exclusivity for branded products. Such generic competition often results in very significant decreases in the overall sales or prices at which branded products can be sold.

If we are unable to maintain or scale adequate sales, marketing, market access and product distribution capabilities for our products or enter into or maintain agreements with third parties to do so, we may be unable to maximize product revenues, which could have a material adverse impact on our business, financial condition and results of operations.

Maintaining our sales, marketing, market access and product distribution capabilities requires significant resources, and there are numerous risks involved with managing such a commercial organization, including our potential inability to successfully recruit, train, retain and incentivize adequate numbers of qualified and effective sales and marketing personnel. We are competing for talent with numerous commercial-stage oncology-focused biotech companies seeking to build out their commercial organizations, as well as other large pharmaceutical organizations that have extensive, well-funded, and more experienced sales and marketing operations, and we may be unable to maintain or adequately scale our commercial organization as a result of such competition. If we cannot maintain effective sales, marketing, market access and product distribution capabilities, we may be unable to maximize the commercial potential of CABOMETYX and COMETRIQ in their approved indications. Also, to the extent that the commercial opportunities for CABOMETYX grow over time, we may not properly judge the requisite size and experience of our current commercialization teams or the level of distribution necessary to market and sell CABOMETYX successfully in multiple indications. If we are unable to maintain or scale our organization appropriately, we may not be able to maximize product revenues, which could have a material adverse impact on our business, financial condition and results of operations.

Our ability to successfully commercialize our products will depend, in part, on the extent to which we are able to adequately distribute the products to eligible patients. We currently rely on third-party providers to handle storage and distribution for our commercial supplies of both CABOMETYX and COMETRIQ in the U.S. Furthermore, we rely on our

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collaboration partners for ongoing and further commercialization and distribution of CABOMETYX and COMETRIQ in their respective territories outside of the U.S., as well as for access and distribution activities for the approved products under named patient use programs (or similar programs) with the effect of introducing earlier patient access to CABOMETYX and COMETRIQ.

Our current and anticipated future dependence upon the activities, support, and legal and regulatory compliance of third parties may adversely affect our ability to supply CABOMETYX and COMETRIQ to the marketplace on a timely and competitive basis. These third parties may not provide services in the time required 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. If we are unable to contract for these third-party services related to the distribution of CABOMETYX and COMETRIQ on acceptable terms, our commercialization efforts and those of our collaboration partners may be delayed or otherwise adversely affected, which could have a material adverse impact on our business, financial condition and results of operations.

If we are unable to maintain or obtain for our products both sufficient health insurance coverage and adequate reimbursement from third-party payers, our business will suffer.

Our ability to commercialize our products successfully is highly dependent on the extent to which health insurance coverage and adequate reimbursement is, and will be, available from third-party payers, including governmental payers, such as Medicare and Medicaid, and private health insurers. Patients may not be capable of paying for CABOMETYX or COMETRIQ themselves and may rely on third-party payers to pay for, or subsidize, the costs of their medications, among other medical costs. If third-party payers do not provide coverage or adequate reimbursement for CABOMETYX or COMETRIQ, our revenues and results of operations will suffer. In addition, even if third-party payers provide some coverage or reimbursement for CABOMETYX or COMETRIQ, the availability of such coverage or reimbursement for prescription drugs under private health insurance and managed care plans, which often varies based on the type of contract or plan purchased, may not be sufficient for patients to afford CABOMETYX or COMETRIQ. Third-party payers continue to scrutinize and manage the prices charged for pharmaceutical products and services, and many also limit reimbursement for newly-approved products and indications.

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

We are subject to certain healthcare laws and regulations and enforcement by the federal government and the states in which we conduct our business. Should our compliance controls prove ineffective at preventing or mitigating the risk and impact of improper conduct or inaccurate reporting, the laws that may affect our ability to operate include, without limitation:

- the federal Anti-Kickback Statute (AKS), which governs our business activities, including our marketing practices, medical educational programs, pricing policies, and relationships with healthcare providers or other entities. The AKS has been broadly interpreted to apply to manufacturer arrangements with prescribers, purchasers and formulary managers, among others. Among other things, this statute prohibits persons and entities from knowingly and willfully soliciting, receiving, offering or paying remuneration, directly or indirectly, in exchange for or to induce either the referral of an individual for, or the purchase, order or recommendation of, any good or service for which payment may be made under federal healthcare programs such as the Medicare and Medicaid programs. Remuneration is not defined in the AKS and has been broadly interpreted to include anything of value, including for example, gifts, discounts, coupons, the furnishing of supplies or equipment, credit arrangements, payments of cash, waivers of payments, ownership interests, value-added services to customers, and providing anything at less than its fair market value;
- the FDCA and its implementing regulations, which prohibit, among other things, the introduction or delivery for introduction into interstate commerce of any drug that is adulterated or misbranded;
- federal civil and criminal false claims laws, including the civil False Claims Act, 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, or making a

false statement to avoid, decrease or conceal an obligation to pay money to the federal government;

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

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- HIPAA and its implementing regulations, which impose certain requirements relating to the privacy, security and transmission of individually identifiable health information on covered entities and business associates that access such information on behalf of a covered entity;
- state law equivalents of each of the above federal laws, such as anti-kickback and false claims laws, which may apply to items or services reimbursed by any third-party payer, including commercial insurers, and state laws governing the privacy and security of health information in certain circumstances, many of which differ from each other in significant ways and may not have the same effect, thus complicating compliance efforts;
- the PPACA Open Payments program created under the Physician Payments Sunshine Act and its implementing regulations, which requires certain manufacturers of drugs, devices, biologics and medical supplies that are reimbursable under Medicare, Medicaid, or the Children's Health Insurance Program, with specific exceptions, to report annually to the government information related to certain payments and other transfers of value to physicians and teaching hospitals, as well as ownership and investment interests held by physicians and their immediate family members;
- state laws and regulations that require drug manufacturers to file reports relating to pricing and marketing information, which requires tracking gifts and other remuneration and items of value provided to healthcare professionals and entities, as well as state and local laws requiring the registration of pharmaceutical sales representatives;
- 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) and its foreign equivalents;
- federal and state consumer protection and unfair competition laws, which broadly regulate marketplace activities and activities that potentially harm consumers; and
- federal, state and municipal pharmaceutical price and price reporting laws, both existing (e.g., California's SB-17) and under consideration, which require or propose to require us to provide notice of price increases and/or file complex ancillary reports concerning prices and pricing and discount practices. The legal and regulatory landscape, and associated compliance obligations imposed on pharmaceutical companies, may increase general and administrative costs, cause revenue fluctuations due to speculative buying practices by purchasers, or diminish our revenues as a result of the imposition of caps on pricing and price increases.

These federal and state healthcare fraud and abuse laws, FDA rules and regulations, as well as false claims laws, including the civil False Claims Act, govern certain marketing practices, including off-label promotion. If our operations are found to be in violation of any of the laws described above or any other governmental regulations that apply to us, we, or our officers or employees, may be subject to penalties, including administrative civil and criminal penalties, damages, fines, regulatory penalties, the curtailment or restructuring of our operations, exclusion from participation in Medicare, Medicaid and other federal and state healthcare programs, reputational harm, additional reporting requirements and oversight if we become subject to a corporate integrity agreement or similar agreement, any of which would adversely affect our ability to sell our products and operate our business and also adversely affect our financial results. Of particular concern are suits filed under the civil False Claims Act, known as "qui tam" actions, which can be brought by any individual on behalf of the government. These individuals, commonly known as relators or "whistleblowers," may potentially then share in amounts paid by the entity to the government in fines or settlement. The filing of qui tam actions has caused a number of pharmaceutical, medical device and other healthcare companies to have to defend civil False Claims Act actions. When an entity is determined to have violated the civil False Claims Act, it may be required to pay up to three times the actual damages sustained by the government, plus civil penalties for each separate false claim. Defending against any such actions can be costly, time-consuming and may require significant financial and personnel resources. Therefore, even if we are successful in defending against any such actions that may be brought against us, our business may be impaired.

Current healthcare laws and regulations and future legislative or regulatory reforms to the healthcare system may affect our ability to commercialize our marketed products profitably.

The U.S. and some foreign jurisdictions are considering or have enacted a number of legislative and regulatory proposals to change the healthcare system in ways that could affect our ability to continue to commercialize CABOMETYX and COMETRIQ profitably. Among policy makers and payers in the U.S. and elsewhere, there is

significant interest in promoting changes in healthcare systems with the stated goals of containing healthcare costs, improving quality and/or expanding access. In the U.S., the pharmaceutical industry has been a particular focus of these efforts and has been significantly affected by major legislative initiatives.

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Specifically, we may face uncertainties as a result of executive, legislative and administrative efforts to repeal, substantially modify or invalidate some or all of the provisions of the PPACA. On December 14, 2018, a Texas U.S. District Court Judge ruled that the PPACA is unconstitutional in its entirety because the "individual mandate" was repealed by Congress as part of the Tax Cuts and Jobs Act of 2017. While the Texas District Court Judge, as well as the Trump Administration and CMS, have stated that the ruling will have no immediate effect pending an appeal of the decision, it is unclear how this decision, subsequent appeals and other efforts to repeal and replace the PPACA will impact the PPACA. There is no assurance that the PPACA, as currently enacted or as amended in the future, will not have a material adverse impact on our business financial condition and results of operations, and we cannot predict how future federal or state legislative or administrative changes relating to healthcare reform will affect our business.

The Trump Administration has also indicated an intention to regulate prescription drug pricing, and recent Congressional hearings have brought increased public attention to the costs of prescription drugs. These actions and the uncertainty about the future of the PPACA and healthcare laws may put downward pressure on pharmaceutical pricing and increase our regulatory burdens and operating costs.

In August 2017, President Trump signed the FDA Reauthorization Act of 2017, which will reauthorize the FDA user fee programs for prescription drugs, generic drugs, medical devices, and biosimilars, under which manufacturers of such products partially pay for the FDA's pre-market review of their product candidates. The legislation includes, inter alia, measures to expedite the development and approval of generic products, where generic competition is lacking even in the absence of exclusivities or listed patents. The FDA has also released a Drug Competition Action Plan, which proposes actions to broaden access to generic drugs and lower consumers' health care costs by, among other things, improving the efficiency of the generic drug approval process and supporting the development of complex generic drugs, and the FDA has taken steps to implement this plan. Moreover, both Congress and the FDA are considering various legislative and regulatory proposals that would limit or reduce the term for patent exclusivity or regulatory exclusivity in the biopharmaceutical industry. While we cannot currently predict the specific outcome or impact on our business of such regulatory actions or legislation, they do have the potential to facilitate the development and future approval of generic versions of our products or otherwise limit or reduce the term for our market exclusivity, which could result in very significant decreases in the overall sales or prices of our marketed products and materially harm our business and financial condition.

As a result of the overall trend towards cost-effectiveness criteria and managed healthcare in the U.S., third-party payers are increasingly attempting to contain healthcare costs by limiting both coverage and the level of reimbursement of new drugs. Insurers also continue to pursue means of contracting for pharmaceutical "value" or "outcomes." These entities could refuse or limit coverage for CABOMETYX and COMETRIQ, such as by using tiered reimbursement or pressing for new forms of value-based contracting, which would adversely affect demand for CABOMETYX and COMETRIQ. They may also refuse to provide coverage for uses of CABOMETYX and COMETRIQ for medical indications other than those for which the FDA has granted market approval. As a result, significant uncertainty exists as to whether and how much third-party payers will cover newly approved drugs, which in turn will put pressure on the pricing of drugs. Due to the volatility in the current economic and market dynamics, we are unable to predict the impact of any unforeseen or unknown legislative, regulatory, third-party payer or policy actions, which may include cost containment and healthcare reform measures. These policy actions could have a material adverse impact on our business, financial condition and results of operations.

Pricing for pharmaceutical products has come under increasing scrutiny by governments, legislative bodies and enforcement agencies. These activities may result in actions that have the effect of reducing our revenue or harming our business or reputation.

Many companies in our industry have received a governmental request for documents and information relating to drug pricing and patient support programs. Requests could originate in various forms, including through a Congressional inquiry (e.g., from the U.S. Senate Finance Committee) or a subpoena from the U.S. Department of Justice. We could receive a similar request, which would require us to incur significant expense and result in distraction for our management team. Additionally, to the extent there are findings, or even allegations, of improper conduct on the part of the company, these findings could further harm our business, reputation and/or prospects. It is possible that these inquiries could result in: negative publicity or other negative actions that could harm our reputation; changes in our

product pricing and distribution strategies; reduced demand for our approved products; and/or reduced reimbursement of approved products, including by federal health care programs such as Medicare and Medicaid and state health care programs.

Specifically, there have been several recent U.S. Congressional inquiries and proposed and enacted federal legislation designed to, among other things, bring more transparency to drug pricing (including requirements for pharmaceutical manufacturers to report price increases and provide a public justification for these increases if they exceed certain benchmarks), review the relationship between pricing and manufacturer patient programs, reduce the price of drugs

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under Medicare, reform government program reimbursement methodologies for drugs, and facilitate value-based arrangements between manufacturers and payers. Also, the Trump Administration's budget proposal for fiscal year 2019 contains drug price control measures that could be enacted during the 2019 budget process or in other future legislation, including measures to permit Medicare Part D plans to negotiate the price of certain drugs under Medicare Part B, to allow some states to negotiate drug prices under Medicaid, and to eliminate cost sharing for generic drugs for low-income patients. While any proposed measures will require authorization through additional legislation to become effective, both Congress and the Trump Administration have indicated that it will continue to seek new legislative and/or administrative measures to control drug costs. For example, in October 2018, CMS proposed a rule that would require drug manufacturers to disclose drug prices in television advertisements, and in November 2018, CMS proposed a rule that would allow Medicare Part D and Medicare Advantage plans to limit coverage under certain defined circumstances for certain drugs, including cancer medicines, pursuant to exceptions to the existing "protected classes" policy. In addition, the U.S. Department of Health and Human Services (HHS) Office of Inspector General has solicited input for proposed rulemaking related to the potential addition of "safe harbor" regulations for the AKS. This solicitation aims, among other things, at changes to pharmaceutical contracting and discounting (including potentially encouraging value-based contracting). We cannot know what form any final regulations promulgated by CMS or the HHS Office of Inspector General might look like or how they could affect our business.

At the state level, legislatures have increasingly passed legislation and implemented regulations designed to control pharmaceutical and biological product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, to encourage importation from other countries and bulk purchasing, including the National Medicaid Pooling Initiative. With respect to drug pricing transparency, for example, in October 2017, California Governor Jerry Brown signed SB-17, which requires, among other provisions, pharmaceutical manufacturers to provide notice of price increases above a defined threshold to certain purchasers and related reports to the government. SB-17 is currently subject to challenge, but in the meantime, manufacturers must comply with its requirements. We do not know what form legislative proposals concerning drug prices may take in other states or how they would affect us. It is possible that these laws would encourage federal and state healthcare programs to reduce the amount of reimbursements they provide for prescription drugs, and any reduction in reimbursement from these government healthcare programs may result in a similar reduction in payments from private payers. We also believe that pricing transparency requirements, such as the requirement for us, in certain circumstances, to provide lengthy notices of price increases to purchasers, may influence customer ordering patterns for CABOMETYX and COMETRIQ, and that this, in turn, may increase the volatility of our revenues as a reflection of changes in inventory volumes. Therefore, the implementation of these cost cost-containment measures or other healthcare reforms may result in fluctuations in our results of operations and limit our ability to generate product revenue or commercialize our current products and/or those for which we may receive regulatory approval in the future.

Further, in some foreign countries, particularly in the EU, the pricing and reimbursement of prescription pharmaceuticals is subject to governmental control under the respective national health system. In these EU countries, pricing and reimbursement negotiations with governmental authorities or payers can take six to twelve months or longer after the initial marketing authorization is granted for a product, or after the marketing authorization for a new indication is granted. This can substantially delay broad availability of the product. To obtain reimbursement and/or pricing approval in some countries, our collaboration partner, Ipsen, may be required to conduct a study that seeks to establish the cost effectiveness of CABOMETYX compared with other available established therapies. The conduct of such a study could also result in delays in the commercialization of CABOMETYX. Additionally, cost-control initiatives, increasingly based on affordability, could decrease the price we and our collaboration partner, Ipsen, might establish for CABOMETYX, which would result in lower license revenues to us.

Enhanced governmental and private scrutiny over, or investigations or litigation involving, pharmaceutical manufacturer donations to patient assistance programs offered by charitable foundations may require us to modify our programs and could negatively impact our business practices, harm our reputation, divert the attention of management and increase our expenses.

To help patients afford our products, we have a patient assistance program and also occasionally make donations to independent charitable foundations that help financially needy patients. These types of programs designed to assist patients in affording pharmaceuticals have become the subject of scrutiny. In recent years, some pharmaceutical manufacturers were named in class action lawsuits challenging the legality of their patient assistance programs and support of independent charitable patient support foundations under a variety of federal and state laws. Our patient assistance program and support of independent charitable foundations could become the target of similar litigation. At least one insurer also has directed its network pharmacies to no longer accept manufacturer co-payment coupons for certain

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specialty drugs the insurer identified. In addition, certain state and federal enforcement authorities and members of Congress have initiated inquiries about co-pay assistance programs. Some state legislatures have also been considering proposals that would restrict or ban co-pay coupons.

In addition, there has been regulatory review and enhanced government scrutiny of donations by pharmaceutical companies to patient assistance programs operated by charitable foundations. The HHS Office of Inspector General has established specific guidelines permitting pharmaceutical manufacturers to make donations to charitable organizations who provide co-pay assistance to Medicare patients, provided that such organizations are bona fide charities, are entirely independent of and not controlled by the manufacturer, provide aid to applicants on a first-come basis according to consistent financial criteria, and do not link aid to use of a donor's product. If we are deemed not to have complied with laws or regulations in the operation of these programs, we could be subject to damages, fines, penalties or other criminal, civil or administrative sanctions or enforcement actions. Further, numerous organizations, including pharmaceutical manufacturers, have received subpoenas from the U.S. Department of Justice and other enforcement authorities seeking information related to their patient assistance programs and support, and certain of these organizations have entered into, or have otherwise agreed to, significant civil settlements with applicable enforcement authorities. In connection with these civil settlements, the U.S. government has and may in the future require the affected companies to enter into complex corporate integrity agreements that impose significant reporting and other requirements on those companies. We cannot ensure that our compliance controls, policies and procedures will be sufficient to protect against acts of our employees, business partners or vendors that may violate the laws or regulations of the jurisdictions in which we operate. Regardless of whether we have complied with the law, a government investigation could negatively impact our business practices, harm our reputation, divert the attention of management and increase our expenses.

We are subject to government regulations relating to privacy and data protection that have required us to modify certain of our policies and procedures with respect to the collection and processing of personal data, and future regulations may cause us to incur additional expenses or otherwise limit our ability to collect and process personal data. Failure to maintain compliance with these regulations could jeopardize certain business transactions and create additional liabilities for us.

The legislative and regulatory landscape for privacy and data protection in the U.S. 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 state security breach notification laws, state health information privacy laws and federal and state consumer protection laws, that govern the collection, use and disclosure of personal information. For example, in June 2018, California Governor Jerry Brown signed the CCPA, which takes effect on January 1, 2020 and will broadly define personal information, give California residents expanded privacy rights and protections and provide for civil penalties for violations and a private right of action for data breaches. There are similar legislative proposals being advanced in other states, as well as in Congress. In addition, most healthcare providers who are expected to prescribe our products, and from whom we obtain patient health information, are subject to privacy and security requirements under HIPAA. Although we are not directly subject to HIPAA, we could be subject to criminal penalties if we knowingly obtain individually identifiable health information from a HIPAA-covered entity in a manner that is not authorized or permitted by HIPAA. Other countries also have, or are developing, laws governing the collection, use and transmission of personal information. For example, the EU Data Privacy Directive (95/46/EC) and implementing legislation in the various national Member States of the EU was replaced on May 25, 2018 by the more restrictive GDPR, which now regulates the processing of personal data within the EU and between countries in the EU and countries outside of the EU, including the U.S. Switzerland is updating the Swiss Data Protection Act, and updates to data protection laws in other countries may occur in due course. In connection with these new laws, in particular the CCPA and GDPR, we have modified certain of our policies and procedures with respect to the collection and processing of personal data to the extent necessary given our operations and commensurate with similar companies in our industry. We will continue to review all future privacy and other regulations implemented pursuant to the CCPA, GDPR and other applicable laws to assess whether additional procedural safeguards are warranted, which may cause us to incur additional expenses or otherwise limit our ability to collect and process personal data. Failure to provide adequate privacy protections and maintain compliance with these laws and regulations could jeopardize certain

domestic and cross-border business transactions and create additional liabilities for us, including the imposition of sanctions or other penalties, as well as increase our cost of doing business.

If competitors use litigation and regulatory means to obtain approval for generic versions of our marketed products, our business will suffer.

Under the FDCA, the FDA can approve an ANDA for a generic version of a branded drug without the applicant undertaking the human clinical testing necessary to obtain approval to market a new drug. The FDA can also approve a

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505(b)(2) NDA that relies in whole or in part on the agency's findings of safety and/or effectiveness for a previously approved drug. Both the ANDA and 505(b)(2) processes are discussed in more detail above in "Item 1. Business" under the heading "Government Regulation-The Hatch-Waxman Act." In either case, if an ANDA or 505(b)(2) applicant submits an application referencing one of our drugs prior to the expiry of one or more listed patents for the drug, we may end up engaging in litigation with the potential generic competitor to protect our patent rights, which would require us to incur significant expense and result in distraction for our management team, and could also have an adverse impact on our stock price. Moreover, if any such ANDAs or 505(b)(2) NDAs were to be approved, and if our listed patents covering cabozantinib were held to be invalid (or if any such competing generic versions of cabozantinib were found not to infringe our patents), we would have generic competitors in the market, and the resulting generic competition would negatively affect our business, financial condition and results of operations. In particular, generic cabozantinib products would be significantly less costly than ours to bring to market. Companies that produce generic equivalents are generally able to offer their products at lower prices. Thus, regardless of the regulatory approval pathway, the introduction of a generic version of any of our marketed products could result in very significant decreases in the overall sales or prices of these marketed products and materially harm our business and financial condition.

Clinical testing of cabozantinib for new indications, or of new potential product candidates, is a lengthy, costly, complex and uncertain process and may fail to demonstrate safety and efficacy.

Clinical trials are inherently risky and may reveal that cabozantinib, despite its approval for certain indications, or a new potential product candidate, is ineffective or has an unacceptable safety profile with respect to an intended use. Such results may significantly decrease the likelihood of regulatory approval in a particular indication. Moreover, 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 and our other product candidates 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 in new indications, or of our other product candidates, including:

- lack of efficacy or a tolerable safety profile;
- negative or inconclusive clinical trial results may require us to conduct further testing or to abandon projects that we had expected to be promising;
- discovery or commercialization by our competitors of other compounds or therapies that show significantly improved safety or efficacy compared to cabozantinib or our other product candidates;
- our inability to identify and maintain a sufficient number of trial sites, many of which may already be engaged in other clinical trial programs;
- lower-than-anticipated patient registration or enrollment in our clinical testing, resulting in the delay or cancellation of clinical testing;
- failure by our collaborators to provide us on a timely basis with an adequate supply of product that complies with the applicable quality and regulatory requirements for a combination trial;
- failure of our third-party contract research organizations or investigators to satisfy their contractual obligations, including deviating from any trial protocols; and
- regulators or institutional review boards may withhold authorization to commence or conduct clinical trials of cabozantinib or another product candidate, 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 the clinical testing of cabozantinib or our other product candidates 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. Furthermore, we rely on our clinical and commercial collaboration partners to fund a significant portion of the clinical development of cabozantinib and our product candidates. Should one or all of our collaboration partners decline to support future

planned clinical trials, we will be entirely responsible for the financial obligations associated with the further development of cabozantinib or our other product candidates and, as a result, we may be unable to execute our business plans, which could have a material adverse impact on our business, financial condition and results of operations.

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We may not be able to rapidly or effectively continue the further development of cabozantinib or our other product candidates 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 our product candidates or may not result in an approvable product.

The duration and the cost of clinical trials vary significantly as a result of factors relating to the clinical trial, including, among others:

- characteristics of the product candidate under investigation;
- the number of patients who ultimately participate in the clinical trial;
- the duration of patient follow-up that is appropriate in view of the results or required by regulatory authorities;
- the number of clinical sites included in the trials; and
- the length of time required to enroll suitable patient subjects.

Any delay could limit our ability to generate revenues, cause us to incur additional expense and cause the market price of our common stock to decline significantly. Our partners under our collaboration agreements may experience similar risks with respect to the compounds we have out-licensed to them. If any of the events described above were to occur with such programs or compounds, the likelihood of receipt of milestones and royalties under such collaboration agreements could decrease.

The regulatory approval processes of the FDA and comparable foreign regulatory authorities are lengthy and uncertain, and may not result in regulatory approvals for cabozantinib or our other product candidates, which could have a material adverse impact on our business, financial condition and results of operations.

The activities associated with the research, development and commercialization of cabozantinib and our other product candidates are subject to extensive regulation by the FDA and other regulatory agencies in the U.S. and by comparable authorities in other countries. The process of obtaining regulatory approvals in the U.S. 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 sNDA can be submitted to the FDA, or a MAA to the EMA or any application or submission to regulatory authorities in other jurisdictions, the product candidate must undergo extensive clinical trials, which can take many years and require substantial expenditures.

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

In addition, delays or rejections may be encountered based upon changes in regulatory policy for product approval during the period of product development and regulatory agency review, which may cause delays in the approval or rejection of an application for cabozantinib or for our other product candidates.

Even if the FDA or a comparable authority in another jurisdiction approves cabozantinib for one or more indications beyond advanced RCC, previously treated HCC and MTC, or one of our other product candidates, the approval may be limited, imposing significant restrictions on the indicated uses, conditions for use, labeling, distribution, advertising, promotion, marketing and/or production of the product and could 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 a post-marketing requirement to conduct a clinical study comparing a lower dose of cabozantinib to the approved dose of 140 mg daily cabozantinib in progressive, metastatic MTC. Failure to complete any post-marketing requirements in accordance with the timelines and conditions set forth by the FDA could significantly increase costs or delay, limit or eliminate the commercialization of cabozantinib. Further, these agencies may also impose various administrative, civil or criminal sanctions for failure to comply with regulatory requirements, including withdrawal of product approval.

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We may be unable to expand our development pipeline, which could limit our growth and revenue potential.

Our business is focused on the discovery, development and commercialization of new medicines for difficult-to-treat cancers. In this regard, we are pursuing internal drug discovery efforts with the goal of identifying new product candidates to advance into clinical trials. Internal discovery efforts to identify new product candidates require substantial technical, financial and human resources. These internal discovery efforts may initially show promise in identifying potential product candidates, yet ultimately fail to yield product candidates for clinical development for a number of reasons. For example, potential product candidates may, on further study, be shown to have inadequate efficacy, harmful side effects, suboptimal pharmaceutical profiles or other characteristics suggesting that they are unlikely to be commercially viable products.

Apart from our internal discovery efforts, our strategy to expand our development pipeline is also dependent on our ability to successfully identify and acquire or in-license relevant product candidates. However, the in-licensing and acquisition of product candidates is a highly competitive area, and many other companies are pursuing the same or similar product candidates to those that we may consider attractive. In particular, larger companies with more well-established and diverse revenue streams may have a competitive advantage over us due to their size, financial resources and more extensive clinical development and commercialization capabilities. Furthermore, companies that perceive us to be a competitor may be unwilling to assign or license rights to us. We may also be unable to in-license or acquire additional relevant product candidates on acceptable terms that would allow us to realize an appropriate return on our investment. If we are unable to develop suitable product candidates through internal discovery effort or if we are unable to successfully obtain rights to suitable product candidates, our business, financial condition and prospects for growth could suffer. Even if we succeed in our efforts to obtain rights to suitable product candidates, the competitive business environment may result in higher acquisition or licensing costs, and our investment in these potential products will remain subject to the inherent risks associated with the development and commercialization of new medicines. In certain circumstances, we may also be reliant on the licensor for the continued development of the in-licensed technology and their efforts to safeguard their underlying intellectual property.

With respect to acquisitions, we may not be able to integrate the target company successfully into our existing business, maintain the key business relationships of the target, or retain key personnel of an acquired business. Furthermore, we could assume unknown or contingent liabilities or incur unanticipated expenses. Any acquisitions or investments made by us also could result in our spending significant amounts, issuing dilutive securities, assuming or incurring significant debt obligations and contingent liabilities, incurring large one-time expenses and acquiring intangible assets that could result in significant future amortization expense and significant write-offs, any of which could harm our operating results.

Increasing use of social media could give rise to liability and result in harm to our business.

We and our employees are increasingly utilizing social media tools and our website as a means of communication. For example, we use Facebook and Twitter to communicate with the medical community and the investing public, although we do not intend to disclose material, nonpublic information through these means. Despite our efforts to monitor evolving social media communication guidelines and comply with applicable rules, there is risk that the unauthorized use of social media by us or our employees to communicate about our products or business, or inadvertent disclosure of material, nonpublic information through these means, may cause us to be found in violation of applicable laws and regulations, which may give rise to liability and result in harm to our business. In addition, there is also risk of inappropriate disclosure of sensitive information, which could result in significant legal and financial exposure and reputational damages that could potentially have a materially adverse impact on our business, financial condition and results of operations. Furthermore, negative posts or comments about us or our products in social media could seriously damage our reputation, brand image and goodwill.

Risks Related to Our Capital Requirements, Accounting and Financial Results

We may be unable to maintain or increase profitability.

Although we reported net income of $690.1 million for the year ended December 31, 2018 we may not be able to maintain or increase profitability on a quarterly or annual basis, and we are unable to predict the extent of long-range future profits or losses. The amount of our net profits or losses will depend, in part, on: the level of sales of CABOMETYX and COMETRIQ in the U.S.; achievement of clinical, regulatory and commercial milestones, if any,

under our collaboration agreements with Ipsen and Takeda; the amount of royalties from sales of CABOMETYX and COMETRIQ outside of the U.S. under our collaboration agreements with Ipsen and Takeda; other collaboration revenues; and the level of our expenses,

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including development and commercialization activities for cabozantinib and any pipeline expansion efforts. We expect to continue to spend significant additional amounts to fund the continued development of cabozantinib for additional indications and the commercialization of our approved products. In addition, we will continue to expand our product pipeline through our drug discovery efforts and the execution of strategic transactions that align with our oncology drug development expertise, which efforts could involve substantial costs. To offset these costs, we will need to generate substantial revenues. If these costs exceed our expectations, or we fail to achieve anticipated revenue targets, the market value of our common stock may decline.

If additional capital is not available to us when we need it, we may be forced to limit the expansion of our product development programs or commercialization efforts.

As of December 31, 2018, we had $851.6 million in cash and investments, which included $850.5 million available for operations. Our business operations continued to grow substantially during 2018. In order to maintain business growth and maximize the clinical and commercial opportunities for cabozantinib, we plan to continue to execute on the U.S. commercialization plans for CABOMETYX, while reinvesting in our product pipeline through the continued development of cabozantinib, both alone and in combination with other therapies, research and development activities, as well as through strategic transactions. Our ability to execute on these business objectives will depend on many factors including but not limited to:

- the commercial success of both CABOMETYX and COMETRIQ and the revenues we generate from those approved products;
- costs associated with maintaining our expanded sales, marketing, market access, medical affairs and product distribution capabilities for CABOMETYX and COMETRIQ;
- the achievement of stated regulatory and commercial milestones and royalties paid under our collaboration agreements with Ipsen and Takeda;
- the commercial success of and revenues generated by products marketed under our collaboration and license agreements;
- future clinical trial results;
- the level of our investments in the expansion of our pipeline through drug discovery and corporate development activities;
- our ability to control costs;
- the number and size of clinical trials we conduct and the cost of drug supply for such clinical trials evaluating our products with other therapeutic agents;
- trends and developments in the pricing of oncologic therapeutics in the U.S. and abroad, especially in the EU;
- scientific developments in the market for oncologic therapeutics and the timing of regulatory approvals for competing oncologic therapies; and
- the filing, maintenance, prosecution, defense and enforcement of patent claims and other intellectual property rights.

Our commitment of cash resources to CABOMETYX and the reinvestment in our product pipeline through the continued development of cabozantinib and increasing drug discovery activities, as well as through the execution of strategic transactions, could require us to obtain additional capital. We may seek such additional capital through some or all of the following methods: corporate collaborations; licensing arrangements; and public or private debt or equity financings. Our ability to obtain additional capital may depend on prevailing economic conditions and financial, business and other factors beyond our control. Disruptions in the U.S. and global financial markets, including any disruptions resulting from government shutdowns, the UK’s pending withdrawal from the EU, rising interest rate environments, increased or changed tariffs and trade restrictions or otherwise, may adversely impact the availability and cost of credit, as well as our ability to raise money in the capital markets. Economic and capital markets conditions have been, and continue to be, volatile. Continued instability in these market conditions may limit our ability to access the capital necessary to fund and grow our business. Accordingly, we do not know whether additional capital will be available when needed, or that, if available, we will obtain additional capital on terms favorable to us or our stockholders. If we are unable to raise additional funds when we need them, we may be required to limit the expansion of our product development programs or commercialization efforts, which could have a material adverse impact on our business, financial condition and results of operations.

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Our financial results are impacted by management's selection of accounting methods, certain assumptions and estimates and future changes in accounting standards.

Our accounting policies and methods are fundamental to how we record and report our financial condition and results of operations. Our management must exercise judgment in selecting and applying many of these accounting policies and methods so they comply with generally accepted accounting principles and reflect management's judgment of the most appropriate manner to report our financial condition and results of operations. In some cases, management must select the accounting policy or method to apply from two or more alternatives, any of which may be reasonable under the circumstances, yet may result in our reporting materially different results than would have been reported under a different alternative.

Certain accounting policies are critical to the presentation of our financial condition and results of operations. The preparation of our financial statements requires us to make significant estimates, assumptions and judgments that affect the amounts of assets, liabilities, revenues and expenses and related disclosures. We believe our critical accounting policies relating to revenue recognition, clinical trial accruals, inventory and stock-based compensation reflect the more significant estimates and judgments used in the preparation of our Consolidated Financial Statements. Although we base our estimates and judgments on historical experience, our interpretation of existing accounting literature and on various other assumptions that we believe to be reasonable under the circumstances, if our assumptions prove to be materially incorrect, actual results may differ materially from these estimates.

In addition, future changes in financial accounting standards may cause adverse, unexpected revenue fluctuations and affect our financial position or results of operations, particularly those relating to the way we account for revenues and costs. New pronouncements from the Financial Accounting Standards Board (FASB) and varying interpretations of pronouncements have occurred with frequency in the past and are expected to occur again in the future and as a result, we may be required to make changes in our accounting policies. Those changes could adversely affect our reported revenues and expenses, our other results of operations or our current financial position.

The recently passed comprehensive tax reform bill could have a material adverse impact on our business, financial condition and results of operations.

The Tax Cuts and Jobs Act could be amended or subject to technical correction, which could change the financial impacts that were recorded at December 31, 2017 and December 31, 2018, or are expected to be recorded in future periods. Additionally, further guidance may be forthcoming from the FASB and SEC, as well as regulations, interpretations and rulings from federal and state tax agencies, which could result in additional impacts, possibly with retroactive effect.

Our effective tax rate may fluctuate, and we may incur obligations in tax jurisdictions in excess of accrued amounts.

We are subject to income tax in the U.S. as well as numerous U.S. states and territories, municipalities, and other local jurisdictions. As a result, our effective tax rate is derived from various factors including the mix of earnings and applicable tax rates in the various places that we operate, the accounting for stock options and share based awards, and research and development spending. In preparing our financial statements, we estimate the amount of tax that will become payable in each jurisdiction. Our effective tax rate, however, may be different than experienced in the past due to numerous factors, including changes in tax laws such as the passage of the Tax Cuts and Jobs Act, changes in the mix of our earnings from state to state, the results of examinations and audits of our tax filings, or our inability to secure or sustain acceptable agreements with tax authorities. Any of these factors could cause our effective tax rate to fluctuate.

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

As of December 31, 2018, we had federal and state net operating loss carryforwards of approximately $1.1 billion. The federal and state net operating loss carryforwards will begin to expire, if not utilized, beginning in 2028 for federal income tax purposes and 2028 for California state income tax purposes. These net operating loss carryforwards could expire unused and be unavailable to offset future income tax liabilities. Under the Internal Revenue Code (the Code) and similar state provisions, certain substantial changes in our ownership could result in an annual limitation on the amount of net operating loss carryforwards that can be utilized in future years to offset future taxable income. The annual limitation may result in the expiration of net operating losses and credit carryforwards before utilization. Based on our review and analysis, we concluded, as of December 31, 2018, that an ownership change, as defined under

Section 382, had not occurred. However, if there is an ownership change under Section 382 of the Code in the future, we may not be able to utilize a

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material portion of our net operating losses. Furthermore, our ability to utilize our net operating losses is conditioned upon our maintaining profitability and generating U.S. federal taxable income.

The transition away from the London Interbank Offered Rate (LIBOR) could affect the value of certain short-term investments, as well as our ability to seek additional debt financing.

Actions by governmental entities may impact certain financial instruments in which we have invested or may invest in the future. For example, some of these financial instruments may rely in some fashion upon LIBOR, which is an average interest rate, determined by the ICE Benchmark Administration, that banks charge one another for the use of short-term money. The UK's Financial Conduct Authority, which regulates LIBOR, has announced plans to phase out the use of LIBOR by the end of 2021. While only a small percentage of our short-term investments include financial instruments subject to LIBOR, and while we do not currently have any outstanding debt that is subject to LIBOR, there remains uncertainty regarding the future utilization of LIBOR and the nature of any replacement rate, and any potential effects of the transition away from LIBOR on certain instruments in to which we may enter in the future are not known. The transition process may involve, among other things, increased volatility or illiquidity in markets for instruments that currently rely on LIBOR. The transition may also result in reductions in the value of certain instruments or the effectiveness of related transactions such as hedges, increased borrowing costs, uncertainty under applicable documentation, or difficult and costly consent processes. Any such effects of the transition away from LIBOR, as well as other unforeseen effects, result in expenses, difficulties, complications or delays in connection with future financing efforts, which could have a material adverse impact on our business, financial condition and results of operations.

The UK’s pending withdrawal from the EU may have a negative effect on global economic conditions, financial markets and our business.

Brexit has created significant uncertainty concerning the future relationship between the UK and the EU. While discussions between the UK and the EU focused on finalizing withdrawal issues and transition agreements are ongoing, limited progress to date in these negotiations and ongoing uncertainty within the UK government and parliament sustains the possibility of the UK leaving the EU on March 29, 2019 without a withdrawal agreement and associated transition period in place, which is likely to cause significant market and economic disruption. The effects of Brexit will depend on any agreements the UK makes to retain access to EU markets either during a transitional period or more permanently. Brexit could, among other outcomes, disrupt the free movement of goods, services and people between the UK and the EU, undermine bilateral cooperation in key policy areas and significantly disrupt trade between the UK and the EU. In addition, Brexit could lead to legal uncertainty and potentially divergent national laws and regulations as the UK determines which EU laws to replace or adopt.

Given the lack of comparable precedent, it is unclear what financial, trade, regulatory and legal implications the withdrawal of the UK from the EU would have and how such withdrawal would affect us. For example, we rely on third-party contract manufacturing organization facilities located in the UK, which are responsible for packaging, labeling, storing and subsequently distributing supplies of our product to the EU, and any tariffs, differing regulatory requirements and other restrictions on the free movement of goods between the UK and the EU that result from Brexit may have an adverse impact on this part of our supply chain. In addition, trade restrictions, changes to the regulatory approval or drug cost reimbursement systems, and additional administrative costs may impede the ability of our collaborator Ipsen to market our products in Europe. Furthermore, the announcement of Brexit caused significant volatility in global stock markets and currency exchange rate fluctuations, and the pending withdrawal of the UK from the EU may also adversely affect European and global economic and market conditions, which may cause third-party payers, including governmental organizations, to closely monitor their costs and reduce their spending budgets, and which could contribute to instability in the global financial and foreign exchange markets. Any of these effects of Brexit, among others, could have a material adverse impact on our business, financial condition and results of operations.

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Risks Related to Our Relationships with Third Parties

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

We have established collaborations with leading pharmaceutical and biotechnology companies, including, Ipsen, Takeda, Genentech, Daiichi Sankyo and BMS for the development and ultimate commercialization of certain compounds generated from our research and development efforts. Our dependence on our relationships with collaborators for the development and commercialization of compounds subjects us to, a number of risks, including:

- our inability 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;
- the possibility that collaborators may delay clinical trials, fail to supply us on a timely basis with the product required for a combination trial, deliver product that fails to meet appropriate quality and regulatory standards and results in a market recall or withdrawal, 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 that may arise between us and our collaborators that result in the delay or termination of the research, development or commercialization of our drug candidates, or that diminish or delay receipt of the economic benefits we are entitled to receive under the collaboration, or that result in costly litigation or arbitration that diverts management's attention and resources;
- our inability to control the U.S. commercial resourcing decisions made and resulting costs incurred by Genentech for COTELLIC, which costs we are obligated to share, in part, under our collaboration agreement with Genentech;
- the possibility that our collaborators may experience financial difficulties;
- our collaborators' lack of success in their efforts to obtain regulatory approvals in a timely manner, or at all;
- our collaborators' failure to properly maintain or defend our intellectual property rights or their use of our intellectual property rights or proprietary information in such a way as to invite litigation that could jeopardize or invalidate our intellectual property rights or expose us to potential litigation;
- our collaborators' failure to comply with the terms of our collaboration agreements and related ancillary agreements;
- our collaborators' failure to comply with applicable healthcare laws, as well as established guidelines, laws and regulations related to GMP, GCP, GDP and Good Pharmacovigilance Practices;
- 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;
- the possibility that our collaborators could independently move forward with competing drug candidates developed either independently or in collaboration with others, including our competitors;
- our inability to enter into additional collaboration arrangements with other parties in an area or field of exclusivity;
- the possibility that future collaborators may require us to relinquish some important rights, such as marketing and distribution rights; and
- the possibility that collaborations may be terminated or allowed to expire, which would delay, and may increase the cost of development of our drug candidates.

If any of these risks materialize, we may not receive collaboration revenues or otherwise realize anticipated benefits from such collaborations, our product development efforts could be delayed, which could have a material adverse impact on our business, financial condition and results of operations.

If third parties upon which we rely to perform clinical trials for cabozantinib in new indications or for new potential product candidates do not perform as contractually required or expected, we may not be able to obtain regulatory approval for or commercialize cabozantinib or other product candidates beyond currently approved indications.

We do not have the ability to conduct clinical trials for cabozantinib or for new potential product candidates independently, including our post-marketing commitments in connection with the approval of COMETRIQ in progressive,

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metastatic MTC, so we rely on independent third parties for the performance of these trials, such as the U.S. federal government (including NCI-CTEP, a department of the National Institutes of Health, with whom we have our CRADA), third-party contract research organizations, medical institutions, clinical investigators and contract laboratories to conduct our clinical trials. If these third parties do not successfully carry out their contractual duties or regulatory obligations or meet expected deadlines, or if the third parties must be replaced or if the quality or accuracy of the data they generate or provide is compromised due to their failure to adhere to our clinical protocols or regulatory requirements or for other reasons, our preclinical development activities or clinical trials may be extended, delayed, suspended or terminated, and we may not be able to obtain regulatory approval for or commercialize cabozantinib or other product candidates beyond currently approved indications. In addition, due to the complexity of our research initiatives, we may be unable to engage with third-party contract research organizations that have the necessary experience and sophistication to further our drug discovery efforts, which would impede our ability to identify, develop and commercialize our potential product candidates.

We lack internal manufacturing capabilities necessary for us to produce our products for clinical development or for commercial sale and rely on third parties to do so, which subjects us to various risks.

We do not own or operate manufacturing facilities, distribution facilities or resources for clinical or commercial production and distribution of our products. Instead, we have multiple contractual agreements in place with third-party contract manufacturing organizations that, on our behalf, manufacture clinical and commercial supplies of CABOMETYX and COMETRIQ. As our operations expand due to our development and commercial progress, we expect to enter into new agreements with additional third-party contract manufacturers and suppliers as needed. This will continue for the foreseeable future for all of our product candidates and all of our current and future commercial products.

To establish and manage our supply chain requires a significant financial commitment, the creation of numerous third-party contractual relationships and continued oversight of these third parties to ensure compliance with applicable regulatory requirements. Although we maintain significant resources to directly and effectively oversee the activities and relationships with the companies in our supply chain, we do not have direct control over their operations.

Our third-party contract manufacturers may not be able to produce material on a timely basis or manufacture material with the required quality standards, or in the quantity required to meet our development and commercial needs and applicable regulatory requirements. If our third-party contract manufacturers and suppliers do not continue to supply us with our products or product candidates in a timely fashion and in compliance with applicable quality and regulatory requirements, or if they otherwise fail or refuse to comply with their obligations to us under our supply and manufacturing arrangements, we may not have adequate remedies for any breach. Furthermore, their failure to supply us could impair or preclude our ability to meet our commercial supply requirements, or our supply needs for clinical trials, including those being conducted in collaboration with our partners, which could delay our product development efforts and have a material adverse impact on our business, financial condition and results of operations. Through our third-party contract manufacturers and data service providers, we have implemented product serialization designed to comply with the DSCSA, pursuant to which all prescription pharmaceutical products manufactured and distributed in the U.S. were required to be serialized as of November 27, 2018. If our third-party contract manufacturers or data service providers fail to support our efforts to continue to comply with DSCSA and any future federal or state electronic pedigree requirements, we may face legal penalties or be restricted from selling our products.

As part of our collaboration agreements with Ipsen and Takeda, we are responsible for the supply of CABOMETYX and COMETRIQ for global development and commercial purposes. Failure to meet our supply obligations under these collaboration agreements could impair our collaborators' ability to successfully develop and commercialize CABOMETYX and COMETRIQ and generate revenues to which we are entitled under the collaborations.

Our collaborations with outside scientific advisors and collaborators 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, including in drug discovery and preclinical development strategy. These advisors and collaborators are not our employees and may have other commitments or pursue other opportunities 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. There has also been increased scrutiny surrounding the disclosures of payments made to medical researchers from companies in the pharmaceutical industry, and it is possible that the academic and other institutions that employ these medical researchers may prevent us from engaging them as advisors and collaborators or otherwise limit our access to these experts, or that the advisors themselves may now be more reluctant to work with industry partners. In any of these circumstances, we may lose

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work performed by these advisors and collaborators or be unable to engage them in the first place, and our discovery and development efforts with respect to the matters on which they were working or would work in the future may be significantly delayed or otherwise adversely affected. In addition, although our advisors and collaborators sign agreements not to disclose our confidential information, it is possible that valuable proprietary knowledge may become publicly known through them.

Risks Related to Our Information Technology, Data Privacy and Intellectual Property

Data breaches, cyber-attacks and other failures in our information technology infrastructure could compromise our intellectual property or other sensitive information, damage our operations and cause significant harm to our business and reputation.

In the ordinary course of our business, we collect, maintain and transmit sensitive data on our networks and systems, including our intellectual property and proprietary or confidential business information (such as research data and personal information) and confidential information with respect to our customers, clinical trial patients and our business partners. We have also outsourced significant elements of our information technology infrastructure and, as a result, third parties may or could have access to our confidential information. The secure maintenance of this information is critical to our business and reputation, and while we have enhanced and are continuing to enhance our cyber-security efforts commensurate with the growth and complexity of our business, our systems and those of third-party service providers may be vulnerable to a cyber-attack. In addition, we are heavily dependent on the functioning of our information technology infrastructure to carry out our business processes, such as external and internal communications or access to clinical data and other key business information. Accordingly, both inadvertent disruptions to this infrastructure and cyber-attacks could cause us to incur significant remediation or litigation costs, result in product development delays, disrupt key business operations and divert attention of management and key information technology resources.

We believe that companies have been increasingly subject to a wide variety of security incidents, cyber-attacks and other attempts to gain unauthorized access or otherwise compromise information technology systems. In fact, although the aggregate impact of cyber-attacks on our operations and financial condition has not been material to date, we have frequently been the target of threats of this nature and expect them to continue. These threats can come from a variety of sources, ranging in sophistication from an individual hacker to a state-sponsored attack and motive (including corporate espionage). Cyber threats may be generic, or they may be custom-crafted against our information systems. Cyber-attacks continue to become more prevalent and much harder to detect and defend against. Our network and storage applications and those of our contract manufacturing organizations, contract research organizations or vendors may be subject to unauthorized access by hackers or breached due to operator error, malfeasance or other system disruptions. It is often difficult to anticipate or immediately detect such incidents and the damage caused by such incidents. These data breaches and any unauthorized access or disclosure of our information or intellectual property could compromise our intellectual property and expose our sensitive business information (or sensitive business information of our collaboration partners, which may lead to significant liability for us). A data security breach could also lead to public exposure of personal information of our clinical trial patients, employees and others. Any such event that leads to unauthorized access, use or disclosure of personal information, including personal information regarding our patients or employees, could harm our reputation and business, compel us to comply with federal and/or state breach notification laws and foreign law equivalents (including the GDPR), subject us to investigations and mandatory corrective action, and otherwise subject us to liability under laws and regulations that protect the privacy and security of personal information, which could disrupt our business, result in increased costs or loss of revenue, and/or result in significant financial exposure. Furthermore, the costs of maintaining or upgrading our cyber-security systems at the level necessary to keep up with our expanding operations and prevent against potential attacks are increasing, and despite our best efforts, our network security and data recovery measures and those of our vendors may still not be adequate to protect against such security breaches and disruptions, which could cause material harm to our business, financial condition and results of operations.

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

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

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applications may be challenged or may fail to result in issued patents. Our issued patents have been and may in the future be challenged by third parties as invalid or unenforceable under U.S. or foreign laws, or they may be infringed by third parties, and we are from time to time involved in the defense and enforcement of our patents or other intellectual property rights in a court of law, U.S. Patent and Trademark Office inter partes review or reexamination proceeding, foreign opposition proceeding or related legal and administrative proceeding in the U.S. and elsewhere. The costs of defending our patents or enforcing our proprietary rights in post-issuance administrative proceedings and litigation can be substantial and the outcome can be uncertain. An adverse outcome may allow third parties to use our intellectual property without a license and/or allow third parties to introduce generic and other competing products, any of which would negatively impact our business. Third parties may also attempt to invalidate or design around our patents, or assert that they are invalid or otherwise unenforceable, and seek to introduce generic versions of cabozantinib. In addition, should any third parties receive FDA approval of an ANDA for a generic version of cabozantinib or an 505(b)(2) NDA with respect to cabozantinib, and if our patents covering cabozantinib were held to be invalid (or if such competing generic versions of cabozantinib were found to not infringe our patents), then they could introduce generic versions of cabozantinib or other such 505(b)(2) products before our patents expire, and the resulting generic competition would negatively affect our business, financial condition and results of operations.

In addition, because patent applications can take many years to issue, third parties may have pending applications, unknown to us, which may later result in issued patents that cover the production, manufacture, commercialization or use of our product candidates. Our existing patents and any future patents we obtain may not be sufficiently broad to prevent others from practicing our technologies or from developing competing products. Furthermore, others may independently develop similar or alternative technologies or design around our patents. In addition, our patents may be challenged or invalidated or may fail to provide us with any competitive advantages, if, for example, others were the first to invent or to file patent applications for closely related inventions.

The laws of some foreign countries do not protect intellectual property rights to the same extent as the laws of the U.S., 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. Initiatives seeking compulsory licensing of life-saving drugs are also becoming increasingly prevalent in developing countries either through direct legislation or international initiatives. Governments in those developing countries could require that we grant compulsory licenses to allow competitors to manufacture and sell their own versions of our products or product candidates, thereby reducing our product sales. Moreover, the legal systems of certain countries, particularly certain developing countries, do not favor the aggressive enforcement of patent and other intellectual property protection, which makes it difficult to stop infringement. We rely on trade secret protection for some of our confidential and proprietary information. We have taken security measures to protect our proprietary information and trade secrets, but these measures may not provide adequate protection. While we seek to protect our proprietary information by entering into confidentiality agreements with employees, collaborators and consultants, we cannot assure you that our proprietary information will not be disclosed, or that we can meaningfully protect our trade secrets. In addition, our competitors may independently develop substantially equivalent proprietary information or may otherwise gain access to our trade secrets.

Litigation or third-party claims of intellectual property infringement could require us to spend substantial time and money and adversely affect our ability to develop and commercialize products.

Our commercial success depends in part upon our ability to avoid infringing patents and proprietary rights of third parties and not to breach any licenses that we have entered into with regard to our technologies and the technologies of third parties. Other parties have filed, and in the future are likely to file, patent applications covering 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 accomplish or could require substantial time and expense.

In addition, third parties may obtain patents that relate to our technologies and claim that use of such technologies infringes on their patents or otherwise employs their proprietary technology without authorization. Regardless of their merit, such claims could require us to incur substantial costs, including the diversion of management and technical

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personnel, in defending ourselves against any such claims or enforcing our own 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 these third parties, subjecting us to substantial royalty payment obligations. We may not be able to obtain these licenses on commercially reasonable terms, or at all. Defense of any lawsuit or failure to obtain any of these licenses could adversely affect our ability to develop and commercialize products.

We may be subject to damages resulting from claims that we, our employees or independent contractors have wrongfully used or disclosed alleged trade secrets of their former employers.

Many of our employees and independent contractors were previously employed at universities or other biotechnology, biopharmaceutical or pharmaceutical companies, including our competitors or potential competitors. We may be subject to claims that we or these employees or independent contractors 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 damages, 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 develop or commercialize certain product candidates, which could severely harm our business.

Risks Related to Employees and Location

If we are unable to manage our growth, there could be a material adverse impact on our business, financial condition and results of operations, and our prospects may be adversely affected.

We have experienced and expect to continue to experience growth in the number of our employees and in the scope of our operations. This growth places significant demands on our management, operational and financial resources, and our current and planned personnel, facilities, systems, procedures and controls may not be adequate to support our growth. To effectively manage our growth, we must continue to improve existing, and implement new, operational and financial systems, procedures and controls and must expand, train and manage our growing employee base, and there can be no assurance that we will effectively manage our growth without experiencing operating inefficiencies or control deficiencies. We expect that we may need to increase our management personnel to oversee our expanding operations, and recruiting and retaining qualified individuals is difficult. If we are unable to manage our growth effectively, or are unsuccessful in recruiting qualified management personnel, there could be a material adverse impact on our business, financial condition and results of operations, and our prospects may be adversely affected.

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

We are highly dependent upon the principal members of our management, as well as clinical, commercial and scientific staff, the loss of whose services might adversely impact the achievement of our objectives. Also, we may not have sufficient personnel to execute our business plans. Retaining and, where necessary, recruiting qualified clinical, commercial and scientific personnel will be critical to support activities related to advancing the development program for cabozantinib and our other compounds, successfully executing upon our commercialization plan for cabozantinib and our internal proprietary research and development efforts. Competition is intense for experienced clinical, commercial and scientific personnel, and we may be unable to retain or recruit such personnel with the expertise or experience necessary to allow us to successfully develop and commercialize our products. Further, all of our employees are employed "at will" and, therefore, may leave our employment at any time.

Additionally, in the second quarter of 2018, we moved our corporate headquarters from South San Francisco, California to Alameda, California. This relocation may make it more difficult to retain certain employees, and any resulting loss of talent and need to recruit and train new employees could be disruptive to our business.

Our operations might be interrupted by the occurrence of a natural disaster or other catastrophic event.

Our headquarters in Alameda, California is located in the San Francisco Bay Area, and therefore our facilities are vulnerable to damage from earthquakes. We have limited earthquake insurance, which may not cover all of the damage we may suffer in the event of an earthquake. We are also vulnerable to damage from other types of disasters, including fires and floods, which have become a significant danger in California during recent years, as well as power loss, communications failures, terrorism and similar events, and any insurance we may maintain may be inadequate to

cover our losses. If any

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disaster were to occur, our ability to operate our business at our facilities could be seriously, or potentially completely, impaired. In addition, a disaster could cause significant delays in our programs and make it difficult for us to recover due to the unique nature of our research activities. Accordingly, an earthquake or other disaster could materially and adversely harm our ability to conduct business.

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

Any break-in or trespass at our facilities that results in the misappropriation, theft, sabotage or any other type of security breach with respect to our proprietary and confidential information, including research or clinical data, or that results in damage to our research and development equipment and assets, or that results in physical or psychological harm to any of our employees, could subject us to liability and have a material adverse impact on our business, financial condition and results of operations.

Risks Related to Environmental and Product Liability

We use hazardous chemicals 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 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, any 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 or commercialize 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 products and product candidates, injury to our reputation, withdrawal of patients from our clinical trials, product recall, substantial monetary awards to third parties and the inability to commercialize any products that we may develop in the future. 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 $20.0 million per occurrence and $20.0 million in the aggregate. However, our insurance may not reimburse us or may not be sufficient to reimburse us for expenses or losses we may suffer. Moreover, if insurance coverage becomes more expensive, we may not be able to maintain insurance coverage at a reasonable cost or in sufficient amounts to protect us against losses due to liability. On occasion, juries have awarded large judgments in class action lawsuits for claims based on drugs that had unanticipated side effects. In addition, the pharmaceutical, biopharmaceutical and biotechnology industries, in general, have been subject to significant medical malpractice litigation. A successful product liability claim or series of claims brought against us could harm our reputation and business and would decrease our cash reserves.

Risks Related to Our Common Stock

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

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

- the commercial success of both CABOMETYX and COMETRIQ and the revenues we generate from those approved products;

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- customer ordering patterns for CABOMETYX and COMETRIQ, which may vary significantly from period to period as a result of multiple factors, including pricing information required to be disclosed by us pursuant to drug pricing transparency laws;
- the overall level of demand for CABOMETYX and COMETRIQ, including the impact of any competitive products and the duration of therapy for patients receiving CABOMETYX or COMETRIQ;
- the achievement of stated regulatory and commercial milestones and royalties paid under our collaboration agreements with Ipsen and Takeda;
- the commercial success of and revenues generated by products marketed under our collaboration and license agreements;
- changes in the amount of deductions from gross sales, including changes to the discount percentage of rebates and chargebacks mandated by the government programs in which we participate, including increases in the government discount percentage resulting from price increases we have taken or may take in the future, or due to different levels of utilization by entities entitled to government rebates and chargebacks and changes in patient demographics;
- costs associated with maintaining our sales, marketing, market access, medical affairs and product distribution capabilities for CABOMETYX and COMETRIQ;
- the achievement of stated regulatory and commercial milestones under our collaboration agreements;
- the progress and scope of other development and commercialization activities for cabozantinib and our other compounds;
- future clinical trial results;
- our future investments in the expansion of our pipeline through drug discovery and business development activities;
- the inability to obtain adequate product supply for any approved drug product or inability to do so at acceptable prices;
- recognition of upfront licensing or other fees or revenues;
- payments of non-refundable upfront or licensing fees, or payment for cost-sharing expenses, to third parties;
- 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;
- the termination or non-renewal of existing collaborations or third-party vendor relationships;
- regulatory actions with respect to our product candidates and any approved products or our competitors' products;
- disputes or other developments relating to proprietary rights, including patents, litigation matters and our ability to obtain patent protection for our technologies;
- the timing and amount of expenses incurred for clinical development and manufacturing of cabozantinib;
- adjustments to expenses accrued in prior periods based on management's estimates after the actual level of activity relating to such expenses becomes more certain;
- the impairment of acquired goodwill and other assets;
- significant fluctuations in interest rates or foreign currency exchange rates;
- general and industry-specific economic conditions that may affect our or our collaborators' research and development expenditures; and
- other factors described in this "Risk Factors" section.

In addition, in the fourth quarter of 2018, we determined, based on our facts and circumstances, that it was more likely than not that a substantial portion of our deferred tax assets would be realized and, as a result, substantially all of our valuation allowance against deferred tax assets was released. Therefore, beginning in 2019, we expect to commence recording income tax expense at an estimated tax rate that will likely approximate statutory tax rates, which would result in a significant reduction in our net income and net income per share.

Due to the possibility of such 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

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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 has been and may in the future be highly 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 or inconclusive results or announcements related to our or our collaborators' clinical trials or delays in those clinical trials;
- the announcement of FDA approval or non-approval, or delays in the FDA review process with respect to cabozantinib, our collaborators' product candidates being developed in combination with cabozantinib, or our competitors' product candidates;
- the commercial success of both CABOMETYX and COMETRIQ and the revenues we generate from those approved products;
- the timing of achievement of our clinical, regulatory, partnering and other milestones, such as the commencement of clinical development, the completion of a clinical trial, the filing for regulatory approval or the establishment of collaborative arrangements for cabozantinib or any of our other programs or compounds;
- actions taken by regulatory agencies, both in the U.S. and abroad, with respect to cabozantinib or our clinical trials for cabozantinib;
- unanticipated regulatory actions taken by the FDA as a result of changing FDA standards and practices concerning the review of product candidates, including approvals at earlier stages of clinical development or with lesser developed data sets and expedited reviews;
- the announcement of new products or clinical trial data by our competitors;
- the announcement of regulatory applications seeking a path to U.S. approval of generic versions of our marketed products;
- quarterly variations in our or our competitors' results of operations;
- developments in our relationships with our collaborators, including the termination or modification of our agreements;
- the announcement of an in-licensed product candidate or strategic acquisition;
- 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;
- the entry into new financing arrangements;
- developments in the biotechnology, biopharmaceutical or pharmaceutical industry;
- sales of large blocks of our common stock or sales of our common stock by our executive officers, directors and significant stockholders;
- additions and departures of key personnel or board members;
- the extent to which coverage and adequate reimbursement is available for both CABOMETYX and COMETRIQ from government and health administration authorities, private health insurers, managed care programs and other third-party payers;
- disposition of any of our 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. In addition, the stock markets in general, and the markets for biotechnology and pharmaceutical stocks in particular, have historically experienced significant volatility that has often been unrelated or disproportionate to the operating performance of particular companies. For example, negative publicity regarding drug pricing and price increases by pharmaceutical companies has negatively impacted, and may continue to negatively impact,

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the markets for biotechnology and pharmaceutical stocks. Likewise, as a result of the pending Brexit and/or significant changes in U.S. social, political, regulatory and economic conditions or in laws and policies governing foreign trade and health care spending and delivery, including possible repeal and/or replacement of all or portions of PPACA or increases or changes in tariffs and other trade restrictions stemming from Trump administration and foreign government policies, or future U.S. federal government shutdowns, the financial markets could experience significant volatility that could also negatively impact the markets for biotechnology and pharmaceutical stocks. These broad market fluctuations have adversely affected, and may in the future adversely affect the trading 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 adverse impact on our business, financial condition and results of operations.

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

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

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

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

Item 1B. Unresolved Staff Comments

None.

Item 2. Properties

We lease a total of 134,765 square feet of office and research facilities in the San Francisco Bay Area. The lease expires in January 2028. We have two five-year options to extend the lease and a one-time option to terminate the lease without cause on the last day of the 8th year of the initial term. We believe that our existing leased facilities as well as our rights to acquire additional space under our existing lease arrangements are sufficient to accommodate our current and near-term needs.

Item 3. Legal Proceedings

We are not a party to any material legal proceedings. We may from time to time become a party or subject to various legal proceedings and claims, either asserted or unasserted, which arise in the ordinary course of business. Some of these proceedings have involved, and may involve in the future, claims that are subject to substantial uncertainties and unascertainable damages.

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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 under the symbol “EXEL” since April 11, 2000.

Holders

On February 12, 2019, there were 398 holders of record of our common stock. The number of record holders is based upon the actual number of holders registered on our books at such date and does not include holders of shares in “street names” or persons, partnerships, associations, corporations or other entities identified in security position listings maintained by depository trust companies.

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.

Unregistered Sales of Equity Securities

There were no unregistered sales of equity securities by us during the year ended December 31, 2018.

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Performance

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, 2018, the cumulative total stockholder return for our common stock, the Nasdaq Composite Index and the Nasdaq Biotechnology Index. The graph assumes that $100 was invested on December 31, 2013 in each of our common stock, the Nasdaq Composite 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.

	December 31,					
	2013	2014	2015	2016	2017	2018
Exelixis, Inc.	100	28	95	251	513	328
Nasdaq Composite Index	100	114	120	130	166	158
Nasdaq Biotechnology Index	100	136	150	117	142	127

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Item 6. Selected Financial Data

The following Selected Financial Data has been derived from our audited Consolidated Financial Statements and should be read in conjunction with Part II, Item 7. “Management’s Discussion and Analysis of Financial Condition and Results of Operations” and Part II, Item 8. “Financial Statements and Supplementary Data” contained in this Annual Report on Form 10-K. The consolidated financial information as of December 31, 2018 and 2017 and for the years ended, December 31, 2018, 2017, and 2016 are derived from audited Consolidated Financial Statements included elsewhere in this Annual Report on Form 10-K. The consolidated financial information as of December 31, 2016, 2015 and 2014, and for each of the years ended December 31, 2015 and 2014, are derived from audited Consolidated Financial Statements not included in this Annual Report on Form 10-K.

	Year Ended December 31,				
	2018	2017	2016	2015	2014
	(In thousands, except per share data)				
Consolidated Statements of Operations Data:					
Revenues	$853,826	$452,477	$191,454	$37,172	$25,111
Operating expenses:					
Cost of goods sold	26,348	15,066	6,552	3,895	2,043
Research and development	182,257	112,171	95,967	96,351	189,101
Selling, general and administrative	206,366	159,362	116,145	57,305	50,829
Restructuring (recovery) charge	—	(32)	914	1,042	7,596
Total operating expenses	414,971	286,567	219,578	158,593	249,569
Income (loss) from operations	438,855	165,910	(28,124)	(121,421)	(224,458)
Other income (expenses), net	13,237	(7,333)	(42,098)	(40,268)	(37,021)
Income (loss) before income taxes	452,092	158,577	(70,222)	(161,689)	(261,479)
Income tax benefit (provision)	237,978	(4,350)	—	(55)	182
Net income (loss)	$690,070	$154,227	$(70,222)	$(161,744)	$(261,297)
Net income (loss) per share, basic	$2.32	$0.52	$(0.28)	$(0.77)	$(1.34)
Net income (loss) per share, diluted	$2.21	$0.49	$(0.28)	$(0.77)	$(1.34)
Shares used in computing net income (loss) per share, basic	297,892	293,588	250,531	209,227	194,299
Shares used in computing net income (loss) per share, diluted	312,803	312,003	250,531	209,227	194,299

	December 31,				
	2018	2017	2016	2015	2014
	(In thousands)				
Consolidated Balance Sheet Data:					
Cash and investments	$851,621	$457,176	$479,554	$253,310	$242,760
Working capital (deficit)	$791,544	$369,704	$200,215	$126,414	$(3,188)
Total assets	$1,422,286	$655,294	$595,739	$332,223	$323,256
Long-term obligations	$29,361	$255,163	$237,635	$420,897	$312,163
Accumulated deficit	$(880,363)	$(1,829,172)	$(1,983,147)	$(1,912,925)	$(1,751,181)
Total stockholders’ equity (deficit)	$1,287,453	$284,961	$89,318	$(140,806)	$(159,324)

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Item 7. Management's Discussion and Analysis of Financial Condition and Results of Operations

Some of the statements under in this "Management's Discussion and Analysis of Financial Condition and Results of Operations" 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. 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.

We have adopted a 52- or 53-week fiscal year policy that generally ends on the Friday closest to December 31st. Fiscal year 2016 ended on December 30, 2016; fiscal year 2017 ended on December 29, 2017; fiscal year 2018 ended on December 28, 2018; and fiscal year 2019 will end on January 3, 2020. For convenience, references in this report as of and for the fiscal years ended (or ending, as applicable) December 30, 2016, December 29, 2017, December 28, 2018 and January 3, 2020 are indicated as being as of and for the years ended (or ending, as applicable) December 31, 2016, 2017, 2018 and 2019, respectively. The annual period and quarterly period ending January 3, 2020 are a 53-week fiscal year and a 14-week fiscal quarter, respectively; all other annual periods presented are 52-week fiscal years and all interim periods presented are 13-week fiscal quarters.

Overview

We are an oncology-focused biotechnology company that aims to accelerate the discovery, development and commercialization of new medicines for difficult-to-treat cancers. Since we were founded in 1994, four products resulting from our discovery efforts have progressed through clinical development and received regulatory approval; three have a growing commercial presence in markets worldwide, and we expect that the fourth will soon enter the marketplace in Japan. Two are derived from cabozantinib, our flagship molecule, an inhibitor of multiple tyrosine kinases including MET, AXL, VEGF receptors and RET. These are: CABOMETYX tablets approved for advanced RCC and previously treated HCC, and COMETRIQ capsules approved for progressive, metastatic MTC. The two other products resulting from our discovery efforts are: COTELLIC, an inhibitor of MEK approved as part of a combination regimen to treat advanced melanoma and marketed under a collaboration with Genentech; and MINNEBRO, an oral, non-steroidal, selective blocker of the MR approved for the treatment of hypertension in Japan and licensed to Daiichi Sankyo.

CABOMETYX was first approved by the FDA, for previously treated patients with advanced RCC in April 2016, and then in December 2017, approximately two months ahead of the assigned PDUFA action date, the FDA expanded CABOMETYX's approval in this indication to include previously untreated patients with advanced RCC. Additionally, in January 2019, the FDA approved CABOMETYX as a treatment for patients with HCC who have been previously treated with sorafenib. This most recent approval was based on results from CELESTIAL, our phase 3 pivotal trial evaluating cabozantinib in patients with previously treated HCC, which demonstrated a statistically significant and clinically meaningful improvement in OS versus placebo. We are highly focused on optimizing the execution of this commercial launch in HCC in the U.S. through our commercial and medical affairs organizations and established distribution network.

To develop and commercialize CABOMETYX and COMETRIQ outside the U.S., we have entered into license agreements with Ipsen and Takeda. Ipsen has been granted rights to cabozantinib outside of the U.S. and Japan, and Takeda has been granted rights to cabozantinib in Japan. Both partners also contribute financially and operationally to the further global development and commercialization of cabozantinib in other potential indications, and we continue to work closely with them on these activities. Utilizing its regulatory expertise and established international oncology marketing network, since the initiation of our collaboration Ipsen has continued to execute on its commercialization plans, most recently receiving regulatory approval from the EC for CABOMETYX as a treatment for HCC in adults who have previously been treated with sorafenib, and Takeda continues to conduct clinical development activities in both RCC and HCC, with the goal of supporting future regulatory filings in Japan.

In addition to our regulatory and commercialization efforts in the U.S. and the support provided to our partners for rest of world regulatory and commercialization activities, we are also focused on the next wave of cabozantinib's clinical development program, pursuing other indications that have the potential to expand the number of cancer patients who could benefit from this medicine. We are evaluating cabozantinib, both as a single agent and in combination with other

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therapies, in a broad development program comprising over 75 ongoing or planned clinical trials across multiple indications. We, along with our clinical and commercial collaboration partners, sponsor some of the trials, and independent investigators conduct the remaining trials through our CRADA with NCI-CTEP or our IST program. Informed by the available data from these clinical trials, we continue to advance cabozantinib's late-stage development program. One pivotal trial that has resulted from this effort is COSMIC-311, our phase 3 trial evaluating cabozantinib in patients with RAI-refractory DTC who have progressed after up to two VEGF receptor-targeted therapies initiated in October 2018.

We are particularly interested in examining cabozantinib's potential in combination with ICIs to determine if such combinations further improve outcomes for patients. Building on preclinical and clinical observations that cabozantinib may promote a more immune-permissive tumor environment potentially resulting in cooperative activity of cabozantinib in combination with these products, we are evaluating cabozantinib in combination with a variety of ICIs in multiple clinical trials. The most advanced of these combination studies include Checkmate 9ER, a phase 3 pivotal trial evaluating cabozantinib in combination with nivolumab in previously untreated advanced or metastatic RCC, and Checkmate 040, a phase 1/2 trial evaluating cabozantinib in combination with nivolumab and in combination with both nivolumab and ipilimumab in patients with both previously treated and previously untreated advanced HCC. Both trials are in collaboration with BMS. As a further part of our clinical collaboration with BMS, we also plan to evaluate cabozantinib and nivolumab with or without ipilimumab in various other tumor types, including UC. Diversifying our exploration of combinations with ICIs, we have also initiated COSMIC-312, a phase 3 pivotal trial evaluating cabozantinib in combination with Roche's ICI, atezolizumab, versus sorafenib in previously untreated advanced HCC, and COSMIC-021, a phase 1b dose escalation study evaluating the safety and tolerability of cabozantinib in combination with atezolizumab in patients with locally advanced or metastatic solid tumors. The COSMIC-021 study comprises eighteen tumor expansion cohorts, including multiple therapeutic settings of RCC, UC, and NSCLC and single therapeutic settings of HCC, CRPC, TNBC, EOC, endometrial cancer, gastric or gastroesophageal junction adenocarcinoma, colorectal adenocarcinoma, DTC and head and neck cancer of squamous cell histology, and is currently enrolling. Findings from the dose escalation stage of the study demonstrate that the combination was well-tolerated and showed encouraging anti-tumor activity in patients with advanced RCC. Depending on the results from COSMIC-021, we may also evaluate this combination in various other tumor types, including NSCLC. COSMIC-021 also includes two exploratory cohorts that will evaluate cabozantinib as a single-agent therapy in NSCLC and UC indications.

As we continue to work to maximize the clinical, therapeutic and commercial potential of cabozantinib, we also remain committed to building our product pipeline by discovering and developing new cancer therapies for patients. In this regard, we have reinitiated internal drug discovery efforts with the goal of identifying new product candidates to advance into clinical trials. Notably, these efforts are led by some of the same experienced scientists responsible for the discovery of cabozantinib and cobimetinib, which have been approved for commercialization by regulatory authorities, as well as other promising compounds we have discovered, many of which are in various stages of clinical, regulatory and commercial development pursuant to our collaborations with Daiichi Sankyo and BMS. Using our expertise in medicinal chemistry, tumor biology and pharmacology, we are advancing drug candidates toward and through preclinical development. Furthest along in these internal drug discovery efforts is XL092, a next-generation oral TKI that is currently the subject of an active IND.

These internal drug discovery activities are augmented by efforts to identify and in-license promising, early-stage oncology assets and then further develop them utilizing our established clinical development infrastructure. In furtherance of this strategy, in January 2018, we entered into an exclusive global collaboration and license agreement with StemSynergy for the discovery and development of novel oncology compounds aimed to inhibit tumor growth by targeting CK1 , a component of the Wnt signaling pathway implicated in key oncogenic processes. Under the terms of this agreement, we have partnered with StemSynergy to conduct preclinical and clinical studies with compounds targeting CK1 . Additionally, in May 2018, we entered into a collaboration and license agreement with Invenra which is focused on developing next-generation biologics, to discover and develop multispecific antibodies for the treatment of cancer. Invenra is responsible for antibody lead discovery and generation while we will lead IND-enabling studies, manufacturing, clinical development in single-agent and combination therapy regimens, and future regulatory and

commercialization activities. The collaboration agreement also provides that we will receive an exclusive, worldwide license to one preclinical asset, and that we will pursue up to six additional discovery projects during the term of the collaboration, which in total are directed to three discovery programs. To date, we have initiated two such discovery projects.

For additional information regarding our business, see “Business” in Part I, Item 1 of this Annual Report on Form 10-K.

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2018 Business Updates and Financial Highlights

During 2018, we continued to execute on our commercial, development and financial objectives, generating significant revenue from operations and enabling the business to maximize the clinical and commercial potential of our CABOMETYX and our other internally discovered, commercially available products and to expand the product pipeline. Significant business updates and financial highlights for 2018 and subsequent to year end include:

Business Updates

- In January and June 2018, we announced amendments to the protocol for COSMIC-021, the phase 1b trial of cabozantinib in combination with atezolizumab in patients with locally advanced or metastatic solid tumors, to add new expansion cohorts to the trial (for an aggregate of eighteen cohorts), which now includes patients with RCC, UC, NSCLC, CRPC, HCC, TNBC, EOC, endometrial cancer, gastric or gastroesophageal junction adenocarcinoma, colorectal adenocarcinoma, DTC and head and neck cancer of squamous cell histology.
- In January 2018, we entered into an exclusive collaboration and license agreement with StemSynergy for the discovery and development of novel oncology compounds aimed to inhibit tumor growth by targeting CK1 .
- In February 2018, we announced updated results from the NCI-CTEP-sponsored phase 1 trial of cabozantinib in combination with nivolumab, with or without ipilimumab, in patients with refractory genitourinary tumors. The updated results demonstrated an acceptable tolerability profile and high rates of durable responses in the previously treated metastatic UC and metastatic RCC cohorts.
- In April 2018, we appointed Maria C. Freire, Ph.D. to our Board of Directors. Dr. Freire serves as President and Executive Director and as a member of the board of directors of the Foundation for the National Institutes of Health, an independent 501(c)(3) charitable organization established by Congress to support the National Institutes of Health by raising private funds for biomedical research and fostering partnerships and alliances around the world.
- In May 2018, we entered into a collaboration and license agreement with Invenra to discover and develop multispecific antibodies for the treatment of cancer.
- In May 2018, Ipsen received regulatory approval from the EC for CABOMETYX as a treatment for adult patients with previously untreated, intermediate- or poor-risk advanced RCC. The EC's approval of CABOMETYX was based on results from CABOSUN, a randomized phase 2 trial comparing cabozantinib with sunitinib in patients with previously untreated advanced RCC with intermediate- or poor-risk disease that demonstrated a statistically significant and clinically meaningful improvement in PFS and ORR versus sunitinib.
- In May 2018, we announced that IMblaze370, Genentech's phase 3 pivotal trial evaluating the combination of cobimetinib with atezolizumab in patients with CRC, did not meet its primary endpoint. However, Genentech continues to pursue the cobimetinib development program, either as a single-agent or in combination studies.
- In June 2018, clinical data from cabozantinib were the subject of fifteen presentations at the ASCO 2018 Annual Meeting, including a poster presentation covering a sub-group analysis of CELESTIAL, our phase 3 pivotal trial evaluating cabozantinib in patients with previously treated HCC, comparing outcomes by duration of sorafenib treatment in patients whose only prior treatment was sorafenib and outcomes based on age. The findings showed that cabozantinib improved OS and PFS compared with placebo irrespective of duration of prior sorafenib treatment or age category.
- In July 2018, we were added to Standard & Poor's (S&P's) MidCap 400 index and are classified under S&P's Global Industry Classification Standard Biotechnology Sub-Industry index.
- In July 2018, the NEJM published results from CELESTIAL, our phase 3 pivotal trial evaluating cabozantinib in patients with previously treated HCC. The data demonstrate that cabozantinib provided a statistically significant and clinically meaningful improvement in OS versus placebo.
- In September 2018, NCCN updated its Clinical Practice Guidelines to include favorable new recommendations for CABOMETYX as a treatment for patients with advanced RCC, regardless of patient risk status. As part of this update, NCCN also designated CABOMETYX as the only preferred TKI treatment option for previously untreated patients with poor- or intermediate-risk, and the only preferred TKI treatment option for previously treated patients.
- In September 2018, Ipsen received regulatory approval from Health Canada for CABOMETYX as a treatment in Canada for adult patients with advanced RCC who have received prior VEGF-targeted therapy. Health Canada's approval of CABOMETYX was based on results from METEOR, our phase 3 trial in which CABOMETYX provided

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a statistically significant and clinically meaningful improvement in OS, PFS and ORR as compared with everolimus in patients with advanced RCC who have received prior anti-angiogenic therapy.

- In October 2018, we initiated COSMIC-311, a phase 3 pivotal trial evaluating cabozantinib in patients with RAI-refractory DTC who have progressed after up to two VEGFR-targeted therapies. This trial was informed by cabozantinib's encouraging clinical activity in patients with RAI-refractory DTC in phase 1 and 2 studies for which updated data was presented at the 2018 Multidisciplinary Head and Neck Cancers Symposium in February 2018.
- In October 2018, clinical data from cabozantinib were the subject of thirteen presentations at ESMO, including a poster presentation covering the results from the dose escalation stage of COSMIC-021, our phase 1b study evaluating the safety and tolerability of cabozantinib in combination with Roche's atezolizumab in patients with locally advanced or metastatic solid tumors. Findings from the dose escalation phase of the trial demonstrate that the combination was well-tolerated and showed encouraging anti-tumor activity in patients with advanced RCC. In another poster presentation, data were presented from an analysis that evaluated the effect of PD-L1 expression on clinical outcomes with cabozantinib in advanced RCC from the CABOSUN and METEOR trials. This analysis showed that cabozantinib's activity was independent of PD-L1 expression. Additionally, a separate retrospective analysis of RCC patients found that cabozantinib was active following prior treatment with immune checkpoint inhibitor therapy either alone or in combination with VEGF-targeted or other prior therapy.
- In October 2018, Ipsen received approvals from both the Agência Nacional de Vigilância Sanitária in Brazil for CABOMETYX as a treatment for both previously treated and previously untreated advanced RCC and from the Taiwan Food and Drug Administration for CABOMETYX as a treatment for patients with advanced RCC who have received prior anti-angiogenic therapy.
- In November 2018, Ipsen received regulatory approval from the EC for CABOMETYX as a treatment for HCC in adults who have previously been treated with sorafenib. The EC's approval of CABOMETYX was based on results from CELESTIAL, our phase 3 pivotal trial evaluating cabozantinib in patients with previously treated HCC, which demonstrated a statistically significant and clinically meaningful improvement in OS versus placebo.
- In December 2018, we initiated COSMIC-312, a phase 3 pivotal trial evaluating cabozantinib in combination with atezolizumab versus sorafenib in patients with previously untreated advanced HCC. We are sponsoring COSMIC-312, and Ipsen will co-fund the trial. Ipsen will have access to the results to support potential future regulatory submissions outside of the U.S. and Japan. Roche is providing atezolizumab free of charge.
- In January 2019, we announced that our partner Daiichi Sankyo received approval from the MHLW for MINNEBRO as a treatment for patients with hypertension in Japan. MINNEBRO is a compound identified during our research collaboration with Daiichi Sankyo, which the companies entered into in March 2006, and has been subsequently developed by Daiichi Sankyo.
- In January 2019, the FDA approved CABOMETYX as a treatment for patients with HCC who have been previously treated with sorafenib. The FDA's approval of CABOMETYX was based on results from CELESTIAL, our phase 3 pivotal trial evaluating cabozantinib in patients with previously treated HCC, which demonstrated a statistically significant and clinically meaningful improvement in OS versus placebo.
- In January 2019, the FDA accepted our IND for XL092, a next-generation oral TKI and the first compound to advance from our new discovery organization. The phase 1 dose escalation trial will evaluate its pharmacokinetics, safety and tolerability in patients with advanced solid tumors, with the primary objective of determining a dose for daily oral administration of XL092 suitable for further evaluation.

2018 Financial Highlights

- Net income for 2018 was $690.1 million, or $2.32 per share, basic and $2.21 per share, diluted, compared to $154.2 million, or $0.52 per share, basic and $0.49 per share diluted, for 2017.
- Total revenues for 2018 increased to $853.8 million, compared to $452.5 million for 2017.
- Net product revenues for 2018 increased to $619.3 million, compared to $349.0 million for 2017.
- Research and development expenses for 2018 increased to $182.3 million, compared to $112.2 million for 2017.
- Selling, general and administrative expenses for 2018 increased to $206.4 million, compared to $159.4 million for 2017.

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- Cash and investments increased to $851.6 million at December 31, 2018, compared to $457.2 million at December 31, 2017.
- During the second quarter of 2018, Ipsen reached $150.0 million in cumulative net sales of cabozantinib, which resulted in an increase in the minimum royalty rate earned by us to 22% of net sales by Ipsen. Previously we had been entitled to receive a tiered royalty of 2% to 12%. Since reaching that milestone, we are entitled to receive a tiered royalty of 22% to 26% of annual net sales.
- During the fourth quarter of 2018, we released substantially all of our valuation allowance against our deferred tax assets which resulted in a $244.1 million income tax benefit.

See “Results of Operations” below for a discussion of the detailed components and analysis of the amounts above.

Challenges and Risks

We will continue to face a number of challenges and risks to our business that may impact our ability to execute on our 2019 business objectives. In particular, we anticipate that for the foreseeable future our ability to maintain or meaningfully increase unrestricted cash flow to fund our commercial operations and our development and discovery programs will be dependent upon the continued successful commercialization of CABOMETYX for the treatment of RCC and HCC, in each case in territories where it has been approved and according to the terms of such regulatory approvals, and in potential other indications for which we are in late-stage development, such as previously treated RAI-refractory DTC. The commercial opportunity for CABOMETYX as a treatment of RCC and HCC remains subject to a variety of factors, most importantly, CABOMETYX’s perceived benefit/risk profile as compared to the benefit/risk profiles of other treatments available or currently in development for the treatment of these conditions. Our ability to maintain or meaningfully increase product revenues from CABOMETYX is also affected by a number of other factors, including the highly competitive markets for which we intend to pursue regulatory approval of cabozantinib and the prospect for new competitive therapies and generic competition, and the extent to which coverage and reimbursement for CABOMETYX is available from government and other third-party payers. Obtaining and maintaining appropriate coverage and reimbursement for CABOMETYX is increasingly challenging due to, among other things, the focus healthcare cost containment and other potential austerity measures being discussed in the U.S. and worldwide, as well as increasing interest amongst legislators and policymakers in the U.S. in restricting drug prices through the imposition of pharmaceutical drug price controls. Our ability to fulfill the commercial potential of cabozantinib also depends on whether data generated by our clinical development activities will support regulatory approval of cabozantinib in additional indications. Achievement of our 2019 business objectives will also depend on the success of our development and commercialization strategy formulated to navigate increased competition, including that from, but not limited to, ICIs, as well as the use of combination therapy to treat cancer. Furthermore, our research and development objectives may be impeded as we work to scale our organization to meet the demands of expanded drug development and discovery activities. In connection with efforts to expand our product pipeline, we may be unsuccessful in discovering new drug candidates or we may not be able to successfully identify appropriate candidates for in-licensing or acquisition.

Some of these challenges and risks are specific to our business, and others are common to companies in the pharmaceutical industry with development and commercial operations. For a complete discussion of challenges and risks we face, see “Risk Factors” in Part I, Item 1A of this Annual Report on Form 10-K.

Results of Operations

Revenues

Revenues by category were as follows (dollars in thousands):

	Year Ended December 31,			Percentage Change - 2018 v. 2017		Percentage Change - 2017 v. 2016	
	2018	2017	2016				
Net product revenues	$619,279	$349,008	135,375	77	%	158	%
Collaboration revenues	234,547	103,469	56,079	127	%	85	%
Total revenues	$853,826	$452,477	$191,454	89	%	136	%

Collaboration revenues for the year ended December 31, 2018 were impacted by our adoption of Accounting Standards Update No. 2014-09, Revenue from Contracts with Customers (Topic 606). For additional information on our adoption of Topic 606, see “Note 1. Organization and Summary of Significant Accounting Policies—Recently Adopted

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Accounting Pronouncements," "Note 2. Revenues" and "Note 3. Collaboration Agreements" in our "Notes to Consolidated Financial Statements" contained in Part II, Item 8 of this Annual Report on Form 10-K.

Net Product Revenues

Net product revenues by product were as follows (dollars in thousands):

	Year Ended December 31,			Percentage Change - 2018 v. 2017	Percentage Change - 2017 v. 2016
	2018	2017	2016		
CABOMETYX	$599,946	$324,000	$93,481	85 %	247 %
COMETRIQ	19,333	25,008	41,894	(23)%	(40)%
Net product revenues	$619,279	$349,008	$135,375	77 %	158 %

The increases in net product revenues for CABOMETYX for the year ended December 31, 2018, as compared to 2017 and 2016, were primarily due to a 72% and 228% increase, respectively, in the number of units of CABOMETYX sold, and, to a lesser extent, increases in the average selling price of the product. The increases in CABOMETYX sales volumes reflects the continued growth of CABOMETYX in advanced RCC following regulatory approvals of CABOMETYX for the treatment of patients with advanced RCC who have received prior anti-angiogenic therapy in April 2016 and for previously untreated patients with advanced RCC in December 2017. The decreases in net product revenues for COMETRIQ for the year ended December 31, 2018, as compared to 2017 and 2016, were primarily due to a 26% and 53% decline, respectively, in the number of units of COMETRIQ sold. COMETRIQ sales volume has continued to decrease since the launch of CABOMETYX in April 2016. The adoption of Topic 606 did not impact our net product revenues.

We recognize product revenues net of discounts and allowances that are described in "Note 1. Organization and Summary of Significant Accounting Policies" to our "Notes to Consolidated Financial Statements" contained in Part II, Item 8 of this Annual Report on Form 10-K. The increase in the reserve balances for discounts and allowances from December 31, 2017 to December 31, 2018 was primarily the result of an increase in product sales volume, and to a lesser extent, higher discounts and participation in government programs, and an increase in commercial contracting. The increase in the reserve balances for discounts and allowances from December 31, 2016 to December 31, 2017 was the result of an increase in product sales volume, and to a lesser extent, additional reserves for goods in the channel expected to have higher discounts during early 2018, as well as a higher volume in government programs. Those increases were partially offset by payments, the issuance of customer credits and the prior period adjustments for chargebacks and certain rebates. We expect our discounts and allowances as a percentage of gross product revenues to increase during 2019 as our business evolves and the number of patients participating in government programs increases, the discounts and rebates paid to government payers increase and as a result of the engagement in commercial contracting that may result in additional discounts or rebates.

Collaboration Revenues

Collaboration revenues were as follows (dollars in thousands):

	Year Ended December 31,			Percentage Change - 2018 v. 2017	Percentage Change - 2017 v. 2016
	2018	2017	2016		
Collaboration revenues:					
License revenues [1]	$192,188	$96,637	$56,286	99 %	72 %
Research and development service revenues [2]	39,501	8,737	—	352 %	n/m
Other collaboration revenues [3]	2,858	(1,905)	(207)	n/m	820 %
Total collaboration revenues	$234,547	$103,469	$56,079	127 %	85 %

(1) Upon the adoption of Topic 606 as of January 1, 2018, the allocation of proceeds from our collaboration partners, including upfront and milestone payments, between intellectual property licenses and research and development services as well as the resulting timing of recognition have changed. License revenues for the year ended

December 31, 2018 included the immediate recognition of the portion of milestones that were allocated to the transfer of intellectual property licenses for those milestones for which it had become probable that a significant revenue reversal would not occur, as well as royalty revenues from Ipsen and Genentech. License revenues for the years ended December 31, 2017 and 2016 included the full recognition of substantive

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milestones achieved during the period, recognition of deferred revenues from upfront payments and a non-substantive milestone, which were being amortized over various periods, as well as royalty revenues from Ipsen and Genentech.

(2) Research and development service revenues for the year ended December 31, 2018 included the recognition of deferred revenue for the portion of the upfront and milestone payments that have been allocated to the research and development service performance obligations which are being amortized through early 2030, as well as development cost reimbursements earned on our collaboration agreements. As described above, prior to the adoption of Topic 606, we did not allocate any of our upfront payments or milestones to research and development services; therefore, Research and development service revenues for the years ended December 31, 2017 included only development cost reimbursements earned on our collaboration agreements.

(3) Other collaboration revenues for the year ended December 31, 2018 included royalties we paid to GSK on Ipsen's sales of products containing cabozantinib, the profit on the U.S. commercialization of COTELLIC from Genentech and product supply revenues. Other collaboration revenues for the years ended years ended December 31, 2017 and 2016 included only royalties we paid to pay GSK on Ipsen's sales of products containing cabozantinib and product supply revenues, as the profits and losses on the U.S. commercialization of COTELLIC for the period were included in Selling, general and administrative expenses.

Collaboration revenues were $234.5 million, $103.5 million and $56.1 million for the years ended December 31, 2018, 2017 and 2016, respectively. The increases in collaboration revenues were primarily the result of increases in milestones revenues, royalties under our collaboration agreement with Ipsen, development cost reimbursement revenues and profit sharing under our collaboration agreement with Genentech; those increases were partially offset by decreases in the recognition of deferred revenue due to the adoption of Topic 606 and increases in the royalties we paid to GSK on Ipsen's sales of products containing cabozantinib.

Milestone revenues were $164.4 million, $57.5 million and $40.0 million for the years ended December 31, 2018, 2017 and 2016, respectively. Milestone revenues related primarily to development, regulatory and commercial achievements under our collaboration agreement with Ipsen. Under our Ipsen collaboration, during the year ended December 31, 2018, we recognized three developmental and regulatory milestones totaling $115.0 million and a commercial milestone for $25.0 million, as compared to two developmental and regulatory milestones totaling $40.0 million during 2017. See "Note 3. Collaboration Agreements" in our "Notes to Consolidated Financial Statements" contained in Part II, Item 8 of this Annual Report on Form 10-K for additional information about the timing and amounts of revenue associated with the achievement of these milestones. Due to uncertainties surrounding the timing and achievement of regulatory and development milestones, it is difficult to predict future milestone revenues and such milestones can vary significantly from year to year.

Royalties on net sales of cabozantinib by Ipsen outside of the U.S. and Japan were $32.3 million, $3.8 million and $0.2 million for the years ended December 31, 2018, 2017 and 2016, respectively. Ipsen's net sales of cabozantinib have continued to grow since their first commercial sale of the product in the fourth quarter of 2016, primarily due to increased demand and approvals of CABOMETYX in additional indications and/or jurisdictions outside of the U.S. We were initially entitled to receive a tiered royalty of 2% to 12% on the initial $150.0 million of net sales; this amount was reached in the second quarter of 2018. As of December 31, 2018 and going forward, we are entitled to receive a tiered royalty of 22% to 26% on annual net sales (with separate tiers for Canada); these 22% to 26% royalty tiers reset each calendar year. In Canada, we are entitled to receive a tiered royalty of 22% on the first CAD$30.0 million of annual net sales and a tiered royalty thereafter to 26% on annual net sales; these 22% to 26% royalty tiers for Canada will also reset each calendar year. For 2019, we expect the royalty revenues to increase as a result of achieving the 22% minimum royalty tier.

Development cost reimbursements in connection with our collaboration arrangements with Ipsen and Takeda were $24.9 million and $8.7 million for the years ended December 31, 2018 and 2017, respectively. The increase for the year ended December 31, 2018, was primarily the result of Ipsen's and Takeda's participation in the CheckMate 9ER study. There were no such development cost reimbursements during the year ended December 31, 2016.

Profits on the U.S. commercialization of COTELLIC and royalties on ex-U.S. net sales of COTELLIC under our collaboration agreement with Genentech totaled $13.6 million for the year ended December 31, 2018. During the years ended December 31, 2017 and 2016 collaboration revenues included royalties on ex-U.S. net sales of

COTELLIC of $6.4 million and $2.8 million, respectively. Profits and losses on the U.S. commercialization of COTELLIC for the years ended December 31, 2017 and 2016 were included in Selling, general and administrative expenses. We achieved a profit on the U.S. commercialization of COTELLIC in 2018, as compared to a loss in 2017, as Genentech scaled back the personal promotion of COTELLIC resulting in a reduction in commercial expenditures while revenues from the sale of COTELLIC remained relatively flat.

Revenues from the amortization of deferred revenue related to the recognition of a portion of the upfront payments received in connection with our February 2016 collaboration agreement with Ipsen and the upfront payment

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received in connection with our January 2017 collaboration agreement with Takeda. Such revenues were $4.5 million, $28.9 million and $13.3 million for the years ended December 31, 2018, 2017 and 2016, respectively. The decrease in the recognition of such revenues for the year ended December 31, 2018, as compared to 2017 was a result of the adoption of Topic 606; Upon adopting Topic 606 on January 1, 2018, we recorded a $236.7 million reduction of the unrecognized upfront and non-substantive milestone payments previously received from our collaboration partners that had been included in deferred revenue at December 31, 2017 along with a corresponding reduction of our opening accumulated deficit. For the year ended December 31, 2017, we recognized $18.5 million and $10.4 million of such revenue in connection with the Ipsen collaboration agreement and the Takeda collaboration agreement, respectively. For the year ended December 31, 2016, we recognized $13.3 million of such revenue in connection with the Ipsen collaboration agreement. No such revenue was recognized in connection with the Takeda collaboration agreement during 2016. The increase in such revenues for the year ended December 31, 2017, as compared to 2016, is due to the timing of the execution of those agreements.

For the years ended December 31, 2018, 2017 and 2016, collaboration revenues were reduced by $5.4 million, $2.0 million and $0.2 million, respectively, for the 3% royalty we are required to pay GSK on the net sales by Ipsen of any product incorporating cabozantinib. As royalty generating sales of cabozantinib by Ipsen have increased as described above, our royalty payments to GSK have also increased.

Cost of Goods Sold

The Cost of goods sold and our gross margins were as follows (dollars in thousands):

	Year Ended December 31,			Percentage Change - 2018 v. 2017	Percentage Change - 2017 v. 2016
	2018	2017	2016		
Cost of goods sold	$26,348	$15,066	$6,552	75 %	130 %
Gross margin	96 %	96 %	95 %		

Cost of goods sold is related to our product revenues and consists primarily of a 3% royalty we are required to pay GSK on U.S. net sales by us of any product incorporating cabozantinib, indirect labor costs, the cost of manufacturing the product, write-downs related to expiring and excess inventory, and other third-party logistics costs. Portions of the manufacturing costs for inventory were incurred prior to the regulatory approval of CABOMETYX and COMETRIQ and, therefore, were expensed as research and development costs when incurred, rather than capitalized as inventory. Cost of goods sold included a 2%, 3% and 7% reduction related to materials that had been previously expensed during the years ended December 31, 2018, 2017 and 2016, respectively. There were no amounts remaining related to previously expensed materials in our inventory balances as of December 31, 2018. Write-downs related to excess and expiring inventory were $1.1 million, $1.1 million and $0.5 million for the years ended December 31, 2018, 2017 and 2016, respectively.

The increases in Cost of goods sold for the year ended December 31, 2018, as compared to 2017, were primarily related to the growth in sales of CABOMETYX. The increase in Cost of goods sold for the year ended December 31, 2017, as compared to 2016, primarily reflects the growth in product sales of CABOMETYX following the product's launch in late April 2016 and an increase in market share.

We do not expect our gross margin to change significantly during the year ending December 31, 2019.

Research and Development Expenses

Research and development expenses were as follows (dollars in thousands):

	Year Ended December 31,			Percentage Change - 2018 v. 2017	Percentage Change - 2017 v. 2016
	2018	2017	2016		
Research and development expenses	$182,257	$112,171	$95,967	62 %	17 %

Research and development expenses consist primarily of clinical trial costs, personnel expenses, consulting and outside services, stock-based compensation, the allocation of general corporate costs and license costs.

The increase in Research and development expenses for the year ended December 31, 2018, as compared to 2017, were primarily related to increases in clinical trial costs, personnel expenses, license costs and stock-based compensation. Clinical trial costs, which includes services performed by third-party contract research organizations and other vendors who support our clinical trials, increased $26.1 million for the year ended December 31, 2018, as compared to 2017. The

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increase in clinical trial costs was primarily due to increased costs associated with: CheckMate 9ER, COSMIC-311, COSMIC-312 and the preparation for further pivotal phase 3 trials that are expected to be initiated in 2019. Personnel expenses increased $21.5 million for the year ended December 31, 2018, as compared to 2017, primarily due to an increase in headcount to support our development and discovery efforts. License costs increased $8.2 million for the year ended December 31, 2018, as compared to 2017, primarily as a result of our entry into the collaboration agreements with Invenra and StemSynergy. Stock-based compensation increased $5.5 million for the year ended December 31, 2018, as compared to 2017, primarily due to an increase in headcount.

The increase in Research and development expenses for the year ended December 31, 2017, as compared to 2016, was primarily related to an increase in personnel expenses and clinical trial costs. Personnel expenses increased $8.5 million for the year ended December 31, 2017, as compared to 2016, primarily due to support for our development efforts and our medical affairs organization. Clinical trial costs increased $4.4 million for the year ended December 31, 2017, as compared to 2016 primarily due to start-up costs associated with CheckMate 9ER and COSMIC-021, partially offset by decreases in costs related to METEOR.

We do not track fully-burdened Research and development expenses on a project-by-project basis. We group our Research and development expenses into three categories: Development, Drug discovery and Other. Our development group leads the development and implementation of our clinical and regulatory strategies and prioritizes disease indications in which our compounds are being or may be studied in clinical trials. Our drug discovery group utilizes a variety of technologies to enable the rapid discovery, optimization and extensive characterization of lead compounds such that we are able to select development candidates with the best potential for further evaluation and advancement into clinical development. Research and development expenses by category were as follows (in thousands):

	Year Ended December 31,		
	2018	2017	2016
Research and development expenses:			
Development:			
Clinical trial costs	$66,434	$40,315	$35,947
Personnel expenses	48,114	30,076	22,936
Consulting and outside services	9,693	8,492	8,176
Other development costs	13,505	12,967	11,478
Total development	137,746	91,850	78,537
Drug discovery [(1)]	21,944	6,334	1,220
Other [(2)]	22,567	13,987	16,210
Total research and development expenses	$182,257	$112,171	$95,967

(1) Primarily includes personnel expenses, consulting and outside services and laboratory supplies for all periods presented and license costs for our collaboration and license agreements with Invenra and StemSynergy during the year ended December 31, 2018.

(2) Includes stock-based compensation and the allocation of general corporate costs to research and development.

In addition to reviewing the three categories of Research and development expenses described above, we principally consider qualitative factors in making decisions regarding our research and development programs. Such factors include enrollment in clinical trials for our drug candidates, preliminary data from and final results of clinical trials, the potential indications for our drug candidates, the clinical and commercial potential for our drug candidates, and competitive dynamics. We also make our research and development decisions in the context of our overall business strategy.

We are focusing our development efforts primarily on cabozantinib to maximize the therapeutic and commercial potential of this compound, and as a result, we expect our near-term research and development expenses to primarily relate to the clinical development of cabozantinib. We expect to continue to incur significant development costs for cabozantinib in future periods as we evaluate its potential in a broad development program comprising over 75 ongoing or planned clinical trials across multiple indications. Notable studies of this program include: CheckMate 9ER and CheckMate 040, each in collaboration with BMS; company-sponsored COSMIC-021 and COSMIC-312, for

which Roche is providing atezolizumab free of charge; and company-sponsored COSMIC-311. In addition, post-marketing commitments in connection with the approval of COMETRIQ in progressive, metastatic MTC dictate that we conduct an additional study in that indication.

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We are also committed to building our product pipeline by discovering and developing new cancer therapies for patients. In this regard, we have reinitiated internal drug discovery efforts with the goal of identifying new product candidates to advance into clinical trials. These internal drug discovery activities are augmented by efforts to identify and in-license promising, early-stage oncology assets and then further develop them utilizing our established clinical development infrastructure. As a result, for 2019 we expect our Research and development expenses to increase as we continue to expand the cabozantinib development program and our product pipeline.

The length of time required for clinical development of a particular product candidate and our development costs for that product candidate may be impacted by the scope and timing of enrollment in clinical trials for the product candidate, our decisions to develop a product candidate for additional indications and whether we pursue development of the product candidate or a particular indication with a collaborator or independently. For example, cabozantinib is being developed in multiple indications, and we do not yet know for how many of those indications we will ultimately pursue regulatory approval. In this regard, our decisions to pursue regulatory approval of cabozantinib for additional indications depend on several variables outside of our control, including the strength of the data generated in our prior, ongoing and potential future clinical trials. Furthermore, the scope and number of clinical trials required to obtain regulatory approval for each pursued indication is subject to the input of the applicable regulatory authorities, and we have not yet sought such input for all potential indications that we may elect to pursue. Even after having given such input, applicable regulatory authorities may subsequently require additional clinical studies prior to granting regulatory approval based on new data generated by us or other companies, or for other reasons outside of our control. As a condition to any regulatory approval, we may also be subject to post-marketing development commitments, including additional clinical trial requirements. As a result of the uncertainties discussed above, we are unable to determine the duration of or complete costs associated with the development of cabozantinib or any of our other research and development projects.

In any event, our potential therapeutic products are subject to a lengthy and uncertain regulatory process that may not result in our receipt of the necessary regulatory approvals. Failure to receive the necessary regulatory approvals would prevent us from commercializing the product candidates affected, including cabozantinib in any additional indications. In addition, clinical trials of our potential product candidates may fail to demonstrate safety and efficacy, which could prevent or significantly delay regulatory approval. A discussion of the risks and uncertainties with respect to our research and development activities, including completing the development of our product candidates, and the consequences to our business, financial position and growth prospects can be found in “Risk Factors” in Part I, Item 1A of this Annual Report on Form 10-K.

Selling, General and Administrative Expenses

Selling, general and administrative expenses were as follows (dollars in thousands):

	Year Ended December 31,			Percentage Change - 2018 v. 2017	Percentage Change - 2017 v. 2016
	2018	2017	2016		
Selling, general and administrative expenses	$206,366	$159,362	$116,145	29 %	37 %

Selling, general and administrative expenses consist primarily of personnel expenses, consulting and outside services, stock-based compensation, marketing costs and corporate giving.

The increases in Selling, general and administrative expenses for the year ended December 31, 2018, as compared to 2017, were primarily related to increases in personnel expenses, consulting and outside services, stock-based compensation, corporate giving and marketing costs. Personnel expenses increased $14.7 million for the year ended December 31, 2018, as compared to 2017, primarily due to increases in general and administrative headcount to support our commercial and research and development organizations. Consulting and outside services and marketing costs increased $11.7 million and $6.1 million, respectively, for the year ended December 31, 2018 as compared to 2017, primarily due to increases in marketing activities in connection with preparations for the CABOMETYX launch in HCC, which were partially offset by a $2.1 million decrease in the losses on the U.S. commercialization of COTELLIC. For the year ended December 31, 2017, such losses on the U.S. commercialization of COTELLIC were included in Selling, general and administrative expenses whereas for the year ended December 31, 2018, the profit on

the U.S. commercialization of COTELLIC was included in Collaboration revenues. Stock-based compensation increased $11.1 million for the year ended December 31, 2018, as compared to 2017, primarily due to increases in headcount. Corporate giving, consisting predominantly of donations to independent patient support foundations, increased $6.4 million for the year ended December 31, 2018, as compared to 2017.

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The increase in Selling, general and administrative expenses for the year ended December 31, 2017, as compared to 2016, was primarily related to increases in personnel expenses, consulting and outside services, marketing costs and charitable contribution expenses. Personnel expenses increased $11.3 million for the year ended December 31, 2017, as compared to 2016, primarily due to an increase in general and administrative headcount to support our commercial and research and development organizations. Consulting and outside services increased $10.7 million for the year ended December 31, 2017, as compared to 2016, primarily due to increases in consulting for marketing activities. Marketing costs increased $6.6 million for the year ended December 31, 2017, as compared to 2016, primarily due to an increase in losses recognized under our collaboration agreement with Genentech. In December 2016, Genentech stated that it changed, both retroactively and prospectively, the manner in which it allocates promotional expenses of the COTELLIC plus Zelboraf combination therapy. As a result of Genentech's decision to change its cost allocation approach, we were relieved of our obligation to pay certain disputed costs that had been accrued by us; we were also able to invoice Genentech for certain expenses, with interest, that we had previously paid. Accordingly, during the year ended December 31, 2016, we offset Selling, general and administrative expenses with a $13.3 million recovery of disputed losses that we had recognized and recorded prior to 2016. Marketing costs also included a loss of $2.1 million for activities during the year ended December 31, 2017 under our collaboration agreement with Genentech, as compared to a loss of $4.5 million for activities during 2016. Corporate giving increased $5.2 million for the year ended December 31, 2017, as compared to 2016.

For 2019, we expect modest growth in Selling, general and administrative expenses in 2019 to support our overall organizational growth.

Other Income (Expenses), Net

Other income (expenses), net, were as follows (dollars in thousands):

	Year Ended December 31,			Percentage Change - 2018 v. 2017	Percentage Change - 2017 v. 2016
	2018	2017	2016		
Interest income	$12,840	$4,883	$2,578	163 %	89 %
Interest expense	—	(8,679)	(33,060)	(100)%	(74)%
Other, net	397	(3,537)	(11,616)	n/m	(70)%
Total other income (expenses), net	$13,237	$(7,333)	$(42,098)	n/m	(83)%

The increases in Interest income for the year ended December 31, 2018, as compared to 2017 and 2016, respectively, were the result of both an increase in our investment balances and an increase in the yield earned on those investments.

The decreases in Interest expense for the year ended December 31, 2018, as compared to 2017 and 2016, were due to the repayment of the Secured Convertible Notes due 2018 held by entities associated with Deerfield Management Company, L.P. (Deerfield Notes), in June 2017, the repayment of the our $80.0 million term loan with Silicon Valley Bank in March 2017, and the conversions and the redemption of the 4.25% convertible senior subordinated notes due 2019 (2019 Notes), during the third and fourth quarters of 2016.

The changes in Other, net for the year ended December 31, 2018, as compared to 2017 and 2016, were primarily due to a loss on extinguishment of debt and gains on the sale of other equity investments that both occurred in 2017 and 2016. During the years ended December 31, 2017 and 2016 we recognized a $6.2 million and $13.9 million loss on extinguishment of debt, respectively, due to the repayment of the Deerfield Notes in June 2017 and the conversions and the redemption of the 2019 Notes during the third and fourth quarters of 2016. There was no such retirement of debt during the year ended December 31, 2018. Other, net also included gains of $0.2 million, $3.0 million and $2.5 million, respectively, during the years ended December 31, 2018, 2017 and 2016, respectively, related to the August 2016 sale of our 9% interest in Akarna Therapeutics, Ltd. (Akarna) to Allergan Holdco UK Limited (Allergan). We acquired our interest in Akarna in 2015 in exchange for intellectual property rights related to the Exelixis discovered compound XL335. We are eligible to earn additional such gains in the future as Allergan continues its development of XL335.

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Income Tax Benefit (Provision)

The income tax benefit (provision) were as follows (in thousands):

	Year Ended December 31,		
	2018	2017	2016
Income tax benefit (provision)	$237,978	$(4,350)	$ —

The income taxes benefit for the year ended December 31, 2018 included a $244.1 million benefit related to the release of substantially all of our valuation allowance against our deferred tax assets. The decision to release the valuation allowance was made after we determined that it was more likely than not that these deferred tax assets, including net operating losses and tax credits, would be realized, and was based on the evaluation and weighting of both positive and negative evidence, including our achievement of a cumulative three-year income position as of December 31, 2018 and forecasts of future operating results, as well as considering the utilization of net operating losses and tax credits prior to their expiration. Due to the release of the valuation allowance in 2018, starting in 2019, we expect to record a provision for income taxes on our pretax income using an estimated effective tax rate between 21% and 23%.

Other than the benefit we recorded for the release of our valuation allowance during the year ended 2018, the provision for income taxes for the years ended December 31, 2018 and 2017 primarily related to taxes in states for which we do not have net operating loss carryforwards due to a limited operating history. Our historical losses were sufficient to fully offset our federal taxable income for the years ended December 31, 2018 and 2017.

Impact of Duration of Fiscal Years

We have adopted a 52- or 53-week fiscal year policy that generally ends on the Friday closest to December 31st. 2019 will be a 53-week fiscal year as compared to 52-week fiscal years for 2018, 2017 and 2016. Accordingly, the 53-week fiscal year in 2019 may result in a modest increase in revenues and expenses, as compared to 2018, 2017 and 2016.

Liquidity and Capital Resources

As of December 31, 2018, we had $851.6 million in cash and investments, which included $850.5 million available for operations. We anticipate that the aggregate of our current cash and cash equivalents, short-term investments available for operations, product revenues and collaboration revenues will enable us to maintain our operations for a period of at least 12 months following the filing date of this report. The sufficiency of our cash resources depends on numerous assumptions, including assumptions related to product sales and operating expenses, as well as the other factors set forth in “Risk Factors” under the headings “Risks Related to our Capital Requirements, Accounting and Financial Results,” in Part I, Item 1A of this Annual Report on Form 10-K. Our assumptions may prove to be wrong or other factors may adversely affect our sources of cash, and as a result we may not have the cash resources to fund our operations as currently planned, which would have a material adverse effect on our business.

We expect to continue to spend significant amounts to fund the continued development and commercialization of cabozantinib. In addition, we intend to rebuild our product pipeline through our reinitiated drug discovery efforts and the execution of strategic transactions that align with our oncology drug expertise. Financing these activities could materially impact our liquidity and capital resources and may require us to incur debt or raise additional funds through the issuance of equity. Furthermore, even if we believe we have sufficient funds for our current and future operating plans, we may choose to incur debt or raise additional funds through the issuance of equity due to market conditions or strategic considerations.

Sources and Uses of Cash

The following table summarizes our cash flow activities (in thousands):

	Year Ended December 31,		
	2018	2017	2016
Net cash provided by operating activities	$415,720	$165,611	$210,404
Net cash (used in) provided by investing activities	$(297,850)	$36,795	$(214,548)
Net cash provided by (used in) financing activities	$9,691	$(169,928)	$15,696

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Operating Activities

Our operating activities provided cash of $415.7 million for the year ended December 31, 2018, compared to $165.6 million during 2017 and $210.4 million during 2016.

Cash flows provided by operating activities represent the cash receipts and disbursements related to all of our activities other than investing and financing activities. Cash provided by operating activities is derived by adjusting our net income for: non-cash operating items such as depreciation and amortization, share-based compensation charges and the release of our valuation allowance against our deferred tax assets; and changes in operating assets and liabilities which reflect timing differences between the receipt and payment of cash associated with transactions and when they are recognized in our Consolidated Results of Operations.

The most significant factors that contributed to the increase in cash provided by operating activities for the year ended December 31, 2018, as compared to 2017, was a $270.3 million increase in net product revenues and $42.5 million increase in cash received for milestones. These were partially offset by a $128.4 million increase in operating expenses for the year ended December 31, 2018, as compared to 2017, and by the impact of the upfront nonrefundable payment of $50.0 million received from Takeda in 2017 in consideration for the exclusive license and other rights contained in our collaboration agreement with Takeda.

The most significant factors that contributed to the decrease in cash provided by operating activities for the year ended December 31, 2017, as compared to 2016, include the upfront nonrefundable payment of $200.0 million received from Ipsen in 2016 in consideration for the exclusive license and other rights contained in our collaboration agreement with Ipsen along with a $67.0 million increase in operating expenses. These were offset by a $213.6 million increase in net product revenues and the upfront nonrefundable payment of $50.0 million received from Takeda in the year ended December 31, 2017 in consideration for the exclusive license and other rights contained in our collaboration agreement with Takeda.

Investing Activities

Our investing activities used cash of $297.9 million for the year ended December 31, 2018, as compared to $36.8 million of cash provided during 2017 and $214.5 million of cash used during 2016.

Cash used in investing activities for the year ended December 31, 2018 was primarily due to investment purchases of $557.8 million and Property and equipment purchases of $33.3 million, primarily related to our new corporate headquarters and research facilities in Alameda, California, offset by cash provided from the maturity and sale of investments of $280.8 million and $11.9 million, respectively.

Cash provided by investing activities for the year ended December 31, 2017 was primarily due to cash received from the sale and maturity of investments of $373.9 million, offset by cash used for investment purchases of $319.1 million. During 2017 we also invested $21.1 million in property and equipment.

Cash used by investing activities for the year ended December 31, 2016 was primarily due to investment purchases of $369.2 million, offset by cash provided by the maturity and sale of investments of $153.8 million.

Financing Activities

Our financing activities provided cash of $9.7 million for the year ended December 31, 2018, as compared to $169.9 million of cash used during 2017 and $15.7 million of cash provided during 2016.

Cash provided by financing activities for the year ended December 31, 2018 was primarily the result of $9.7 million in proceeds from the issuance of common stock under our equity incentive plans, net of taxes paid related to net share settlements.

Cash used in financing activities for the year ended December 31, 2017 was primarily the result of $185.8 million paid for all amounts outstanding under the Deerfield Notes and our term loan with Silicon Valley Bank. Those payments were partially offset by $15.9 million of proceeds from the issuance of common stock under our equity incentive plans, net of taxes paid related to net share settlements.

Cash provided by financing activities for the year ended December 31, 2016 was primarily the result of $23.4 million of proceeds from the issuance of common stock under our equity incentive plans, net of taxes paid related to net

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share settlements. Those proceeds were partially offset by cash payments from the conversion and redemption of the 2019 Notes totaling $7.7 million.

Contractual Obligations

We have contractual obligations in the form of leases and purchase obligations. The following chart details our contractual obligations as of December 31, 2018 (in thousands):

	Payments Due by Period			
Contractual Obligations [1]	Total	Less than 1 year	1-3 Years	More than 3 Years
Operating leases	28,187	2,794	5,727	19,666
Purchase and other long-term obligations [2]	27,143	24,067	2,908	168
Total contractual cash obligations	$55,330	$26,861	$8,635	$19,834

(1) In addition to the above, we have committed to make potential future milestone payments to Invenra or StemSynergy as part of our collaboration agreements with those parties. Payments under those agreements generally become due and payable only upon achievement of certain developmental, regulatory and sales-based milestones. Because the achievement of those milestones is neither probable nor reasonably estimable, such contingencies have not been recorded on our Consolidated Balance Sheets and have not been included in the table above. For more information about these obligations, see “Note 3. Collaboration Agreements” in our “Notes to Consolidated Financial Statements” contained in Part II, Item 8 of this Annual Report on Form 10-K.

(2) Purchase obligations include firm purchase commitments related to manufacturing and maintenance of inventory, software services and other long term contractual obligations.

Off-Balance Sheet Arrangements

We do not have any off-balance-sheet arrangements, as defined by applicable SEC regulations.

Critical Accounting Estimates

The preparation of our Consolidated Financial Statements conforms to accounting principles generally accepted in the U.S. which requires management to make judgments, estimates and assumptions that affect the reported amounts of assets, liabilities, equity, revenues and expenses, and related disclosures. An accounting policy is considered to be critical if it requires an accounting estimate to be made based on assumptions about matters that are highly uncertain at the time the estimate is made, and if different estimates that reasonably could have been used, or changes in the accounting estimates that are reasonably likely to occur periodically, could materially impact our Consolidated Financial Statements. On an ongoing basis, management evaluates its estimates including, but not limited to: those related to revenue recognition, including determining the nature and timing of satisfaction of performance obligations, and determining the standalone selling price of performance obligations, and variable consideration such as rebates, chargebacks, sales returns and sales allowances as well as milestones included in collaboration arrangements; the amounts of revenues and expenses under our profit and loss sharing agreement; recoverability of inventory; operating lease assets and liabilities; the amounts of deferred tax assets and liabilities including the related valuation allowance; the accrual for certain liabilities including accrued clinical trial liabilities; and valuations of equity awards used to determine stock-based compensation, including certain awards with vesting subject to market or performance conditions. We base our estimates on historical experience and on various other market-specific and other relevant assumptions that we believe to be reasonable under the circumstances, the results of which form the basis for making judgments about the carrying values of assets and liabilities that are not readily apparent from other sources. Our senior management has discussed the development, selection and disclosure of these estimates with the Audit Committee of our Board of Directors. Actual results could differ materially from those estimates.

We believe our critical accounting policies relating to revenue recognition, inventory, clinical trial accruals, stock option valuation and income taxes reflect the more significant estimates and assumptions used in the preparation of our Consolidated Financial Statements.

For a complete description of our significant accounting policies, see “Note 1. Organization and Summary of Significant Accounting Policies” in the “Notes to Consolidated Financial Statements” contained in Part II, Item 8 of this

Annual Report on Form 10-K.

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Revenue Recognition

Net Product Revenues and Discounts and Allowances

We recognize revenue when our customers obtain control of promised goods or services, in an amount that reflects the consideration to which we are entitled to in exchange for those goods or services. We calculate gross product revenues based on the price that we charge to the specialty pharmacies and distributors in the U.S. We estimate our domestic net product revenues by deducting from our gross product revenues: (a) trade allowances, such as discounts for prompt payment; (b) estimated government rebates and chargebacks; (c) certain other fees paid to specialty pharmacies and distributors; and (d) returns. Discounts and allowances are complex and require significant judgment by management. Estimates are assessed each period and updated to reflect current information.

We initially record estimates for these deductions at the time we recognize the related gross product revenue. Our estimates for the expected utilization are based on customer and payer data received from the specialty pharmacies and distributors and historical utilization rates as well as third-party market research data. For a further description of our discounts and allowances, see “Note 1. Organization and Summary of Significant Accounting Policies” to our “Notes to Consolidated Financial Statements” contained in Part II, Item 8 of this Annual Report on Form 10-K.

Collaboration Revenues

We enter into collaboration arrangements, under which we license certain rights to our intellectual property to third parties. The terms of these arrangements typically include payment to us for one or more of the following: non-refundable, up-front license fees; development, regulatory and commercial milestone payments; product supply services; development cost reimbursements; profit sharing arrangements; and royalties on net sales of licensed products. As part of the accounting for these arrangements, we must develop assumptions that require judgment to determine the standalone selling price for each performance obligation identified in the contract. We use key assumptions to determine the standalone selling price, which may include forecast revenues and costs, clinical development timelines and costs, reimbursement rates for personnel costs, discount rates and probabilities of technical and regulatory success. At the inception of each arrangement that includes development milestone payments, we evaluate whether the milestones are considered probable of being reached and estimate the amount to be included in the transaction price using the most likely amount method. At the end of each subsequent reporting period, we re-evaluate the probability of earning of such development milestones and any related constraint, and if necessary, adjust our estimate of the overall transaction price. In addition, in recording revenues for our research and development services performance obligation, we use internal development projected cost estimates to determine the amount of revenue to record as we satisfy this performance obligation, known as the inputs method.

We record royalty revenues and U.S. profits and losses under the collaboration agreement with Genentech based on estimates of the sales that occurred during the period. The relevant period estimates of sales are based on interim data provided by licensees and analysis of historical activity, adjusted for any changes in facts and circumstances, as appropriate. We base our estimates on the best information available at the time provided to us by our collaboration partners. However, additional information may subsequently become available to us, which may allow us to make a more accurate estimate in future periods. In this event, we are required to record adjustments in future periods when the actual level of activity becomes more certain. Such increases or decreases are generally considered to be changes in estimates and will be reflected in our Consolidated Statements of Operations in the period they become known.

Inventory

We value inventory at the lower of cost or net realizable value. We determine the cost of inventory using the standard-cost method, which approximates actual cost based on a first-in, first-out method. We analyze our inventory levels quarterly and write down inventory subject to expiry in excess of expected requirements, or that has a cost basis in excess of its expected net realizable value. On a quarterly basis, we analyze our estimated production levels for the following twelve month period, which is our normal operating cycle, and reclassify inventory we expect to use or sell in periods beyond the next twelve months into Other long-term assets in the Consolidated Balance Sheets.

Clinical Trial Accruals

All of our clinical trials have been executed with support from contract research organizations and other vendors. We accrue costs for clinical trial activities performed by contract research organizations based upon the estimated amount of work completed on each trial. For clinical trial expenses, the significant factors used in estimating accruals include

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number of patients enrolled, the activities to be performed for each patient, the number of active clinical sites and the duration for which the patients will be enrolled in the trial. We monitor patient enrollment levels and related activities to the extent possible through internal reviews, correspondence with contract research organizations and review of contractual terms. We base our estimates on the best information available at the time. However, additional information may become available to us, which may allow us to make a more accurate estimate in future periods. If we do not identify costs that we have begun to incur or if we underestimate or overestimate the level of services performed or the costs of these services, our actual expenses could differ from our estimates.

Stock Option Valuation

Our estimate of compensation expense requires us to determine the appropriate fair value model and a number of complex and subjective assumptions including our stock price volatility, employee exercise patterns and related tax effects. The most significant assumptions are our estimates of the expected volatility and the expected term of the stock option.

The value of a stock option is derived from its potential for appreciation. The more volatile the stock, the more valuable the option becomes because of the greater possibility of significant changes in stock price. Because there is a market for options on our common stock, we have considered implied volatilities as well as our historical volatilities when developing an estimate of expected volatility. The expected option term also has a significant effect on the value of the option. The longer the term, the more time the option holder has to allow the stock price to increase without a cash investment and thus, the more valuable the option. Further, lengthier option terms provide more opportunity to exploit market highs. However, empirical data show that employees typically do not wait until the end of the contractual term of a nontransferable option to exercise. Accordingly, we are required to estimate the expected term of the option for input to an option-pricing model. As required under generally accepted accounting principles, we review our valuation assumptions at each grant date and, as a result, from time to time we change the valuation assumptions we use to value stock options granted. The assumptions used in calculating the fair value of stock options represent management’s best estimates, but these estimates involve inherent uncertainties and the application of management judgment. As a result, if factors change and we use different assumptions, our stock-based compensation could be materially different in the future. For additional description of our stock-based compensation, see “Note 7. Stock-based Compensation” to our “Notes to Consolidated Financial Statements” contained in Part II, Item 8 of this Annual Report on Form 10-K.

Income Taxes

Our income tax benefit (provision) is computed under the asset and liability method. Significant estimates are required in determining our income tax benefit (provision). Some of these estimates are based on interpretations of existing tax laws or regulations. We recognize deferred tax assets and liabilities for the expected future tax consequences of events that have been included in the financial statements or tax returns. Under this method, deferred tax assets and liabilities are determined on the basis of the difference between the tax basis of assets and liabilities and their respective financial reporting amounts (temporary differences) at enacted tax rates in effect for the years in which the differences are expected to reverse. A valuation allowance is established for deferred tax assets for which it is more likely than not that some portion or all of the deferred tax assets, including net operating losses and tax credits, will not be realized. We periodically re-assess the need for a valuation allowance against our deferred tax assets based on various factors including our historical earnings experience by taxing jurisdiction, and forecasts of future operating results and utilization of net operating losses and tax credits prior to their expiration. Significant judgment is required in making this assessment and, to the extent that a reversal of any portion of our valuation allowance against our deferred tax assets is deemed appropriate, a tax benefit will be recognized against our income tax provision in the period of such reversal. Prior to 2018, we recorded a valuation allowance that fully offset our deferred tax assets. In the fourth quarter of 2018, based on our evaluation of various factors, including our achievement of a cumulative three-year income position as of December 28, 2018 and forecasts of future operating results, we released substantially all of our valuation allowance against our deferred tax assets and recorded a corresponding income tax benefit as described in “Note 8. Income Taxes”, below. We continue to maintain a valuation allowance against our California state deferred tax assets.

Recent Accounting Pronouncements

For a description of the expected impact of recent accounting pronouncements, see “Note 1. Organization and Summary of Significant Accounting Policies” in the “Notes to Consolidated Financial Statements” contained in Part II, Item 8 of this Annual Report on Form 10-K.

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Item 7A. Quantitative and Qualitative Disclosures About Market Risk

As of December 31, 2018 and 2017, our exposure to market risk for changes in interest rates relates primarily to our investment portfolio. As of December 31, 2018 and 2017, we had cash and investments of $851.6 million and $457.2 million, respectively. Our investments are subject to interest rate risk, and our interest income may fluctuate due to changes in interest rates. We manage market risk through diversification requirements mandated by our investment policy, which limits the amount of our portfolio that can be invested in a single issuer. We limit our credit risk by limiting purchases to high-quality issuers. For our investments, we obtain the estimated effects of hypothetical interest rate changes from the same third-party pricing sources we use to value our investments. As of December 31, 2018 and 2017, an increase in the interest rates of one percentage point would have had a net adverse change in the fair value of interest rate sensitive assets of $3.4 million and $1.6 million, respectively.

Royalty revenues and sales-based milestones we receive from our collaboration agreements with Ipsen and Genentech are a percentage of the net sales made by those partners from sales made in countries outside the U.S. and are denominated in currencies in which the product is sold, which is predominantly the Euro. The royalty payments on these ex-U.S. sales are calculated initially in the currency in which the sale is made and are then converted into the U.S. dollar to determine the amount our partners pay us. Fluctuations in the exchange ratio of the U.S. dollar and these foreign currencies will have the effect of increasing or decreasing our revenues even if the amount of units sold does not change. For example, if the U.S. dollar strengthens against a foreign currency, then our royalty revenues will decrease for the same number of units sold in that foreign currency and the date we achieve sales-based milestones would be delayed. For the year ended December 31, 2018 and 2017, an average 10% strengthening of the U.S. dollar relative to the currencies in which these products are sold would have resulted in revenues being reduced by approximately $3.8 million and $1.0 million, respectively.

Item 8. Financial Statements and Supplementary Data

EXELIXIS, INC.

INDEX TO CONSOLIDATED FINANCIAL STATEMENTS

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Report of Independent Registered Public Accounting Firm

To the Stockholders and the Board of Directors of Exelixis, Inc.

Opinion on the Financial Statements

We have audited the accompanying consolidated balance sheets of Exelixis, Inc. (the "Company") as of December 28, 2018 and December 29, 2017, the related consolidated statements of operations, comprehensive income (loss), stockholders' equity (deficit) and cash flows for each of the three fiscal years in the period ended December 28, 2018, and the related notes (collectively referred to as the "consolidated financial statements"). In our opinion, the consolidated financial statements present fairly, in all material respects, the financial position of the Company at December 28, 2018 and December 29, 2017, and the results of its operations and its cash flows for each of the three fiscal years in the period ended December 28, 2018, in conformity with U.S. generally accepted accounting principles. We also have audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States) (PCAOB), the Company's internal control over financial reporting as of December 28, 2018, based on criteria established in Internal Control-Integrated Framework issued by the Committee of Sponsoring Organizations of the Treadway Commission (2013 Framework) and our report dated February 22, 2019 expressed an unqualified opinion thereon.

Adoption of ASU No. 2014-09

As discussed in Note 1 to the consolidated financial statements, the Company changed its method for recognizing revenue as a result of the adoption of Accounting Standards Update No. 2014-09, Revenue from Contracts with Customers (Topic 606), effective December 30, 2017.

Basis for Opinion

These financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on the Company's financial statements based on our audits. We are a public accounting firm registered with the PCAOB and are required to be independent with respect to the Company in accordance with the U.S. federal securities laws and the applicable rules and regulations of the Securities and Exchange Commission and the PCAOB. We conducted our audits in accordance with the standards of the PCAOB. Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the financial statements are free of material misstatement, whether due to error or fraud. Our audits included performing procedures to assess the risks of material misstatement of the financial statements, whether due to error or fraud, and performing procedures that respond to those risks. Such procedures included examining, on a test basis, evidence regarding the amounts and disclosures in the financial statements. Our audits also included evaluating the accounting principles used and significant estimates made by management, as well as evaluating the overall presentation of the financial statements. We believe that our audits provide a reasonable basis for our opinion.

/s/ Ernst & Young LLP

We have served as the Company's auditor since 2002.

Redwood City, California

February 22, 2019

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EXELIXIS, INC.
CONSOLIDATED BALANCE SHEETS
(in thousands, except share and per share data)

	December 31,	
	2018	2017
ASSETS		
Current assets:		
Cash and cash equivalents	$314,775	$183,164
Short-term investments	378,559	204,607
Short-term restricted cash and investments	—	504
Trade receivables, net	162,771	77,300
Other receivables	16,056	3,892
Inventory, net	9,838	6,657
Prepaid expenses and other current assets	15,017	8,750
Total current assets	897,016	484,874
Long-term investments	157,187	64,255
Long-term restricted cash and investments	1,100	4,646
Property and equipment, net	50,897	25,743
Operating lease right-of-use assets	5,867	—
Deferred tax assets, net	244,111	—
Goodwill	63,684	63,684
Other long-term assets	2,424	12,092
Total assets	$1,422,286	$655,294
LIABILITIES AND STOCKHOLDERS' EQUITY		
Current liabilities:		
Accounts payable	$10,901	$9,575
Accrued compensation and benefits	32,142	21,073
Accrued clinical trial liabilities	18,231	19,849
Rebates and fees due to customers	14,954	7,565
Accrued collaboration liabilities	7,419	8,974
Current portion of deferred revenue	—	31,984
Other current liabilities	21,825	16,150
Total current liabilities	105,472	115,170
Long-term portion of deferred revenue	15,897	238,520
Long-term portion of lease liabilities	12,178	14,938
Other long-term liabilities	1,286	1,705
Total liabilities	134,833	370,333
Commitments		
Stockholders' equity:		
Preferred stock, $0.001 par value, 10,000,000 shares authorized and no shares issued	—	—
Common stock, $0.001 par value; 400,000,000 shares authorized; issued and outstanding: 299,876,080 and 296,209,426 at December 31, 2018 and 2017, respectively	300	296
Additional paid-in capital	2,168,217	2,114,184
Accumulated other comprehensive loss	(701)	(347)
Accumulated deficit	(880,363)	(1,829,172)
Total stockholders' equity	1,287,453	284,961
Total liabilities and stockholders' equity	$1,422,286	$655,294

The accompanying notes are an integral part of these Consolidated Financial Statements.

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EXELIXIS, INC.
CONSOLIDATED STATEMENTS OF OPERATIONS
(in thousands, except per share data)

	Year Ended December 31,		
	2018	2017	2016
Revenues:			
Net product revenues	$619,279	$349,008	$135,375
Collaboration revenue	234,547	103,469	56,079
Total revenues	853,826	452,477	191,454
Operating expenses:			
Cost of goods sold	26,348	15,066	6,552
Research and development	182,257	112,171	95,967
Selling, general and administrative	206,366	159,362	116,145
Restructuring (recovery) charge	—	(32)	914
Total operating expenses	414,971	286,567	219,578
Income (loss) from operations	438,855	165,910	(28,124)
Other income (expense), net:			
Interest income	12,840	4,883	2,578
Interest expense	—	(8,679)	(33,060)
Other, net	397	(3,537)	(11,616)
Total other income (expense), net:	13,237	(7,333)	(42,098)
Income (loss) before income taxes	452,092	158,577	(70,222)
Income tax benefit (provision)	237,978	(4,350)	—
Net income (loss)	$690,070	$154,227	$(70,222)
Net income (loss) per share, basic	$2.32	$0.52	$(0.28)
Net income (loss) per share, diluted	$2.21	$0.49	$(0.28)
Shares used in computing net income (loss) per share, basic	297,892	293,588	250,531
Shares used in computing net income (loss) per share, diluted	312,803	312,003	250,531

The accompanying notes are an integral part of these Consolidated Financial Statements.

EXELIXIS, INC.
CONSOLIDATED STATEMENTS OF COMPREHENSIVE INCOME (LOSS)
(in thousands)

	Year Ended December 31,		
	2018	2017	2016
Net income (loss)	$690,070	$154,227	$(70,222)
Other comprehensive income (loss) [1]	(354)	69	(184)
Comprehensive income (loss)	$689,716	$154,296	$(70,406)

(1) Other comprehensive income (loss) consisted solely of unrealized gains or losses, net, on available-for-sale securities arising during the periods presented. There were nominal or no reclassification adjustments to net income (loss) resulting from realized gains or losses on the sale of securities. During the year ended December 31, 2018, there was a tax benefit of $0.2 million related to other comprehensive income as a result of the release of our valuation allowance for our deferred tax assets; there was no income tax benefit or provision related to other comprehensive income (loss) during the remaining periods presented.

The accompanying notes are an integral part of these Consolidated Financial Statements.

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EXELIXIS, INC.
CONSOLIDATED STATEMENTS OF STOCKHOLDERS' EQUITY (DEFICIT)
(in thousands, except share data)

	Common Stock		Additional Paid-in Capital	Accumulated Other Comprehensive Loss	Accumulated Deficit	Total Stockholders' Equity (Deficit)
	Shares	Amount				
Balance at December 31, 2015	227,960,943	$ 228	1,772,123	(232)	(1,912,925)	$(140,806)
Net loss	—	—	—	—	(70,222)	(70,222)
Other comprehensive loss	—	—	—	(184)	—	(184)
Issuance of common stock in settlement of convertible notes	54,009,279	54	253,026	—	—	253,080
Issuance of common stock under equity incentive and stock purchase plans	7,953,576	8	24,530	—	—	24,538
Stock-based compensation	—	—	22,912	—	—	22,912
Balance at December 31, 2016	289,923,798	290	2,072,591	(416)	(1,983,147)	89,318
Adoption of Accounting Standards Update (ASU) No. 2016-09, Compensation—Stock Compensation (Topic 718): Improvements to Employee Share-Based Payment Accounting	—	—	252	—	(252)	—
Net income	—	—	—	—	154,227	154,227
Other comprehensive income	—	—	—	69	—	69
Issuance of common stock under equity incentive and stock purchase plans	5,408,177	5	17,404	—	—	17,409
Issuance of common stock on exercise of warrants	877,451	1	(1)	—	—	—
Stock-based compensation	—	—	23,938	—	—	23,938
Balance at December 31, 2017	296,209,426	296	2,114,184	(347)	(1,829,172)	284,961
Adoption of ASU No. 2014-09, Revenue from Contracts with Customers (Topic 606)	—	—	—	—	258,505	258,505
Adoption of ASU No. 2016-02, Leases (Topic 842)	—	—	—	—	234	234
Net income	—	—	—	—	690,070	690,070
Other comprehensive loss	—	—	—	(354)	—	(354)
Issuance of common stock under equity incentive and stock purchase plans	3,666,654	4	13,407	—	—	13,411
Stock-based compensation	—	—	40,626	—	—	40,626
Balance at December 31, 2018	299,876,080	$ 300	$2,168,217	$ (701)	$(880,363)	$1,287,453

The accompanying notes are an integral part of these Consolidated Financial Statements.

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EXELIXIS, INC.
CONSOLIDATED STATEMENTS OF CASH FLOWS
(in thousands)

	Year Ended December 31,		
	2018	2017	2016
Net income (loss)	$690,070	$154,227	$(70,222)
Adjustments to reconcile net income (loss) to net cash provided by operating activities:			
Depreciation and amortization	4,915	1,187	1,002
Stock-based compensation	40,626	23,938	22,912
401(k) matching contributions made in common stock	3,696	1,640	1,036
Amortization of right-of-use assets	2,854	—	—
Deferred taxes	(244,111)	—	—
Loss on extinguishment of debt	—	6,239	13,901
Amortization of debt discounts and debt issuance costs	—	182	8,432
Interest paid in kind	—	(11,825)	8,008
Gain on other equity investments	(209)	(2,980)	(2,494)
Other	(2,358)	(51)	562
Changes in operating assets and liabilities:			
Trade receivables, net	(85,471)	(43,299)	(38,680)
Other receivables	(4,410)	2,460	3,362
Inventory, net	(3,181)	(3,319)	(722)
Prepaid expenses and other current assets	(3,029)	(3,268)	(1,610)
Other long-term assets	(1,086)	430	1,077
Accounts payable	856	3,010	164
Accrued compensation and benefits	11,069	739	16,705
Accrued clinical trial liabilities	(1,618)	5,718	(3,940)
Rebates and fees due customers	7,389	4,145	3,866
Accrued collaboration liability	(1,555)	6,928	(10,938)
Deferred revenue	271	13,745	256,759
Long-term portion of lease liabilities	(1,225)	14,938	—
Other current and long-term liabilities	2,227	(9,173)	1,224
Net cash provided by operating activities	415,720	165,611	210,404
Cash flows from investing activities:			
Purchases of property and equipment	(33,297)	(21,143)	(1,703)
Proceeds from sale of property and equipment	308	164	97
Purchases of investments	(557,832)	(319,090)	(369,187)
Proceeds from maturities of investments	280,826	336,590	151,485
Proceeds from sale of investments	11,936	37,294	2,266
Proceeds from other equity investments	209	2,980	2,494
Net cash (used in) provided by investing activities	(297,850)	36,795	(214,548)
Cash flows from financing activities:			
Proceeds from exercise of stock options	12,076	17,555	25,327
Proceeds from employee stock purchase plan	5,202	4,868	2,187
Taxes paid related to net share settlement of equity awards	(7,574)	(6,563)	(4,108)
Principal payments on financing lease obligation	(13)	—	—
Principal repayments of debt	—	(185,788)	(575)
Payments on conversion of convertible notes	—	—	(7,135)
Net cash provided by (used in) financing activities	9,691	(169,928)	15,696

Net increase in cash, cash equivalents and restricted cash	127,561	32,478	11,552
Cash, cash equivalents and restricted cash at beginning of period	188,314	155,836	144,284
Cash, cash equivalents and restricted cash at end of period	$315,875	$188,314	$155,836

Continued on next page

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EXELIXIS, INC.
CONSOLIDATED STATEMENTS OF CASH FLOWS - continued
(in thousands)

	Year Ended December 31,		
	2018	2017	2016
Supplemental cash flow disclosure:			
Cash paid for interest	$—	$20,460	$21,044
Cash paid for taxes	$10,677	$538	$190
Non-cash investing and financing activities:			
Property and equipment deemed to have been acquired in build-to-suit lease	$—	$14,530	$—
Right-of-use assets obtained in exchange for lease obligations [(1)]	$17,180	—	$—
Unpaid liabilities incurred to acquire Property and equipment	$802	$524	$—
Issuance of common stock in settlement of convertible notes	$—	$—	$286,925

(1) Amounts for the year ended December 31, 2018 include the transition adjustment for the adoption of Topic 842.

The accompanying notes are an integral part of these Consolidated Financial Statements.

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EXELIXIS, INC.
NOTES TO CONSOLIDATED FINANCIAL STATEMENTS
NOTE 1. ORGANIZATION AND SUMMARY OF SIGNIFICANT ACCOUNTING POLICIES

Organization

Exelixis, Inc. (Exelixis, we, our or us) is an oncology-focused biotechnology company that strives to accelerate the discovery, development and commercialization of new medicines for difficult-to-treat cancers. Since we were founded in 1994, four products resulting from our discovery efforts have progressed through clinical development and received regulatory approval; three have a growing commercial presence in markets worldwide, and we expect that the fourth will soon enter the marketplace in Japan. Two are derived from cabozantinib, an inhibitor of multiple tyrosine kinases including MET, AXL, VEGF receptors and RET. These are: CABOMETYX® (cabozantinib) tablets approved for advanced renal cell carcinoma (RCC) and previously treated hepatocellular carcinoma (HCC) and COMETRIQ® (cabozantinib) capsules approved for progressive, metastatic medullary thyroid cancer (MTC). Other commercially available products resulting from our discovery efforts include COTELLIC® (cobimetinib), an inhibitor of MEK approved as part of a combination regimen to treat advanced melanoma and marketed under a collaboration with Genentech, Inc. (a member of the Roche Group) (Genentech), and MINNEBRO™ (esaxerenone), an oral, non-steroidal, selective blocker of the mineralocorticoid receptor (MR) approved for the treatment of hypertension in Japan and licensed to Daiichi Sankyo Company, Limited (Daiichi Sankyo).

Basis of Consolidation

The accompanying Consolidated Financial Statements include the accounts of Exelixis and those of our wholly-owned subsidiaries. These entities' functional currency is the U.S. dollar. All intercompany balances and transactions have been eliminated.

Basis of Presentation

We have adopted a 52- or 53-week fiscal year policy that generally ends on the Friday closest to December 31st. Fiscal year 2016 ended on December 30, 2016; fiscal year 2017 ended on December 29, 2017; and fiscal year 2018 ended on December 28, 2018. For convenience, references in this report as of and for the fiscal years ended (or ending, as applicable) December 30, 2016, December 29, 2017, and December 28, 2018 are indicated as being as of and for the years ended (or ending, as applicable) December 31, 2016, 2017 and 2018, respectively. All annual periods presented are 52-week fiscal years and all interim periods presented are 13-week fiscal quarters.

Segment Information

We operate in one business segment that focuses on discovery, development and commercialization of new medicines to improve care and outcomes for people with cancer. Our Chief Executive Officer, as the chief operating decision-maker, manages and allocates resources to our operations on a total consolidated basis. Consistent with this decision-making process, our Chief Executive Officer uses consolidated, single-segment financial information for purposes of evaluating performance, forecasting future period financial results, allocating resources and setting incentive targets.

All of our long-lived assets are located in the U.S. See "Note 2. Revenues" for enterprise-wide disclosures about product sales, revenues from major customers and revenues by geographic region.

Use of Estimates

The preparation of the accompanying Consolidated Financial Statements conforms to accounting principles generally accepted in the U.S., which requires management to make judgments, estimates and assumptions that affect the reported amounts of assets, liabilities, equity, revenues and expenses, and related disclosures. On an ongoing basis, management evaluates its estimates including, but not limited to: those related to revenue recognition, including determining the nature and timing of satisfaction of performance obligations, and determining the standalone selling price of performance obligations, and variable consideration such as rebates, chargebacks, sales returns and sales allowances as well as milestones included in collaboration arrangements; the amounts of revenues and expenses under our profit and loss sharing agreement; recoverability of inventory; operating lease assets and liabilities; the amounts of deferred tax assets and liabilities including the related valuation allowance; the accrual for certain liabilities including accrued clinical trial liabilities; and valuations of equity awards used to determine stock-based compensation, including certain awards with vesting subject to market or performance conditions. We base our estimates on

historical experience and on various other market-specific

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and other relevant assumptions that we believe to be reasonable under the circumstances, the results of which form the basis for making judgments about the carrying values of assets and liabilities that are not readily apparent from other sources. Actual results could differ materially from those estimates.

Recently Adopted Accounting Pronouncements

Restricted Cash

In January 2018, we adopted ASU No. 2016-18, Statement of Cash Flows (Topic 230): Restricted Cash (a consensus of the FASB Emerging Issues Task Force), (ASU 2016-18). ASU 2016-18 requires that a statement of cash flows explain the change during the period in the total of cash, cash equivalents, and amounts generally described as restricted cash. Therefore, amounts generally described as restricted cash are included with cash when reconciling the beginning-of-period and end-of-period total amounts shown on the statement of cash flows. ASU 2016-18 was adopted using the retrospective transition method in the accompanying Consolidated Financial Statements.

As a result of the adoption of ASU 2016-18, we no longer include purchases of restricted cash and proceeds from maturities of restricted cash in our cash flows from investing activities. Accordingly, the adoption of ASU 2016-18 resulted in a $1.0 million and $1.5 million increase in Net cash provided by investing activities for the years ended December 31, 2017 and 2016, respectively.

See “Note 4. Cash and Investments—Cash, Cash Equivalents and Restricted Cash” for a reconciliation of cash and cash equivalents presented in our previously published Consolidated Statement of Cash Flows for the years ended December 31, 2017 and 2016 and Cash, cash equivalents and restricted cash reported in the accompanying Consolidated Statement of Cash Flows for the same periods.

Revenue

On January 1, 2018, we adopted Topic 606 using the modified retrospective method applied to those contracts that were not completed as of January 1, 2018. Results for the year ended December 31, 2018 are presented under Topic 606, while prior period amounts are not adjusted and continue to be reported in accordance with our historic accounting under previous revenue recognition guidance, Accounting Standards Codification (ASC) Topic 605: Revenue Recognition (Topic 605).

Leases

On July 1, 2018 we early adopted Topic 842. We adopted Topic 842 using the modified retrospective approach with a cumulative-effect adjustment as of January 1, 2018 in accordance with ASU No. 2018-11, Leases (Topic 842) - Targeted Improvements. Results for the year ended December 31, 2018 are presented under Topic 842. Prior period amounts have not been adjusted and continue to be reported in accordance with our historical accounting under previous lease guidance, ASC Topic 840: Leases (Topic 840). We elected the package of practical expedients permitted under the transition guidance within the new standard, which among other things, allowed us to carry forward the historical lease classification of those leases in place as of January 1, 2018.

Impact of Adoption of Topic 606 and Topic 842

We recorded a net reduction of $258.5 million to opening accumulated deficit as of January 1, 2018, due to the cumulative impact of adopting Topic 606, with the impact primarily relating to a change in the recognition of upfront and non-substantive milestone payments received related to our collaboration arrangements with Ipsen Pharma SAS (Ipsen) and Takeda Pharmaceutical Company Ltd. (Takeda). The adoption of Topic 606 did not have an impact on our recognition of revenue from product sales.

We also recorded a net reduction of $0.2 million to opening accumulated deficit as of January 1, 2018, due to the cumulative impact of adopting Topic 842, with the impact relating to a change in the classification of certain of our buildings in our Lease Agreement (the Lease) with Ascentris 105, LLC (Ascentris) from a build to suit lease to an operating lease. For a description of the Lease, see “Note 11. Commitments.”

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The impact of the adoption of Topic 606 and Topic 842 on the accompanying Consolidated Balance Sheet as of January 1, 2018 was as follows (in thousands):

	December 31, 2017	Adjustments Due to the Adoption of Topic 606	Adjustments Due to the Adoption of Topic 842	January 1, 2018
Contract assets: unbilled collaboration revenue, gross:				
Current portion	$—	$9,588	$ —	$9,588
Long-term portion	$—	$12,247	$ —	$12,247
Other receivables	$3,892	$—	$ 7,743	$11,635
Property and equipment, net	$25,743	$—	$ (14,530)	$11,213
Operating lease right-of-use assets	$—	$—	$ 8,579	$8,579
Contract liabilities: deferred revenue, gross:				
Current portion	$31,984	$(23,591)	$ —	$8,393
Long-term portion	$238,520	$(213,079)	$ —	$25,441
Operating lease liabilities:				
Other current liabilities[(1)]	$16,150	$—	$ 3,173	$19,323
Long-term portion of lease liabilities [(2)]	$14,938	$—	$ (1,615)	$13,323
Accumulated deficit	$(1,829,172)	$258,505	$ 234	$(1,570,433)

(1) Includes deferred rent and current portion of operating lease liabilities.

(2) Long-term portion of operating lease liabilities and Financing obligation for build-to-suit lease.

The adjustments due to the adoption of Topic 606 primarily related to a reduction in deferred revenue driven by the allocation of the transaction price to our license performance obligations in the Ipsen and Takeda collaborations, which were determined to be functional intellectual property that was transferred at a point in time and as a result, revenue was recorded at a point in time. Previously under Topic 605, revenue related to the upfront payments and one non-substantive milestone payment earned in 2016 had been deferred over the estimated period of performance pursuant to the terms of the contract. Contract assets as of January 1, 2018 primarily related to estimated revenue for reimbursements for our continuing research and development services and the $10.0 million milestone from Ipsen's filing with the European Medicines Agency (EMA) for cabozantinib as a treatment for patients with previously treated HCC, that was deemed probable under Topic 606 prior to January 1, 2018. Deferred revenue as of January 1, 2018 was related to the up-front, nonrefundable, fees and milestones earned that were allocated to our research and development services performance obligation which had not been satisfied as of that date. Contract assets and liabilities are netted by collaboration agreement in our Consolidated Balance Sheets; however, for illustration purposes the above amounts are shown prior to netting.

The adjustments due to the adoption of Topic 842 primarily related to the recognition of an operating lease right-of-use asset and operating lease liability for the Lease. In addition, the adoption of Topic 842 resulted in a change in classification of the build-to-suit component of the Lease under Topic 840 to an operating lease under Topic 842 and as a result we derecognized the estimated fair value of the building shells that were included in Property and equipment, net as of December 31, 2017, as we had been deemed to own these buildings under Topic 840. For a description of the Lease, see "Note 11. Commitments" in these Consolidated Financial Statements.

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The impact of the adoption of Topic 606 and Topic 842 on the accompanying Consolidated Statements of Operations for year ended December 31, 2018 was as follows (in thousands):

	Year Ended December 31, 2018			
	As Reported	Effect of Adoption of Topic 606 Higher / (Lower)	Effect of Adoption of Topic 842 Higher / (Lower)	Balances Without the Adoption of Topic 606 or 842
Collaboration revenues	$234,547	$(35,882)	$ —	$270,429
Total revenues	$853,826	$(35,882)	$ —	$889,708
Selling, general and administrative expenses	$206,366	$—	$ 1,204	$205,162
Total operating expenses	$414,971	$—	$ 1,204	$413,767
Interest expense	$—	$—	$ (631)	$(631)
Total other income (expense), net	$13,237	$—	$ 631	$12,606
Income before income taxes	$452,092	$(35,882)	$ (573)	$488,547
Income tax benefit (provision)	$237,978	$(48,325)	$ 73	$286,230
Net income	$690,070	$(84,207)	$ (500)	$774,777
Net income per share, basic	$2.32	$(0.28)	$ —	$2.60
Net income per share, diluted	$2.21	$(0.27)	$ —	$2.48

If we had not adopted Topic 606, we would also have recognized a $10.0 million milestone in the first quarter of 2018 upon the validation of Ipsen's filing with the EMA for cabozantinib as a treatment for patients with previously treated HCC that was recognized under Topic 606 as part of our adoption transition adjustment on January 1, 2018. The adoption of Topic 606 also resulted in a reduction of previously reported deferred revenue that was recorded as part of our adoption transition adjustment as of January 1, 2018.

Cash and Investments

We consider all highly liquid investments purchased with an original maturity of three months or less to be cash equivalents. Cash equivalents include high-grade, short-term investments in money market funds and marketable debt securities which are subject to minimal credit and market risk.

We have designated all investments in marketable debt securities as available-for-sale and therefore, such investments are reported at fair value, with unrealized gains and losses recorded in accumulated other comprehensive loss. For securities sold prior to maturity, the cost of securities sold is based on the specific identification method. Realized gains and losses on the sale of investments are included in Interest and other income, net in the accompanying Consolidated Statements of Operations.

We classify those investments that we do not require for use in current operations and that mature in more than 12 months as Long-term investments in the accompanying Consolidated Balance Sheets.

All of our investments are subject to a quarterly impairment review. We recognize an impairment charge when a decline in the fair value of an investment below its cost basis is judged to be other-than-temporary. Factors considered in determining whether a loss is temporary include the length of time and extent to which the investments fair value has been less than their cost basis, the financial condition and near-term prospects of the issuer, extent of the loss related to credit of the issuer, the expected cash flows from the security, our intent to sell the security and whether or not we will be required to sell the security before we are able to recover our carrying value.

Accounts Receivable

Trade accounts receivable are recorded net of allowances for chargebacks and cash discounts for prompt payment, as described further below. Estimates of our allowance for doubtful accounts are determined based on existing contractual payment terms, historical payment patterns of our customers and individual customer circumstances, an analysis of days sales outstanding by geographic region and a review of the local economic environment and its potential impact on government funding and reimbursement practices. Historically, the amounts of uncollectible accounts receivable that have been written off were nominal.

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Fair Value Measurements

Fair value reflects the amounts that would be received upon sale of an asset or paid to transfer a liability in an orderly transaction between market participants at the measurement date (exit price). We disclose the fair value of financial instruments for assets and liabilities for which the value is practicable to estimate. For those financial instruments measured and recorded at fair value on a recurring basis, we also provide fair value hierarchy information in these Notes to Consolidated Financial Statements. The fair value hierarchy has the following three levels:

Level 1 – Fair values are determined utilizing quoted prices (unadjusted) in active markets for identical assets and liabilities that the reporting entity can access at the measurement date.

Level 2 – Fair values are determined utilizing observable inputs that are observable either directly or indirectly, other than quoted prices in active markets for identical assets and liabilities. These inputs include using prices from independent pricing services based on quoted prices in active markets for similar instruments or on industry models using data inputs, such as interest rates and prices that can be directly observed or corroborated in active markets.

Level 3 – Fair values are determined utilizing inputs that are both significant to the fair value measurement and unobservable.

A review of the fair value hierarchy classification is conducted on a quarterly basis. Changes in the observability of valuation inputs may result in a reclassification of levels for certain investments within the fair value hierarchy.

Inventory

We value inventory at the lower of cost or net realizable value. We determine the cost of inventory using the standard-cost method, which approximates actual cost based on a first-in, first-out method. We analyze our inventory levels quarterly and write down inventory subject to expiry in excess of expected requirements, or that has a cost basis in excess of its expected net realizable value. These inventory-related costs are recognized as Cost of goods sold in the accompanying Consolidated Statements of Operations.

On a quarterly basis, we analyze our estimated production levels for the following twelve month period, which is our normal operating cycle, and reclassify inventory we expect to use or sell in periods beyond the next twelve months into Other long-term assets in the accompanying Consolidated Balance Sheets.

Property and Equipment

Property and equipment are recorded at cost and depreciated using the straight-line method over the following estimated useful lives once it is placed into service:

Asset Category	Estimated Useful Life
Lab equipment	5 years
Furniture and fixtures	7 years
Office equipment	5 years
Computer equipment and software	3 years
Leasehold improvements	7 to 15 years

Leasehold improvements are depreciated over the lesser of their estimated useful lives or the remainder of the lease term. Capitalized software includes certain internal use computer software costs. Repairs and maintenance costs are charged to expense as incurred.

Goodwill

Goodwill amounts have been recorded as the excess purchase price over tangible assets, liabilities and intangible assets acquired based on their estimated fair value. Goodwill is not subject to amortization. We assess the recoverability of our goodwill annually, or more frequently whenever events or changes in circumstances indicate that the carrying amount of a reporting unit may exceed its fair value. The assessment of recoverability may first consider qualitative factors to determine whether the existence of events or circumstances leads to a determination that it is more likely than not that the fair value of a reporting unit is less than its carrying amount. A quantitative assessment is performed if the qualitative assessment results in a more-likely-than-not determination or if a qualitative assessment is not performed. The quantitative

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assessment considers whether the carrying amount of a reporting unit exceeds its fair value, in which case an impairment charge is recorded to the extent the carrying amount of the reporting unit's goodwill exceeds its implied fair value. We continue to operate in one segment, which is also considered to be our sole reporting unit and therefore, goodwill was tested for impairment at the enterprise level as of December 31, 2018 and 2017. We did not recognize any impairment charges in any of the periods presented.

Long-Lived Assets

The carrying value of our long-lived assets, which includes property and equipment, is reviewed for impairment whenever events or changes in circumstances indicate that the asset may not be recoverable. An impairment loss would be recognized when estimated future cash flows expected to result from the use of the asset and its eventual disposition is less than its carrying amount.

Revenue

Topic 606 supersedes all previous revenue recognition requirements in accordance with generally accepted accounting principles. This standard applies to all contracts with customers, except for contracts that are within the scope of other standards, such as leases, insurance, collaboration arrangements and financial instruments. Under Topic 606, an entity recognizes revenue when its customer obtains control of promised goods or services, in an amount that reflects the consideration to which the entity is entitled to in exchange for those goods or services. To determine revenue recognition for arrangements that we determine are within the scope of Topic 606, we perform the following five steps: (i) identify the contract(s) with a customer; (ii) identify the performance obligations in the contract; (iii) determine the transaction price; (iv) allocate the transaction price to the performance obligations in the contract; and (v) recognize revenue when (or as) we satisfy a performance obligation. We only apply the five-step model to contracts when it is probable that we will collect the consideration we are entitled to in exchange for the goods or services we transfer to the customer.

Net Product Revenues

We sell our products principally to specialty distributors and specialty pharmacy providers, or collectively, our Customers. These Customers subsequently resell our products to health care providers and patients. In addition to distribution agreements with Customers, we enter into arrangements with health care providers and payors that provide for government-mandated and/or privately-negotiated rebates, chargebacks and discounts with respect to the purchase of our products. Revenues from product sales are recognized when the Customer obtains control of our product, which occurs at a point in time, typically upon delivery to the Customer.

Product Sales Discounts and Allowances

Revenues from product sales are recorded at the net sales price (transaction price), which includes estimates of variable consideration for which reserves are established and that result from discounts, chargebacks, rebates, co-pay assistance, returns and other allowances that are offered within contracts between us and our Customers, health care providers, payors and other indirect customers relating to the sales of our products. These reserves are based on the amounts earned or to be claimed on the related sales and are classified as reductions of accounts receivable (if the amount is payable to the Customer) or a current liability (if the amount is payable to a party other than a Customer). Where appropriate, these estimates take into consideration a range of possible outcomes that are probability-weighted for relevant factors such as our historical experience, current contractual and statutory requirements, specific known market events and trends, industry data and forecasted Customer buying and payment patterns. Overall, these reserves reflect our best estimates of the amount of consideration to which we are entitled based on the terms of our contracts. The amount of variable consideration that is included in the transaction price may be constrained, and is included in the net sales price only to the extent that it is probable that a significant reversal in the amount of the cumulative revenue recognized will not occur in a future period. Actual amounts of consideration ultimately received may differ from our estimates. If actual results in the future vary from our estimates, we will adjust these estimates, which would affect net product revenues and earnings in the period such variances become known.

Chargebacks: Chargebacks are discounts that occur when contracted customers purchase directly from a specialty distributor. Contracted customers, which currently consist primarily of Public Health Service institutions, non-profit clinics, Federal government entities purchasing via the Federal Supply Schedule and Group Purchasing Organizations,

and health maintenance organizations, generally purchase the product at a discounted price. The specialty distributor, in turn, charges back to us the difference between the price initially paid by the specialty distributor and the discounted price paid to the

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specialty distributor by the customer. The allowance for chargebacks is based on an estimate of sales to contracted customers.

Discounts for Prompt Payment: Our Customers in the U.S. receive a discount of 2% for prompt payment. We expect our Customers will earn 100% of their prompt payment discounts and, therefore, we deduct the full amount of these discounts from total product sales when revenues are recognized.

Rebates: Allowances for rebates include mandated discounts under the Medicaid Drug Rebate Program, other government programs and commercial contracts. Rebate amounts owed after the final dispensing of the product to a benefit plan participant are based upon contractual agreements or legal requirements with public sector benefit providers, such as Medicaid. The allowance for rebates is based on statutory or contractual discount rates and expected utilization. Our estimates for the expected utilization of rebates are based on customer and payer data received from the specialty pharmacies and distributors and historical utilization rates. Rebates are generally invoiced by the payer and paid in arrears, such that the accrual balance consists of an estimate of the amount expected to be incurred for the current quarter's shipments to our customers, plus an accrual balance for known prior quarters' unpaid rebates. If actual future rebates vary from estimates, we may need to adjust our accruals, which would affect net product revenues in the period of adjustment.

Allowances for rebates also include amounts related to the Medicare Part D Coverage Gap Discount Program. In the U.S., the Medicare Part D prescription drug benefit mandates participating manufacturers to fund 50%, and increasing to 70% in 2019, of the Medicare Part D insurance coverage gap for prescription drugs sold to eligible patients. Our estimates for expected Medicare Part D coverage gap amounts are based on customer and payer data received from specialty pharmacies and distributors and historical utilization rates. Funding of the coverage gap is invoiced and paid in arrears so that the accrual balance consists of an estimate of the amount expected to be incurred for the current quarter's shipments to customer, plus an accrual balance for known prior quarters' unpaid claims. If actual future funding varies from estimates, we may need to adjust our accruals, which would affect net product revenues in the period of adjustment.

Co-payment Assistance: Patients who have commercial insurance and meet certain eligibility requirements may receive co-payment assistance. We accrue a liability for co-payment assistance based on actual program participation and estimates of program redemption using customer data provided by the specialty distributor that administers the copay program.

Other Customer Credits: We pay fees to our Customers for account management, data management and other administrative services. To the extent the services received are distinct from the sale of products to the Customer, these payments are classified in Selling, general and administrative expenses in our Consolidated Statements of Operations.

Collaboration Revenues

We enter into collaboration arrangements, under which we license certain rights to our intellectual property to third parties. The terms of these arrangements typically include payment to us for one or more of the following: non-refundable, up-front license fees; development, regulatory and commercial milestone payments; product supply services; development cost reimbursements; profit sharing arrangements; and royalties on net sales of licensed products. Except for profit sharing arrangements and payments for product supply services, each of these payment types were within the scope of Topic 606 during the year ended December 31, 2018. As part of the accounting for these arrangements, we must develop assumptions that require judgment to determine the standalone selling price for each performance obligation identified in the contract. These key assumptions may include forecasted revenues, clinical development timelines and costs, reimbursement rates for personnel costs, discount rates and probabilities of technical and regulatory success. Prior period amounts continue to be reported in accordance with our historic accounting under previous revenue recognition guidance, Topic 605. See " — Recently Adopted Accounting Pronouncements — Impact of Adoption of Topic 606 and Topic 842" above, for more information about the impact of the adoption on Topic 606.

Up-front License Fees: If the license to our intellectual property is determined to be distinct from the other performance obligations identified in the arrangement, we recognize revenues from nonrefundable, up-front fees allocated to the license when the license is transferred to the licensee and the licensee is able to use and benefit from

the license. For licenses that are bundled with other promises, we utilize judgment to assess the nature of the combined performance obligation to determine whether the combined performance obligation is satisfied over time or at a point in time and, if over time, the appropriate method of measuring progress for purposes of recognizing revenue from non-refundable, up-front fees. We evaluate the measure of progress each reporting period and, if necessary, adjust the measure of performance and related revenue recognition.

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Regulatory and Development Milestone Payments: At the inception of each arrangement that includes development milestone payments, we evaluate whether the milestones are considered probable of being reached and estimate the amount to be included in the transaction price using the most likely amount method. If it is probable that a significant revenue reversal would not occur, the associated milestone value is included in the transaction price. Milestone payments that are not within our or the licensee's control, such as regulatory approvals, are not considered probable of being achieved until uncertainty associated with the approvals has been resolved. The transaction price is then allocated to each performance obligation, on a relative standalone selling price basis, for which we recognize revenue as or when the performance obligations under the contract are satisfied. At the end of each subsequent reporting period, we re-evaluate the probability of achieving such development and regulatory milestones and any related constraint, and if necessary, adjust our estimate of the overall transaction price. Any such adjustments are recorded on a cumulative catch-up basis, which would affect Collaboration revenues and earnings in the period of adjustment.

Product Supply Services: Arrangements that include a promise for future supply of drug product for either clinical development or commercial supply at the licensee's discretion are generally considered as options. We assess if these options provide a material right to the licensee and if so, they are accounted for as separate performance obligations.

Development Cost Reimbursements: Our Ipsen and Takeda arrangements include promises of future clinical development and drug safety services, as well as participation on certain joint committees. We have determined that these services collectively are distinct from the licenses provided to Ipsen and Takeda and as such, these promises are accounted for as a separate performance obligation recorded over time. We record revenue for these services as the performance obligations are satisfied, which we estimate using internal development costs incurred and projections through the term of the arrangements.

Profit Sharing Arrangements: Under the terms of our collaboration agreement with Genentech for cobimetinib, we are entitled to a share of U.S. profits and losses received in connection with commercialization of cobimetinib. We are also entitled to low double-digit royalties on ex-U.S. net sales. We account for such arrangements in accordance with ASC Topic 808: Collaborative Arrangements (Topic 808). We have determined that we are an agent under the agreement and therefore revenues are recorded net of costs incurred. We record U.S. profits and losses under the collaboration agreement in the period earned based on our estimate of those amounts. We recognized an annual profit under the agreement for the year ending December 31, 2018 and accordingly, those profits are recognized as Collaboration revenues in the accompanying Consolidated Statements of Operations. Prior to 2018, the commercialization of cobimetinib in the U.S. had not been profitable for any annual period and accordingly, losses for periods prior to 2018 were recognized as Selling, general and administrative expenses in the accompanying Consolidated Statements of Operations.

Sales-based Milestone Payments and Royalties: For arrangements that include sales-based royalties, including milestone payments based on the volume of sales, the license is deemed to be the predominant item to which the royalties or sales-based milestones relate and we recognize revenue at the later of (i) when the related sales occur, or (ii) when the performance obligation to which some or all of the royalty has been allocated has been satisfied (or partially satisfied).

Cost of Goods Sold

Cost of goods sold is related to our product revenues and consists primarily of a 3% royalty we are required to pay GlaxoSmithKline (GSK) on all net sales of any product incorporating cabozantinib, indirect labor costs, the cost of manufacturing, write-downs related to expiring and excess inventory, shipping and other third-party logistics and distribution costs for our product.

We consider regulatory approval of product candidates to be uncertain and product manufactured prior to regulatory approval may not be sold unless regulatory approval is obtained. As such, the manufacturing costs for product candidates incurred prior to regulatory approval were not capitalized as inventory but are expensed as research and development costs. Portions of the manufacturing costs for inventory sold during the years ended December 31, 2018, 2017 and 2016 were incurred prior to the regulatory approval of CABOMETYX and COMETRIQ and, therefore, were expensed as research and development costs when incurred, rather than capitalized as inventory. There were no amounts remaining related to previously expensed materials in our inventory balances as of December 31, 2018.

Research and Development Expenses

Research and development costs are expensed as incurred and include costs associated with research performed pursuant to collaborative agreements. Research and development costs consist of direct and indirect internal costs related to specific projects as well as fees paid to other entities that conduct certain research activities on our behalf.

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Substantial portions of our preclinical studies and all of our clinical trials have been executed with support from third-party contract research organizations and other vendors. We accrue expenses for preclinical studies performed by our vendors based on certain estimates over the term of the service period and adjust our estimates as required. We accrue expenses for clinical trial activities performed by contract research organizations based upon the estimated amount of work completed on each trial. For clinical trial expenses, the significant factors used in estimating accruals include the number of patients enrolled, the number of active clinical sites, and the duration for which the patients will be enrolled in the trial. We monitor patient enrollment levels and related activities to the extent possible through internal reviews, correspondence with contract research organizations and review of contractual terms. We base our estimates on the best information available at the time. However, additional information may become available to us which may allow us to make a more accurate estimate in future periods. In this event, we may be required to record adjustments to research and development expenses in future periods when the actual level of activity becomes more certain.

Leases

We determine if an arrangement includes a lease at inception. Operating leases are included in operating lease right-of-use assets, other current liabilities, and long-term lease liabilities in our Consolidated Balance Sheet at December 31, 2018. Right-of-use assets represent our right to use an underlying asset for the lease term and lease liabilities represent our obligation to make lease payments arising from the lease. Operating lease right-of-use assets and liabilities are recognized at the lease commencement date based on the present value of lease payments over the lease term. In determining the net present value of lease payments, we use our incremental borrowing rate based on the information available at the lease commencement date. The operating lease right-of-use assets also include any lease payments made and exclude lease incentives. Our leases may include options to extend or terminate the lease which are included in the lease term when it is reasonably certain that we will exercise any such options. Lease expense is recognized on a straight-line basis over the expected lease term. We have elected not to apply the recognition requirements of Topic 842 for short-term leases.

For lease agreements entered into after the adoption of Topic 842 that include lease and non-lease components, such components are generally accounted for separately. For our building leases, as a result of us having elected to adopt the package of practical expedients permitted under the Topic 842 transition guidance, we account for the lease and non-lease components, such as common area maintenance charges, as a single lease component.

Prior period amounts continue to be reported in accordance with our historic accounting under previous lease guidance, Topic 840. See “ — Recently Adopted Accounting Pronouncements — Impact of Adoption of Topic 606 and Topic 842” above, for more information about the impact of the adoption on Topic 842.

Stock-Based Compensation

The expense for stock-based compensation is based on the grant date fair value of the award. The grant date fair value of restricted stock units (RSUs) is estimated as the value of the underlying shares of our common stock. The grant date fair value of stock-options is estimated using a Monte Carlo simulation pricing model for stock options that include market vesting conditions and a Black-Scholes Merton option pricing model for other stock options. Because there is a market for options on our common stock, we have considered implied volatilities as well as our historical realized volatilities when developing an estimate of expected volatility. We estimate the term using historical data. We recognize compensation expense on an accelerated basis over the requisite service period for awards with a market or performance condition and on a straight-line basis over the requisite service period for all other awards. Compensation expense relating to awards subject to performance conditions is recognized when management determines that it is probable that the performance goals will be achieved; the probability of achievement is assessed on a quarterly basis. We have made an election to record forfeitures when they occur.

Foreign Currency Translation and Remeasurement

Monetary assets and liabilities denominated in currencies other than the functional currency are remeasured using exchange rates in effect at the end of the period and related gains or losses are recorded in Other, net. Gains and losses on the remeasurement of monetary assets and liabilities were not material for any of the years presented. We do not have any nonmonetary assets or liabilities denominated in currencies other than the U.S. dollar.

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Income Taxes

Our income tax benefit (provision) is computed under the asset and liability method. Significant estimates are required in determining our income tax benefit (provision). Some of these estimates are based on interpretations of existing tax laws or regulations. We recognize deferred tax assets and liabilities for the expected future tax consequences of events that have been included in the financial statements or tax returns. Under this method, deferred tax assets and liabilities are determined on the basis of the difference between the tax basis of assets and liabilities and their respective financial reporting amounts (temporary differences) at enacted tax rates in effect for the years in which the differences are expected to reverse. A valuation allowance is established for deferred tax assets for which it is more likely than not that some portion or all of the deferred tax assets, including net operating losses and tax credits, will not be realized. We periodically re-assess the need for a valuation allowance against our deferred tax assets based on various factors including our historical earnings experience by taxing jurisdiction, and forecasts of future operating results and utilization of net operating losses and tax credits prior to their expiration. Significant judgment is required in making this assessment and, to the extent that a reversal of any portion of our valuation allowance against our deferred tax assets is deemed appropriate, a tax benefit will be recognized against our income tax provision in the period of such reversal. Prior to 2018, we recorded a valuation allowance that fully offset our deferred tax assets. In the fourth quarter of 2018, based on our evaluation of various factors, including our achievement of a cumulative three-year income position as of December 28, 2018 and forecasts of future operating results, we released substantially all of our valuation allowance against our deferred tax assets and recorded a corresponding income tax benefit as described in “Note 8. Income Taxes”, below. We continue to maintain a valuation allowance against our California state deferred tax assets.

We recognize tax benefits from uncertain tax positions only if it is more likely than not that the tax position will be sustained upon examination by the tax authorities based on the technical merits of the position. An adverse resolution of one or more of these uncertain tax positions in any period could have a material impact on the results of operations for that period.

Recent Accounting Pronouncements Not Yet Adopted

In November 2018, the Financial Accounting Standards Board (the FASB) issued ASU No. 2018-18, Collaborative Arrangements (Topic 808): Clarifying the Interaction between Topic 808 and Topic 606 (ASU 2018-18). ASU 2018-18 clarifies that certain transactions between collaborative arrangement participants should be accounted for as revenue under Topic 606 when the counterparty is a customer for a distinct good or service (i.e. a unit of account). For units of account that are in the scope of Topic 606, all of the guidance in Topic 606 should be applied, including the guidance on recognition, measurement, presentation and disclosure. ASU 2018-18 also adds a reference in Topic 808 to the unit of account guidance in ASC 606 and requires that it be applied only to assess whether transactions in a collaborative arrangement are in the scope of Topic 606. ASU 2018-18 will preclude entities from presenting amounts related to transactions with a counterparty in a collaborative arrangement that is not a customer as revenue from contracts with customers. ASU 2018-18 is effective for us for all interim and annual reporting periods beginning after December 15, 2019. Early adoption is permitted. We are in the process of assessing the impact of ASU 2018-18 on our Consolidated Financial Statements.

In August 2018, the FASB issued ASU No. 2018-15, Intangibles—Goodwill and Other—Internal-Use Software (Subtopic 350-40): Customer's Accounting for Implementation Costs Incurred in a Cloud Computing Arrangement That Is a Service Contract (ASU 2018-15). ASU 2018-15 aligns the requirements for capitalizing implementation costs incurred in a hosting arrangement that is a service contract with the requirements for capitalizing implementation costs incurred to develop or obtain internal-use software (and hosting arrangements that include an internal-use software license). Accordingly, ASU 2018-15 requires a customer in a hosting arrangement that is a service contract to follow the guidance in Subtopic 350-40 to determine which implementation costs to capitalize as an asset related to the service contract and which costs to expense. ASU 2018-15 also requires us to expense the capitalized implementation costs of a hosting arrangement that is a service contract over the term of the hosting arrangement, which includes reasonably certain renewals. ASU 2018-15 is effective for us for all interim and annual reporting periods beginning after December 15, 2019. Early adoption is permitted. We are in the process of assessing the impact of ASU 2018-15 on our Consolidated Financial Statements.

In January 2017, the FASB issued ASU No. 2017-04, Intangibles—Goodwill and Other (Topic 350): Simplifying the Test for Goodwill Impairment, (ASU 2017-04). ASU 2017-04 eliminated Step 2 from the goodwill impairment test. Instead, under the amendments in ASU 2017-04, an entity should perform its annual, or interim, goodwill impairment test by comparing the fair value of a reporting unit with its carrying amount. An entity should recognize an impairment charge for the amount by which the carrying amount exceeds the reporting unit's fair value; however, the loss recognized should not exceed the total amount of goodwill allocated to that reporting unit. Additionally, an entity should consider income tax

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effects from any tax deductible goodwill on the carrying amount of the reporting unit when measuring the goodwill impairment loss, if applicable. ASU 2017-04 is effective for all interim and annual reporting periods beginning after December 15, 2019. Early adoption is permitted. We do not expect the adoption of ASU 2017-04 to have a material impact on our Consolidated Financial Statements.

NOTE 2. REVENUES

Revenues by disaggregated category were as follows (in thousands):

	Year Ended December 31,		
	2018	2017	2016
Product revenues:			
Gross product revenues	$738,529	$402,569	$151,499
Discounts and allowances	(119,250)	(53,561)	(16,124)
Net product revenues	619,279	349,008	135,375
Collaboration revenues:			
License revenues [1]	192,188	96,637	56,286
Research and development service revenues [2]	39,501	8,737	—
Other collaboration revenues [3]	2,858	(1,905)	(207)
Total collaboration revenues	234,547	103,469	56,079
Total revenues	$853,826	$452,477	$191,454

(1) Upon the adoption of Topic 606 as of January 1, 2018, the allocation of proceeds from our collaboration partners, including upfront and milestone payments, between intellectual property licenses and research and development services as well as the resulting timing of recognition have changed. License revenues for the year ended December 31, 2018 included the immediate recognition of the portion of milestones that were allocated to the transfer of intellectual property licenses for those milestones for which it had become probable that a significant revenue reversal would not occur, as well as royalty revenues from Ipsen and Genentech. License revenues for the years ended December 31, 2017 and 2016 included the full recognition of substantive milestones achieved during the period, recognition of deferred revenues from upfront payments and a non-substantive milestone, which were being amortized over various periods, as well as royalty revenues from Ipsen and Genentech.

(2) Research and development service revenues for the year ended December 31, 2018 included the recognition of deferred revenue for the portion of the upfront and milestone payments that have been allocated to the research and development service performance obligations which are being amortized through early 2030, as well as development cost reimbursements earned on our collaboration agreements. As described above, prior to the adoption of Topic 606, we did not allocate any of our upfront payments or milestones to research and development services; therefore, Research and development service revenues for the years ended December 31, 2017 included only development cost reimbursements earned on our collaboration agreements.

(3) Other collaboration revenues for the year ended December 31, 2018 included royalties we paid to GSK on Ipsen's sales of products containing cabozantinib, the profit on the U.S. commercialization of COTELLIC from Genentech and product supply revenues. Other collaboration revenues for the years ended years ended December 31, 2017 and 2016 included only royalties we paid to GSK on Ipsen's sales of products containing cabozantinib and product supply revenues, as the profits and losses on the U.S. commercialization of COTELLIC for the period were included in Selling, general and administrative expenses.

During the year ended December 31, 2018, Net product revenues and License revenues related to goods and intellectual property licenses transferred at a point in time and Research and development services revenues related to services performed over time. License revenues and Research and development services revenues were recorded in accordance with Topic 606 during 2018 and Topic 605 in prior periods. Other collaboration revenues, which included royalties we paid to GSK on Ipsen's sales of products containing cabozantinib, the profit on the U.S. commercialization of COTELLIC from Genentech and product supply revenue, were recorded in accordance with Topic 808 for all periods presented.

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Net product revenues disaggregated by product were as follows (in thousands):

	Year Ended December 31,		
	2018	2017	2016
CABOMETYX	$599,946	$324,000	$93,481
COMETRIQ	19,333	25,008	41,894
Net product revenues	$619,279	$349,008	$135,375

Total revenues disaggregated by significant customer were as follows (dollars in thousands):

	Year Ended December 31,					
	2018		2017		2016	
	Dollars	Percent of total	Dollars	Percent of total	Dollars	Percent of total
Ipsen	$182,879	21 %	$69,792	15 %	$33,252	17 %
Caremark L.L.C.	110,698	13 %	73,921	16 %	17,746	9 %
Affiliates of McKesson Corporation	99,916	12 %	48,662	11 %	13,143	7 %
Accredo Health, Incorporated	81,028	9 %	50,716	11 %	16,631	9 %
Diplomat Specialty Pharmacy	74,244	9 %	83,059	18 %	63,826	33 %
Others, individually less than 10% of Total revenues for all periods presented	305,061	36 %	126,327	29 %	46,856	25 %
Total revenues	$853,826	100 %	$452,477	100 %	$191,454	100 %

Total revenues disaggregated by geographic region were as follows (in thousands):

	Year Ended December 31,		
	2018	2017	2016
U.S.	$632,927	$367,906	$140,709
Europe	182,879	69,792	35,745
Rest of the world	38,020	14,779	15,000
Total revenues	$853,826	$452,477	$191,454

Net product revenues are attributed to regions based on the ship-to location. Collaboration revenues are attributed to regions based on the location of our collaboration partners' headquarters.

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Product Sales Discounts and Allowances

The activities and ending reserve balances for each significant category of discounts and allowances (which constitute variable consideration) were as follows (in thousands):

	Chargebacks and Discounts for Prompt Payment	Other Customer Credits/Fees and Co-pay Assistance	Rebates	Returns	Total
Balance at December 31, 2016	$ 1,802	$ 794	$2,627	$ 351	$5,574
Provision related to sales made in:					
Current period	33,310	7,301	14,390	—	55,001
Prior periods	(817)	—	(624)	—	(1,441)
Payments and customer credits issued	(32,367)	(6,300)	(10,623)	(351)	(49,641)
Balance at December 31, 2017	1,928	1,795	5,770	—	9,493
Provision related to sales made in:					
Current period	75,543	13,015	31,040	2	119,600
Prior periods	(403)	206	(153)	—	(350)
Payments and customer credits issued	(74,746)	(11,978)	(24,741)	(2)	(111,467)
Balance at December 31, 2018	$ 2,322	$ 3,038	$11,916	$ —	$17,276

Chargebacks and discounts for prompt payment are recorded as a reduction of Trade receivables, net and the remaining reserve balances are classified as Other current liabilities in the accompanying Consolidated Balance Sheets.

Contract Assets and Liabilities

We receive payments from our licensees based on billing schedules established in each contract. Amounts are recorded as accounts receivable when our right to consideration is unconditional. Upfront and milestone payments may require deferral of revenue recognition to a future period until we perform our obligations under these arrangements and are recorded as deferred revenue upon receipt or when due. We may also recognize revenue in advance of the contractual billing schedule and such amounts are recorded as unbilled collaboration revenue when recognized. Changes in our contract assets and liabilities under Topic 606 were as follows (in thousands):

	Contract Assets: Unbilled Collaboration Revenue		Contract Liabilities: Deferred Revenue	
	Current Portion	Long-term Portion	Current Portion	Long-term Portion
Balance at December 31, 2017	$ —	$ —	$31,984	$238,520
Adoption of Topic 606	9,588	12,247	(23,591)	(213,079)
Balance at January 1, 2018	9,588	12,247	8,393	25,441
Increases as a result of a change in transaction price and recognition of revenues as services are performed	37,881	4,545	—	—
Transfer to receivables from contract assets recognized at the beginning of the period	(46,052)	—	—	—
Increases as a result of the deferral of milestones achieved in period, excluding amounts recognized as revenue	—	—	1,718	7,237
Revenue recognized that was included in the contract liability balance at the beginning of the period	—	—	(8,683)	—
Other adjustments [1]	(1,417)	(16,792)	(1,428)	(16,781)
Balance at December 31, 2018	$ —	$ —	$—	$15,897

(1) Includes reclassification of deferred revenue from long-term to current and adjustments made due to netting of contract assets and liabilities by collaboration agreement.

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During the year ended December 31, 2018, we recognized $198.1 million in revenues under Topic 606 for performance obligations satisfied in previous periods. Such revenues primarily related to milestone and royalty payments allocated to our license performance obligations of our collaborations with Ipsen and Daiichi Sankyo.

NOTE 3. COLLABORATION AGREEMENTS

We have established multiple collaborations with leading pharmaceutical companies for the commercialization and further development of cabozantinib, as well as with smaller, discovery-focused biotechnology companies to expand our product pipeline. Additionally, in line with our business strategy prior to the commercialization of our first product, COMETRIQ, we entered into other collaborations with leading pharmaceutical companies including Genentech, Daiichi Sankyo, Merck & Co., Inc. (Merck) and Bristol-Myers Squibb Company (BMS) for other compounds and programs in our portfolio.

Under these collaborations, we are generally entitled to receive milestone and royalty payments, and for certain collaborations, payments for product supply services, development cost reimbursements, and/or profit sharing payments. See “Note 2. Revenues” for information on collaboration revenues recognized during the years ended December 31, 2018, 2017 and 2016.

Cabozantinib Commercial Collaborations

Ipsen Collaboration

Description of the Collaboration

In February 2016, we entered into a collaboration and license agreement with Ipsen for the commercialization and further development of cabozantinib. Pursuant to the terms of the collaboration agreement, Ipsen received exclusive commercialization rights for current and potential future cabozantinib indications outside of the U.S., Canada and Japan. The collaboration agreement was subsequently amended in December 2016 to include commercialization rights in Canada. We have also agreed to collaborate with Ipsen on the development of cabozantinib for current and potential future indications.

Unless terminated earlier, the collaboration agreement has a term that continues, on a product-by-product and country-by-country basis, until the latter of (i) the expiration of patent claims related to cabozantinib, (ii) the expiration of regulatory exclusivity covering cabozantinib or (iii) ten years after the first commercial sale of cabozantinib, other than COMETRIQ. A related supply agreement will continue in effect until expiration or termination of the collaboration agreement. The collaboration agreement may be terminated for cause by either party based on uncured material breach of either the collaboration agreement or the supply agreement by the other party, bankruptcy of the other party or for safety reasons. Upon termination by either party, all licenses granted by us to Ipsen will automatically terminate, and, except in the event of a termination by Ipsen for our material breach, the licenses granted by Ipsen to us shall survive such termination and shall automatically become worldwide, or, if Ipsen were to terminate only for a particular region, then for the terminated region. Following termination by us for Ipsen’s material breach, or termination by Ipsen without cause or because we undergo a change of control by a party engaged in a competing program, Ipsen is prohibited from competing with us for a period of time.

Consideration under the Collaboration

In consideration for the exclusive license and other rights contained in the collaboration agreement, including commercialization rights in Canada, Ipsen paid us aggregate upfront payments of $210.0 million. As of December 31, 2018, we have also achieved aggregate milestones of $275.0 million related to development, regulatory and commercial progress by Ipsen since the inception of the collaboration agreement, including $140.0 million in milestones recognized during 2018.

We are also eligible to receive future development and regulatory milestone payments from Ipsen, totaling an aggregate of $84.0 million upon additional approvals of cabozantinib in future indications and/or jurisdictions, as well as contingent payments of up to $519.5 million associated with sales-based milestones. We will further receive royalties on net sales of cabozantinib by Ipsen outside of the U.S. and Japan. We were initially entitled to receive a tiered royalty of 2% to 12% on the initial $150.0 million of net sales; this amount was reached in the second quarter of 2018. As of December 31, 2018 and going forward, we are entitled to receive a tiered royalty of 22% to 26% on annual net sales (with separate tiers for Canada); these 22% to 26% royalty tiers reset each calendar year. In Canada, we are entitled to receive a tiered royalty of

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22% on the first CAD$30.0 million of annual net sales and a tiered royalty thereafter to 26% on annual net sales; these 22% to 26% royalty tiers for Canada will also reset each calendar year.

Consistent with our historical agreement with GSK, we are required to pay a 3% royalty to GSK on all net sales of any product incorporating cabozantinib, including net sales by Ipsen.

We are primarily responsible for funding cabozantinib-related development costs for those trials in existence at the time we entered into the collaboration agreement with Ipsen; global development costs for additional trials are shared between the parties, with Ipsen reimbursing us for 35% of such costs, provided Ipsen chooses to opt into such trials.

We are responsible for the manufacture and supply of cabozantinib for all development and commercialization activities under the collaboration agreement. In connection with the collaboration agreement, we entered into a supply agreement with Ipsen to supply finished, labeled drug product to Ipsen for distribution in the territories outside of the U.S. and Japan for the term of the collaboration agreement. The product will be supplied at our cost, as defined in the agreement.

Revenues from the Collaboration

Collaboration revenues under the collaboration agreement with Ipsen were as follows (in thousands):

	Year Ended December 31,		
	2018	2017	2016
Ipsen collaboration revenues	$182,879	$69,792	$33,252

As of December 31, 2018, $48.0 million of the transaction price allocated to our research and development services performance obligation had not been satisfied. As of December 31, 2018, the net contract liability for the collaboration agreement with Ipsen was $13.3 million, which was included in Long-term portion of deferred revenue in the accompanying Consolidated Balance Sheets. See “—Performance Obligations and Transaction Prices for our Ipsen and Takeda Collaborations”, below, for additional information related to the revenue recognition for this collaboration.

Takeda Collaboration

Description of the Collaboration

In January 2017, we entered into a collaboration and license agreement with Takeda. Pursuant to this collaboration agreement, Takeda has exclusive commercialization rights for current and potential future cabozantinib indications in Japan, and the parties have agreed to collaborate on the clinical development of cabozantinib in Japan.

Unless earlier terminated, the collaboration agreement has a term that continues, on a product-by-product basis, until the earlier of (i) two years after first generic entry with respect to such product in Japan or (ii) the later of (A) the expiration of patent claims related to cabozantinib and (B) the expiration of regulatory exclusivity covering cabozantinib in Japan. The collaboration agreement may be terminated for cause by either party based on uncured material breach by the other party, bankruptcy of the other party or for safety reasons. For clarity, Takeda’s failure to achieve specified levels of commercial performance, based upon sales volume and/or promotional effort, during the first six years of the collaboration shall constitute a material breach of the collaboration agreement. We may terminate the agreement if Takeda challenges or opposes any patent covered by the collaboration agreement. At any time prior to August 1, 2023, the parties may mutually agree to terminate the collaboration agreement if Japan’s Pharmaceuticals and Medical Devices Agency is unlikely to grant any approval of the marketing authorization application in any cancer indication in Japan. After the commercial launch of cabozantinib in Japan, Takeda may terminate the collaboration agreement upon twelve months’ prior written notice following the third anniversary of the first commercial sale of cabozantinib in Japan. Upon termination by either party, all licenses granted by us to Takeda will automatically terminate, and the licenses granted by Takeda to us shall survive such termination and shall automatically become worldwide.

Consideration under the Collaboration

In consideration for the exclusive license and other rights contained in the collaboration agreement, we received a $50.0 million upfront nonrefundable payment from Takeda. During the year ended December 31, 2018, we also achieved a $10.0 million development related milestone.

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As of December 31, 2018, we were eligible to receive development, regulatory and first-sale milestone payments of up to $90.0 million related to second-line RCC, first-line RCC and second-line HCC, as well as additional development, regulatory and first-sale milestone payments, without limit, for additional potential future indications. The collaboration agreement also provides that we are eligible to receive pre-specified payments of up to $83.0 million associated with sales volume milestones and receive royalties on net sales of cabozantinib in Japan. We are entitled to receive a tiered royalty of 15% to 24% on the initial $300.0 million of net sales, and following this initial $300.0 million of net sales, we are then entitled to receive a tiered royalty of 20% to 30% on annual net sales thereafter; these 20% to 30% royalty tiers will reset each calendar year.

Consistent with our historical agreement with GSK, we are required to pay a 3% royalty to GSK on all net sales of any product incorporating cabozantinib, including net sales by Takeda.

Takeda is responsible for 20% of the costs associated with the global cabozantinib development plan's current and future trials, provided Takeda opts into such trials, and 100% of costs associated with the cabozantinib development activities that are exclusively for the benefit of Japan.

We are responsible for the manufacture and supply of cabozantinib for all development and commercialization activities under the collaboration, and consequently, we entered into a clinical supply agreement covering the supply of cabozantinib to Takeda.

Revenues from the Collaboration

Collaboration revenues under the collaboration agreement with Takeda were as follows (in thousands):

	Year Ended December 31,	
	2018	2017
Takeda collaboration revenues	$18,020	$14,779

As of December 31, 2018, $25.6 million of the transaction price allocated to our research and development services performance obligation had not been satisfied. As of December 31, 2018, the net contract liability for the collaboration agreement with Takeda was $2.6 million, which was included in Long-term portion of deferred revenue in the accompanying Consolidated Balance Sheets.

Performance Obligations and Transaction Prices for our Ipsen and Takeda Collaborations

We identified two performance obligations for both the Ipsen and Takeda collaboration agreements: (1) the transfer of an exclusive license for the commercialization and further development of cabozantinib; and (2) research and development services, which includes certain committed studies for the development of cabozantinib, pharmacovigilance services and participation on various joint committees (as defined in the specific collaboration agreements).

We have allocated the transaction price for each of these collaborations, which are described below, to the identified performance obligations based on our best estimate of their relative standalone selling price. For the licenses, the estimate of the relative standalone selling price was determined using a discounted cash flow valuation utilizing forecasted revenues and costs, and a discount rate. For research and development services the estimate of the relative standalone selling price was determined using an adjusted market assessment approach that relies on internal and external costs and market factors.

The portion of the transaction price allocated to our license performance obligation are recorded immediately as our license represents functional intellectual property that was transferred at a point in time. The portion of the transaction price allocated to our research and development services performance obligation is being recognized as revenue using the inputs method based on our internal development projected cost estimates through the current estimated patent expiration of cabozantinib in the European Union (EU) for the Ipsen Collaboration and Japan for the Takeda Collaboration, both of which are early 2030.

Based on our evaluation of the collaboration agreements as of January 1, 2018, the date adoption of Topic 606, we determined that for both agreements, the up-front, nonrefundable payments, the milestones and royalties achieved as of December 31, 2017, and our estimate for the reimbursements of our research and development services performance obligation over the term of each agreement constituted the amount of the consideration to be included in the transaction

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price as of December 31, 2017. In addition, the transaction price for the Ipsen collaboration agreement included a $10.0 million milestone we expected to achieve during the three months ended March 31, 2018. Other than that $10.0 million milestone, variable consideration for both agreements related to regulatory and development milestones not previously recognized was constrained due to the fact that it was not probable that a significant reversal of cumulative revenue would not occur, given the inherent uncertainty of success with these milestones. Any variable consideration related to sales-based milestones and royalties will be recognized when the related sales occur as these amounts have been determined to relate to the relevant transferred license and therefore are recognized as the related sales occur.

We re-evaluate the transaction price for the collaboration agreements in each reporting period as uncertain events are resolved or other changes in circumstances occur and we allocate those changes in the transaction price between our performance obligations. During the year ended December 31, 2018, the transaction price increased as a result of the achievement of various milestones described above. We further updated the transaction price based upon the impact of research and development services performed during the period and changes in our estimated reimbursements for our future research and development services. The portion of the increase in transaction price that was allocated to the previously satisfied performance obligations for the transfer of an intellectual property license was recognized during the period and the portion allocated to research and development services will be recognized in future periods as those services are delivered through early 2030. As of December 31, 2018, variable consideration related to the remaining unearned regulatory and development milestones for both agreements remained constrained due to the fact that it was not probable that a significant reversal of cumulative revenue would not occur.

Cabozantinib Development Collaborations

BMS

In February 2017, we entered into a clinical trial collaboration agreement with BMS for the purpose of exploring the therapeutic potential of cabozantinib in combination with BMS's immune checkpoint inhibitors (ICIs), nivolumab and/or ipilimumab, to treat a variety of types of cancer. As part of the collaboration, we are evaluating these combinations as treatment options for RCC and HCC in the CheckMate 9ER and CheckMate 040 trials, respectively.

Pursuant to the terms of the collaboration agreement with BMS, each party granted to the other a non-exclusive, worldwide (within the collaboration territory as defined in the collaboration agreement and its supplemental agreements), non-transferable, royalty-free license to use the other party's compounds in the conduct of each clinical trial.

Each party will be responsible for supplying finished drug product for the applicable clinical trial and unless otherwise agreed between the parties, costs for each such trial will be shared equally between the parties, unless two BMS compounds will be utilized in such trial, in which case BMS will bear two-thirds of the costs for such study treatment arms and we will bear one-third of the costs. Unless earlier terminated, the collaboration agreement will remain in effect until the completion of all clinical trials under the collaboration, all related trial data has been delivered to both parties and the completion of any then agreed upon analysis. The collaboration agreement may be terminated for cause by either party based on uncured material breach by the other party, bankruptcy of the other party or for safety reasons. Upon termination by either party, the licenses granted to each party to conduct a combined therapy trial will terminate.

The Roche Group (Roche) Collaboration

In February 2017, we entered into a master clinical supply agreement with Roche for the purpose of evaluating cabozantinib in combination with Roche's ICI, atezolizumab, in locally advanced or metastatic solid tumors. As part of this agreement with Roche, in June 2017, we initiated COSMIC-021, a phase 1b trial evaluating the safety and tolerability of the combination in patients with locally advanced or metastatic tumors, and in December 2018, we initiated COSMIC-312, a phase 3 pivotal trial evaluating the combination versus sorafenib in previously untreated advanced HCC, with an exploratory arm also evaluating cabozantinib monotherapy in previously untreated advanced HCC. We are the trial sponsor, and Roche is providing atezolizumab free of charge.

GSK

In October 2002, we established a product development and commercialization collaboration agreement with GSK. Under the terms of the collaboration agreement, GSK had the right to choose cabozantinib for further development and commercialization, but notified us in October 2008 that it had waived its right to select the compound for such

activities. Although the collaboration agreement was terminated during 2014, GSK continues to be entitled to a 3% royalty we are required to pay on all net sales of any product incorporating cabozantinib by us and our collaboration partners. Royalties

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accruing to GSK in connection with the sales of cabozantinib are included in Cost of goods sold for sales by us and as a reduction of Collaboration revenues for sales by Ipsen. Such royalties were as follows (in thousands):

	Year Ended December 31,		
	2018	2017	2016
Royalties accruing to GSK	$23,950	$12,413	$4,334

StemSynergy Therapeutics, Inc. (StemSynergy) Collaboration

In January 2018, we entered into an exclusive collaboration and license agreement with StemSynergy for the discovery and development of novel oncology compounds targeting Casein Kinase 1 alpha (CK1), a component of the Wnt signaling pathway implicated in key oncogenic processes. Under the terms of the agreement, we will partner with StemSynergy to conduct preclinical and clinical studies with compounds targeting CK1 .

During the year ended December 31, 2018, we paid StemSynergy an upfront payment of $3.0 million in initial research and development funding and provided $1.2 million in additional research and development funding. StemSynergy is eligible for up to $2.3 million in additional such funding on an as needed basis. The research and development funding costs incurred to date were included in Research and development expenses in the accompanying Consolidated Statements of Operations.

StemSynergy will also be eligible for up to $56.5 million in milestones for the first product to emerge from the collaboration, including preclinical and clinical development and regulatory milestone payments, sales-based milestones, as well as single-digit royalties on worldwide sales. We will be solely responsible for the commercialization of products that arise from the collaboration.

Invenra, Inc. (Invenra) Collaboration

In May 2018, we entered into a collaboration and license agreement with Invenra, which is focused on developing next-generation biologics, to discover and develop multispecific antibodies for the treatment of cancer. Invenra is responsible for antibody lead discovery and generation while we will lead Investigational New Drug enabling studies, manufacturing, clinical development in single-agent and combination therapy regimens, and future regulatory and commercialization activities. The collaboration agreement also provides that we will receive an exclusive, worldwide license to one preclinical asset, and that we will pursue up to six additional discovery projects during the term of the collaboration, which in total are directed to three discovery programs.

In consideration for the exclusive worldwide license and other rights contained in the collaboration agreement, we paid Invenra an upfront payment of $2.0 million and a project initiation fee of $2.0 million during the year ended December 31, 2018. The payments were included in Research and development expenses in the accompanying Consolidated Statements of Operations. As of December 31, 2018, we also have the right to initiate five additional discovery projects for development subject to an upfront payment of $2.0 million for each project as well as additional global milestone payments and royalties for any products that arise from these discovery efforts. Invenra is eligible to receive payments based on the achievement of specific development and regulatory milestones of up to $131.5 million for a product containing the lead preclinical asset in the first indication and up to $127.5 million for a product developed from each addition project we initiate. Upon successful commercialization of a product, Invenra is eligible to receive global milestone payments up to $325.0 million per product if certain sales thresholds are achieved as well as single digit tiered royalties on net sales of the approved product.

Unless earlier terminated, the collaboration agreement has a term that continues, on a product-by-product and country-by-country basis, until the later of (i) ten years after the first commercial sale of such product in such country or (ii) expiration of patent claims covering the product in such country. We may terminate the collaboration agreement in its entirety or on a project-by-project, basis at any time prior to commercialization, for any or no reason, upon thirty days' written notice to Invenra. The collaboration agreement also may be terminated by either party for a material breach by the other, subject to notice and cure provisions.

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Other Collaborations

Genentech

Profits and losses on U.S. commercialization and Royalty revenues on ex-U.S. sales under the collaboration agreement with Genentech were as follows (in thousands):

	Year Ended December 31,		
	2018	2017	2016
Profits and losses on U.S. commercialization	$8,084	$(2,140)	$8,771
Royalty revenues on ex-U.S. sales	$5,564	$6,398	$2,827

Profits on the U.S. commercialization of COTELLIC for the year ended December 31, 2018 were included Collaboration revenues and profits and losses on for the years ended December 31, 2017 and 2016 were included in Selling, general and administrative expenses. The royalty revenues on ex-U.S. sales were included in Collaboration revenues for all periods presented. See "—Performance Obligations and Transaction Prices for our Other Collaborations", below, for additional information related to revenue recognition for this collaboration.

In December 2006, we out-licensed the development and commercialization of cobimetinib to Genentech pursuant to a worldwide collaboration agreement. Cobimetinib is a reversible inhibitor of MEK, a kinase that is a component of the RAS/RAF/MEK/ERK pathway. Under the terms of the collaboration agreement, we developed cobimetinib through the determination of the maximum tolerated dose in a phase 1 clinical trial, and Genentech had the option to co-develop cobimetinib, an option that Genentech exercised, and in March 2009, we granted to Genentech an exclusive worldwide revenue-bearing license to cobimetinib, at which point Genentech became responsible for completing the phase 1 clinical trial and the subsequent clinical development.

In November 2015, the U.S. Food and Drug Administration (FDA) approved cobimetinib, under the brand name COTELLIC, in combination with Genentech's Zelboraf (vemurafenib) as a treatment for patients with BRAF V600E or V600K mutation-positive advanced melanoma. COTELLIC in combination with Zelboraf has also been approved in Switzerland, the EU, Canada, Australia, Brazil and multiple additional countries for use in the same indication. Prior to the FDA's approval of COTELLIC, in November 2013, we exercised an option under the collaboration agreement to co-promote COTELLIC in the U.S., which allows for us to provide up to 25% of the total sales force for approved cobimetinib indications in the U.S. Between November 2015 and December 2017, we fielded 25% of the sales force promoting COTELLIC in combination with Zelboraf as a treatment for patients with BRAF mutation-positive advanced melanoma in the U.S. However, following a review of the commercial landscape, commencing in January 2018, we and Genentech scaled back the personal promotion of COTELLIC in this indication in the U.S.

Cobimetinib Profit Sharing and Royalty Revenues

Under the terms of our collaboration agreement, as amended in July 2017, we share in the profits and losses received or incurred in connection with COTELLIC's commercialization in the U.S. This profit and loss share has multiple tiers: we receive 50% of profits and losses from the first $200.0 million of U.S. actual sales, decreasing to 30% of profits and losses from U.S. actual sales in excess of $400.0 million. These tiers will reset each calendar year. The revenue for each sale of COTELLIC applied to the profit and loss statement for the collaboration agreement (Genentech Collaboration P&L) is calculated using the average of the quarterly net selling prices of COTELLIC and any additional branded Genentech product(s) prescribed with COTELLIC in such sale. U.S. commercialization costs for COTELLIC are then applied to the Genentech Collaboration P&L, subject to reduction based on the number of Genentech products in any given combination including COTELLIC. In addition to our profit share in the U.S., under the terms of the collaboration agreement, we are entitled to low double-digit royalties on net sales of COTELLIC outside the U.S. We are not eligible for any additional milestone payments under the collaboration agreement with Genentech.

Unless earlier terminated, the collaboration agreement has a term that continues until the expiration of the last payment obligation with respect to the licensed products under the collaboration. Genentech has the right to terminate the collaboration agreement without cause at any time. If Genentech terminates the collaboration agreement without cause, all licenses that were granted to Genentech under the agreement terminate and revert to us. Additionally, if

Genentech terminates the collaboration agreement without cause, or we terminate the collaboration agreement for cause, we would receive, subject to certain conditions, licenses from Genentech to research, develop and commercialize reverted product

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candidates. The collaboration agreement may be terminated for cause by either party based on uncured material breach by the other party.

Cobimetinib Clinical Development Program

Cobimetinib is being evaluated by Genentech in a development program consisting of more than 50 clinical trials. These trials are being sponsored by Genentech or through Genentech's investigator sponsored trial program.

Daiichi Sankyo

Collaboration revenues under the collaboration agreement with Daiichi Sankyo were as follows (in thousands):

	Year Ended December 31,		
	2018	2017	2016
Daiichi Sankyo collaboration revenues	$20,000	$ —	$15,000

See "—Performance Obligations and Transaction Prices for our Other Collaborations", below, for additional information related to revenue recognition for this collaboration.

In March 2006, we entered into a collaboration agreement with Daiichi Sankyo for the discovery, development and commercialization of novel therapies targeted against the 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 esaxerenone, an oral, non-steroidal, selective MR antagonist. Daiichi Sankyo is responsible for all further preclinical and clinical development, regulatory, manufacturing and commercialization activities for the compounds. In January 2019, subsequent to our year-end, Daiichi Sankyo received approval from the Japanese Ministry of Health, Labour and Welfare for MINNEBRO as a treatment for patients with hypertension.

We are eligible to receive additional development, regulatory and sales-based milestone payments of up to $110.0 million under this collaboration agreement, including a $20.0 million milestone payment upon the first arm's-length sale of MINNEBRO in Japan. In addition, we are entitled to receive low double-digit royalties on sales of MINNEBRO. 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. In addition, pursuant to a license agreement we entered into with Ligand Pharmaceuticals, Inc. (Ligand), we are required to pay a royalty of 0.5% to Ligand on net sales of MINNEBRO.

Merck

Collaboration revenues under the collaboration agreement with Merck were as follows (in thousands):

	Year Ended December 31,		
	2018	2017	2016
Merck collaboration revenues	$—	$ —	$5,000

See "—Performance Obligations and Transaction Price for our Other Collaborations", below, for additional information related to revenue recognition for this collaboration.

In December 2011, we entered into an agreement with Merck pursuant to which we granted Merck an exclusive worldwide license to our phosphoinositide-3 kinase-delta (PI3K-) 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- program. Subsequent to December 31, 2018, we have been notified by Merck that they will be terminating their PI3K- program, including their development activities under this collaboration agreement. Upon the termination of the collaboration agreement by Merck, the license granted to Merck will terminate.

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BMS - ROR Collaboration

Collaboration revenues under the ROR collaboration agreement with BMS were as follows (in thousands):

	Year Ended December 31,		
	2018	2017	2016
BMS collaboration revenues	$ —	$ 12,500	$ —

See "—Performance Obligations and Transaction Prices for our Other Collaborations", below, for additional information related to revenue recognition for this collaboration.

In October 2010, we entered into a worldwide collaboration with BMS 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 BMS. Since July 2013, BMS has been solely responsible 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.

We are eligible for additional development and regulatory milestone payments of up to $240.0 million in the aggregate and sales-based milestones of up to $150.0 million in the aggregate, as well as royalties on commercial net sales, depending on the advancement of the product candidate and eventual product.

BMS 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 BMS at will or by us for BMS's uncured material breach, the license granted to BMS 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 BMS to develop and commercialize such product in the related country. In the event of termination by BMS for our uncured material breach, BMS would retain the right to such product, subject to continued payment of milestones and royalties.

Performance Obligations and Transaction Prices for our Other Collaborations

We have evaluated our collaborations agreements with Genentech, Daiichi Sankyo, Merck and BMS and have determined that those collaboration agreements each have one performance obligation: the delivery of intellectual property licenses to the collaboration partner. We have further determined that the licenses we provided represent functional intellectual property that was transferred at a point in time, when the agreements were executed, prior to the adoption of Topic 606. Potential variable consideration for these collaborations related to regulatory and development milestones was constrained due to the fact that it was not probable that a significant reversal of cumulative revenue would not occur, given the inherent uncertainty of success with these milestones and therefore, any additional consideration earned and received from these collaborations will be fully recognized when the milestone is no longer constrained. Any variable consideration related to royalties and other sales-based milestones will be recognized when the related sales occur as these amounts have been determined to relate predominantly to the licenses transferred and therefore are recognized at the later of when the performance obligation is satisfied or the related sales occur.

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NOTE 4. CASH AND INVESTMENTS

Cash, Cash Equivalents and Restricted Cash

A reconciliation of Cash, cash equivalents, and restricted cash reported within our Consolidated Balance Sheets to the amount reported within the accompanying Consolidated Statements of Cash Flows was as follows (in thousands):

	December 31, 2018	December 31, 2017	December 31, 2016
Cash and cash equivalents	$ 314,775	$ 183,164	$ 151,686
Restricted cash included in short-term restricted cash and investments	—	504	—
Restricted cash included in long-term restricted cash and investments	1,100	4,646	4,150
Cash, cash equivalents, and restricted cash as reported within the accompanying Consolidated Statements of Cash Flows	$ 315,875	$ 188,314	$ 155,836

Restricted cash includes certificates of deposit used to collateralize letters of credit and, in prior periods, a purchasing card program.

Cash and Investments

Cash and investments by security type were as follows (in thousands):

	December 31, 2018			
	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Fair Value
Investments available-for-sale:				
Money market funds	$ 47,744	$ —	$ —	$ 47,744
Commercial paper	381,134	—	(1)	381,133
Corporate bonds	344,741	180	(857)	344,064
U.S. Treasury and government sponsored enterprises	55,224	2	(25)	55,201
Total investments available-for-sale	828,843	182	(883)	828,142
Cash and restricted cash	6,883	—	—	6,883
Certificates of deposit	16,596	—	—	16,596
Total cash and investments	$ 852,322	$ 182	$ (883)	$ 851,621

	December 31, 2017			
	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Fair Value
Investments available-for-sale:				
Money market funds	$ 45,478	$ —	$ —	$ 45,478
Commercial paper	199,647	—	—	199,647
Corporate bonds	179,336	18	(332)	179,022
U.S. Treasury and government sponsored enterprises	16,295	—	(32)	16,263
Total investments available-for-sale	440,756	18	(364)	440,410
Cash and restricted cash	3,268	—	—	3,268
Certificates of deposit	13,498	—	—	13,498
Total cash and investments	$ 457,522	$ 18	$ (364)	$ 457,176

Gains and losses on the sales of investments available-for-sale were nominal or zero during the years ended December 31, 2018, 2017 and 2016.

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The fair value of gross unrealized losses on investments available-for-sale in an unrealized loss position were as follows (in thousands):

	December 31, 2018					
	In an Unrealized Loss Position Less than 12 Months		In an Unrealized Loss Position 12 Months or Greater		Total	
	Fair Value	Gross Unrealized Losses	Fair Value	Gross Unrealized Losses	Fair Value	Gross Unrealized Losses
Corporate bonds	$236,162	$ (606)	$39,627	$ (251)	$275,789	$ (857)
U.S. Treasury and government sponsored enterprises	28,105	(16)	9,182	(9)	37,287	(25)
Commercial paper	7,091	(1)	—	—	7,091	(1)
Total	$271,358	$ (623)	$48,809	$ (260)	$320,167	$ (883)

	December 31, 2017					
	In an Unrealized Loss Position Less than 12 Months		In an Unrealized Loss Position 12 Months or Greater		Total	
	Fair Value	Gross Unrealized Losses	Fair Value	Gross Unrealized Losses	Fair Value	Gross Unrealized Losses
Corporate bonds	$140,746	$ (296)	$20,047	$ (36)	$160,793	$ (332)
U.S. Treasury and government sponsored enterprises	13,611	(23)	2,651	(9)	16,262	(32)
Total	$154,357	$ (319)	$22,698	$ (45)	$177,055	$ (364)

There were 199 and 134 investments in an unrealized loss position as of December 31, 2018 and 2017, respectively. During the years ended December 31, 2018, 2017 and 2016 we did not record any other-than-temporary impairment charges on our available-for-sale securities. Based upon our quarterly impairment review, we determined that the unrealized losses were not attributed to credit risk, but were primarily associated with changes in interest rates. Based on the scheduled maturities of our investments and our determination that it was more likely than not that we will hold these investments for a period of time sufficient for a recovery of our cost basis, we concluded that the unrealized losses in our investment securities were not other-than-temporary.

The fair value of investments available-for-sale by contractual maturity were as follows (in thousands):

	December 31,	
	2018	2017
Maturing in one year or less	$674,455	$377,155
Maturing after one year through five years	153,687	63,255
Total investments available-for-sale	$828,142	$440,410

Other Cost Method Equity Investments

During the years ended December 31, 2018, 2017 and 2016, we recognized gains of $0.2 million, $3.0 million and $2.5 million, respectively, related to the August 2016 sale of our 9% interest in Akarna Therapeutics, Ltd. (Akarna) to Allergan Holdco UK Limited (Allergan). We acquired our interest in Akarna in 2015 in exchange for intellectual property rights related to the Exelixis discovered compound XL335. The gain on sale was included in Other, net in the accompanying Consolidated Statements of Operations. We are eligible to earn additional such gains in the future as Allergan continues its development of XL335.

Related Party Transactions

During 2018, BlackRock, Inc. (BlackRock), a global provider of investment, advisory and risk management solutions, reported that their beneficial ownership increased to more than 10% of our outstanding common stock. BlackRock manages a portion of our cash and investments portfolio. As of December 31, 2018 and 2017, respectively, the fair value of cash and

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investments managed by BlackRock was $298.5 million and $141.0 million, which included $3.0 million and $1.0 million invested in the BlackRock Liquidity Money Market Fund. We incurred $0.2 million in fees for BlackRock advisory services performed during the year ended December 31, 2018.

NOTE 5. INVENTORY

Inventory consisted of the following (in thousands):

	December 31,	
	2018	2017
Raw materials	$1,922	$498
Work in process	6,170	3,997
Finished goods	3,836	2,854
Total	$11,928	$7,349
Balance Sheet classification:		
Inventory	$9,838	$6,657
Inventory included in Other long-term assets	2,090	692
Total	$11,928	$7,349

Write-downs related to excess and expiring inventory are charged to either Cost of goods sold or the cost of supplied product included in Collaboration revenues. Such write-downs were $1.1 million, $1.2 million and $0.5 million for the years ended December 31, 2018, 2017 and 2016, respectively.

Inventory expected to be used in production or sold in periods more than 12 months from the date presented is classified as Other long-term assets in the accompanying Consolidated Balance Sheets. As of both December 31, 2018 and 2017, the non-current portion of inventory consisted of a portion of our finished goods.

NOTE 6. PROPERTY AND EQUIPMENT

Property and equipment were as follows (in thousands):

	December 31, 2018	December 31, 2017
Leasehold improvements	$ 33,941	$4,715
Computer equipment and software	15,022	14,146
Furniture and fixtures	12,709	1,609
Laboratory equipment	5,668	5,959
Construction in progress	866	22,114
	68,206	48,543
Less: accumulated depreciation and amortization	(17,309)	(22,800)
Property and equipment, net	$ 50,897	$25,743

Depreciation expense was $4.9 million, $1.2 million and $1.0 million during the years ended December 31, 2018, 2017 and 2016, respectively.

In May 2017, we entered into the Lease for office and research facilities located at 1851, 1801, and 1751 Harbor Bay Parkway, Alameda, California (the Premises). The Lease was amended in October 2017 and June 2018 to increase the space leased to an aggregate of 134,765 square feet. For a description of the Lease, see “Note 11. Commitments.” In June 2018, we relocated our offices and research facilities to the Premises. Accordingly, we placed into service $46.3 million in related Leasehold improvements, Furniture and fixtures and Computer equipment and software, portions of which were included in Construction in progress at prior period ends.

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NOTE 7. STOCK-BASED COMPENSATION

We allocated the stock-based compensation expense for our equity incentive plans and our 2000 Employee Stock Purchase Plan (ESPP) as follows (in thousands):

	Year Ended December 31,		
	2018	2017	2016
Research and development	$13,115	$7,569	$9,366
Selling, general and administrative	27,511	16,369	13,546
Total stock-based compensation	$40,626	$23,938	$22,912

We have several equity incentive plans under which we granted stock options and RSUs to employees and directors. At December 31, 2018, 14,693,867 shares were available for grant under our equity incentive plans. The Board of Directors or a designated Committee of the Board is responsible for administration of our equity incentive plans and determines the term, exercise price and vesting terms of each grant. Stock options have a four-year vesting term, an exercise price equal to the fair market value on the date of grant, and a seven year life from the date of grant. Stock options issued prior to May 2011 have a ten year life from the date of grant. RSUs granted to our employees generally vest annually over a four year term.

We have adopted a Change in Control and Severance Benefit Plan for executives and certain non-executives. Eligible Change in Control and Severance Benefit Plan participants include employees with the title of vice president and above. If a participant’s employment is terminated without cause during a period commencing one month before and ending thirteen months following a change in control, as defined in the plan document, then the Change in Control and Severance Benefit Plan participant is entitled to have the vesting of all its outstanding stock options accelerated with the exercise period being extended to no more than one year.

We have an ESPP that allows for qualified employees (as defined in the ESPP) to purchase shares of our common stock at a price equal to the lower of 85% of the closing price at the beginning of the offering period or 85% of the closing price at the end of each six month purchase period. Compensation expense related to our ESPP was $2.2 million, $1.6 million, and $1.0 million for the years ended December 31, 2018, 2017 and 2016, respectively. As of December 31, 2018, we had 4,722,008 shares available for issuance under our ESPP. Pursuant to the ESPP, we issued 330,492 shares, 434,523 shares, and 559,936 shares of common stock at an average price per share of $15.74, $11.20 and $3.91 during the years ended December 31, 2018, 2017 and 2016, respectively. Cash received from purchases under the ESPP in the years ended December 31, 2018, 2017 and 2016 was $5.2 million, $4.9 million and $2.2 million, respectively.

We used a Monte Carlo simulation pricing model to value stock options that include market vesting conditions and a Black-Scholes Merton option pricing model to value other stock options and ESPP purchases. The weighted average grant-date fair value per share of stock options and ESPP purchases was as follows:

	Year Ended December 31,		
	2018	2017	2016
Stock options	$9.07	$11.42	$4.77
ESPP	$6.40	$6.00	$2.17

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The grant-date fair value of stock option grants and ESPP purchases was estimated using the following assumptions:

	Year Ended December 31,		
	2018	2017	2016
Stock options:			
Risk-free interest rate	2.81 %	1.98 %	1.15 %
Dividend yield	— %	— %	— %
Volatility	55 %	59 %	76 %
Expected life	4.4 years	4.5 years	4.4 years
ESPP:			
Risk-free interest rate	1.93 %	1.09 %	0.55 %
Dividend yield	— %	— %	— %
Volatility	53 %	58 %	65 %
Expected life	6 months	6 months	6 months

We considered our implied volatility and our historical volatility in developing our estimates of expected volatility. The assumptions for the expected life of stock options were based on historical exercise patterns and post-vesting termination behavior. The risk-free interest rate is based on U.S. Treasury rates with the same or similar term as the underlying award. Our dividend rate is based on historical experience and our investors' current expectations.

The fair value of RSUs was based on the closing price of the underlying common stock on the date of grant.

Activity for stock options during the year ended December 31, 2018 was as follows (dollars in thousands, except per share amounts):

	Shares	Weighted Average Exercise Price	Weighted Average Remaining Contractual Term	Aggregate Intrinsic Value
Stock options outstanding at December 31, 2017	22,208,446	$ 6.83		
Granted	3,238,473	$ 19.40		
Exercised	(2,466,579)	$ 4.90		
Forfeited	(288,197)	$ 15.71		
Expired	(18,081)	$ 20.64		
Stock options outstanding at December 31, 2018	22,674,062	$ 8.71	3.7 years	$ 254,201
Exercisable at December 31, 2018	16,463,202	$ 5.65	3.0 years	$ 229,699

During the year ended December 31, 2018, in connection with our long-term incentive compensation program, we granted 308,365 stock options to our President and Chief Executive Officer that have a market vesting condition (PSOs). In addition to the standard service conditions included in our other stock options, these PSOs may not be exercised until, at any time after the grant date, the closing market price of a share of our Common Stock is equal to or greater than 125% of the per share exercise price of the PSO over a period of at least 30 consecutive calendar days. The stock-based compensation expense for the PSO is being recognized over the service period of the award, which commenced on the date of grant.

During the year ended December 31, 2016, the Compensation Committee of the Board of Directors of Exelixis convened to determine we had met certain performance objectives for performance-based stock options granted to employees in 2013, 2014 and 2015. As a result of these determinations, 5,870,303 performance-based stock options vested during 2016 and we recognized $4.1 million in stock-based compensation for those performance-based stock option grants. We did not have any performance-based stock options outstanding during the year ended December 31, 2017 and therefore, did not record any stock-based compensation for performance-based stock options during that year.

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As of December 31, 2018, there was $48.0 million of unrecognized compensation expense related to our unvested stock options, including the PSOs described above. The compensation expense for the unvested stock options will be recognized over a weighted-average period of 2.5 years.

The aggregate intrinsic value in the table above represents the total intrinsic value (the difference between our closing stock price on the last trading day of fiscal 2018 and the exercise prices, multiplied by the number of in-the-money options) that would have been received by the stock option holders had all stock option holders exercised their stock options on December 31, 2018. The total intrinsic value of stock options exercised on the dates of exercise was $39.1 million, $85.2 million and $50.0 million during the years ended December 31, 2018, 2017 and 2016, respectively. Cash received from option exercises during the years ended December 31, 2018, 2017 and 2016 was $12.1 million, $17.6 million and $25.3 million, respectively. The total estimated fair value of stock options vested and recorded as expense during the years ended December 31, 2018, 2017 and 2016 was $18.9 million, $13.1 million and $13.4 million, respectively.

Activity for RSUs during the year ended December 31, 2018 was as follows (dollars in thousands, except per share amounts):

	Shares	Weighted Average Grant Date Fair Value	Weighted Average Remaining Contractual Term	Aggregate Intrinsic Value
RSUs outstanding at December 31, 2017	3,762,990	$ 17.76		
Awarded	2,519,425	$ 18.46		
Vested and released	(1,081,339)	$ 16.05		
Forfeited	(343,742)	$ 18.99		
RSUs outstanding at December 31, 2018	4,857,334	$ 18.42	2.1 years	$ 94,427

During the year ended December 31, 2018, in connection with our long-term incentive compensation program, we awarded 693,131 RSUs that will vest upon the achievement of certain product revenue, late-stage clinical development and pipeline expansion performance targets (PSUs). These PSUs are included in the RSU activity table presented above. The PSUs were designed to drive the performance of our management team toward the achievement of key corporate objectives and will be forfeited if the performance targets are not met by December 31, 2021. Expense recognition for PSUs commences when the attainment of the performance goal is determined by management to be probable. During the year ended December 31, 2018, we did not recognize any compensation expense related to these PSUs. As of December 31, 2018, the total unrecognized compensation expense related to the unvested PSUs was $12.7 million. There were no performance-based RSUs issued prior to 2018.

As of December 31, 2018, there was $81.8 million of unrecognized compensation expense related to our unvested RSUs, including the PSUs described above. The compensation expense for the unvested RSUs will be recognized over a weighted-average period of 3.1 years.

401(k) Retirement Plan

We sponsor the Exelixis, Inc. 401(k) Plan (the 401(k) Plan) whereby eligible employees may elect to contribute up to the lesser of 50% of their annual compensation or the statutorily prescribed annual limit allowable under Internal Revenue Service regulations. During 2018, we made matching contributions in the form of our common stock of 100% of the first $8,500 of each participant’s contributions into the 401(k) Plan. We recorded compensation expense related to the stock match of $3.6 million, $1.7 million, and $1.1 million for the years ended December 31, 2018, 2017 and 2016, respectively. As of December 31, 2018, 571,674 shares were available for issuance under the 401(k) Plan.

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NOTE 8. INCOME TAXES

Our income (loss) before income taxes is derived solely from within the U.S. The Income tax benefit (provision) was as follows (in thousands):

	Year Ended December 31,		
	2018	2017	2016
Current:			
Federal	$—	$—	$ —
State	(6,133)	(4,350)	—
Total current tax expense	(6,133)	(4,350)	—
Deferred:			
Federal	238,675	—	—
State	5,436	—	—
Total deferred tax expense	244,111	—	—
Income tax benefit (provision)	$237,978	$(4,350)	$ —

The income tax benefit for the year ended December 31, 2018 primarily relates to the release of our valuation allowance against significantly all of our deferred tax assets offset by state taxes in jurisdictions outside of California, for which we do not have net operating loss carryforwards due to a limited operating history. Our historical net operating losses are sufficient to fully offset any federal taxable income. The Income tax provision for the year ended December 31, 2017, related to state taxes in jurisdictions outside of California, for which we do not have net operating loss carryforwards due to a limited operating history.

The reconciliation of the U.S. federal income tax (provision) benefit at the statutory federal income tax rates of 21%, 34% and 34% for the years ended December 31, 2018, 2017 and 2016, respectively, to our Income tax benefit (provision) was as follows (in thousands):

	Year Ended December 31,		
	2018	2017	2016
U.S. federal income tax (provision) benefit at statutory rate	$(94,939)	$(53,916)	$23,876
State tax expense	(4,690)	(8,282)	(6,520)
Change in valuation allowance	315,394	34,266	(6,377)
Research credits	18,308	—	—
Stock-based compensation	5,998	20,548	(3,155)
Non-deductible interest	—	(1,367)	(2,680)
Debt extinguishment	—	—	(4,726)
Other	(2,093)	4,401	(418)
Income tax benefit (provision)	$237,978	$(4,350)	$—

Deferred tax assets and liabilities reflect the net tax effects of net operating loss and tax credit carryforwards and temporary differences between the carrying amounts of assets and liabilities for financial reporting and the amounts used for income tax purposes.

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Our deferred tax assets and liabilities were as follows (in thousands):

	December 31,	
	2018	2017
Deferred tax assets:		
Net operating loss carryforwards	$146,701	$244,205
Tax credit carryforwards	98,467	66,770
Book over tax depreciation and amortization	29,929	39,472
Amortization of deferred stock compensation – non-qualified	11,366	8,966
Accruals and reserves not currently deductible	10,425	4,914
Deferred revenue	5,474	53,543
Other assets	1,140	1,088
Total deferred tax assets	303,502	418,958
Valuation allowance	(58,112)	(418,958)
Net deferred tax assets	245,390	—
Deferred tax liabilities:		
Operating lease right-of-use assets	(1,279)	—
Total deferred tax liabilities	(1,279)	—
Net deferred taxes	$244,111	$—

We applied the guidance in the Securities and Exchange Commission's Staff Accounting Bulletin No. 118, Income Tax Accounting Implications of the Tax Cuts and Jobs Act, when accounting for the enactment-date effects of the Tax Cuts and Jobs Act in 2017 and throughout 2018. At December 31, 2017, we had not completed our accounting for all the enactment-date income tax effects of the Tax Cuts and Jobs Act for Section 162(m) related to the deduction limitation for the remuneration of certain employees. As of December 31, 2018, we have now completed our accounting for all of the enactment-date income tax effects of the Tax Cuts and Jobs Act and the impact was not material.

ASC Topic 740: Income Taxes (Topic 740) requires that the tax benefit of net operating losses, temporary differences and credit carry forwards be recorded as an asset to the extent that management assesses that realization is "more likely than not." Realization of the future tax benefits is dependent on our ability to generate sufficient taxable income within the carry forward period. As of each reporting date, management considers new evidence, both positive and negative, that could affect its view of the future realization of deferred tax assets. As of December 31, 2018, based on the evaluation and weighting of both positive and negative evidence, including our achievement of a cumulative three-year income position as of December 31, 2018 and forecasts of future operating results, as well as considering the utilization of net operating losses and tax credits prior to their expiration, management determined that there is sufficient positive evidence to conclude that it is more likely than not the deferred tax assets of $244.1 million are realizable and the valuation allowance was reduced accordingly. As of December 31, 2018, we continue to carry a valuation allowance of $58.1 million against our California state deferred tax assets. Prior to December 31, 2018, because of our history of operating losses, management believed that recognition of the deferred tax assets was not more likely than not (as defined in Topic 740) to be realized and, accordingly, had provided a full valuation allowance. The valuation allowance decreased by $360.8 million and $210.1 million during 2018 and 2017, respectively.

At December 31, 2018, we had federal net operating loss carryforwards of approximately $614 million which expire in the years 2031 through 2036, and federal business tax credits of approximately $102 million which expire in the years 2021 through 2038. We also had state net operating loss carryforwards of approximately $453 million, which expire in the years 2028 through 2036, and California research and development tax credits of approximately $34 million, which do not expire.

Under the Internal Revenue Code and similar state provisions, certain substantial changes in our ownership could result in an annual limitation on the amount of net operating loss and credit carryforwards that can be utilized in future years to offset future taxable income. The annual limitation may result in the expiration of net operating losses and credit carryforwards before utilization. We completed a Section 382 study through December 31, 2018, and concluded

that an ownership change, as defined under Section 382, had not occurred.

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The following table summarizes the activity related to our unrecognized tax benefits (in thousands):

	Year Ended December 31,		
	2018	2017	2016
Beginning balance	$79,342	$61,809	$88,638
Change relating to prior year provision	(4,254)	247	(29,110)
Change relating to current year provision	1,083	17,378	2,304
Reductions based on the lapse of the applicable statutes of limitations	(111)	(92)	(23)
Ending balance	$76,060	$79,342	$61,809

We do not anticipate that the amount of unrecognized tax benefits existing as of December 31, 2018 will significantly change over the next 12 months. As of December 31, 2018, we had $76.1 million in unrecognized tax benefits, of which $46.0 million would reduce our income tax provision and the effective tax rate, if recognized. Interest and penalties were nominal or zero for all periods presented. We have elected to record interest and penalties in the accompanying Consolidated Statements of Operations as a component of income taxes.

We file U.S. and state income tax returns in jurisdictions with varying statues of limitations during which such tax returns may be audited and adjusted by the relevant tax authorities. The 1999 through 2018 tax years generally remain subject to examination by federal and most state tax authorities to the extent net operating losses and credits generated during these periods are being utilized in the open tax periods.

NOTE 9. NET INCOME (LOSS) PER SHARE

The computation of basic and diluted net income (loss) per share was as follows (in thousands, except per share amounts):

	Year Ended December 31,		
	2018	2017	2016
Numerator:			
Net income (loss)	$690,070	$154,227	$(70,222)
Net income allocated to participating securities	—	(367)	—
Net income (loss) allocable to common stock for basic net income (loss) per share	690,070	153,860	(70,222)
Adjustment to net income allocated to participating securities	—	22	—
Net income (loss) allocable to common stock for diluted net income (loss) per share	$690,070	$153,882	$(70,222)
Denominator:			
Weighted-average shares of common stock outstanding used in computing basic net income (loss) per share	297,892	293,588	250,531
Dilutive securities	14,911	18,415	—
Weighted-average shares of common stock outstanding and dilutive securities used in computing diluted net income (loss) per share	312,803	312,003	250,531
Net income (loss) per share, basic	$2.32	$0.52	$(0.28)
Net income (loss) per share, diluted	$2.21	$0.49	$(0.28)

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Potential shares of common stock not included in the computation of diluted net income (loss) per share because to do so would be anti-dilutive was as follows (in thousands):

	Year Ended December 31,		
	2018	2017	2016
Outstanding stock options, unvested RSUs and ESPP contributions	3,968	1,645	27,568
Secured Convertible Notes due 2018 held by entities associated with Deerfield Management Company, L.P. (Deerfield Notes)	—	—	33,890
2014 Warrants	—	—	1,000
Total	3,968	1,645	62,458

The Deerfield Notes were repaid in June 2017. Warrants to purchase an aggregate of 1,000,000 shares of our common stock issued in January 2014 (2014 Warrants) were participating securities. The warrant holders did not have a contractual obligation to share in our losses. The 2014 Warrants were fully exercised in September 2017.

NOTE 10. FAIR VALUE MEASUREMENTS

The classification of our financial assets within the fair value hierarchy that were measured and recorded at fair value on a recurring basis was as follows (in thousands):

	December 31, 2018		
	Level 1	Level 2	Total
Money market funds	$47,744	$—	$47,744
Commercial paper	—	381,133	381,133
Corporate bonds	—	344,064	344,064
U.S. Treasury and government sponsored enterprises	—	55,201	55,201
Total investments available-for-sale	47,744	780,398	828,142
Certificates of deposit	—	16,596	16,596
Total financial assets carried at fair value	$47,744	$796,994	$844,738

	December 31, 2017		
	Level 1	Level 2	Total
Money market funds	$45,478	$—	$45,478
Commercial paper	—	199,647	199,647
Corporate bonds	—	179,022	179,022
U.S. Treasury and government sponsored enterprises	—	16,263	16,263
Total investments available-for-sale	45,478	394,932	440,410
Certificates of deposit	—	13,498	13,498
Total financial assets carried at fair value	$45,478	$408,430	$453,908

We did not have any financial liabilities measured and recorded at fair value on a recurring basis as of December 31, 2018 or December 31, 2017. We did not have any financial assets or liabilities classified as Level 3 in the fair value hierarchy as of December 31, 2018 or December 31, 2017. There were no transfers of financial assets or liabilities between Levels 1, 2 and 3 during the years ended December 31, 2018 or 2017.

When available, we value investments based on quoted prices for those financial instruments, which is a Level 1 input. Our remaining investments are valued using third-party pricing sources, which use observable market prices, interest rates and yield curves observable at commonly quoted intervals for similar assets as observable inputs for pricing, which is a Level 2 input.

See “Note 11. Commitments” regarding the determination of the amount of our operating lease liabilities as of December 31, 2018. Our remaining financial assets and liabilities include cash and restricted cash, Trade receivables, net, Other receivables, Accounts payable, Accrued compensation and benefits, Accrued clinical trial liabilities, Accrued

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collaboration liabilities, Rebates and fees due to customers and other current and long-term liabilities. Those financial assets and liabilities are carried at cost which approximates their fair values.

NOTE 11. COMMITMENTS

Leases

As described further in “Note 1. Organization and Summary of Significant Accounting Policies”, we adopted Topic 842 as of January 1, 2018. Prior period amounts have not been adjusted and continue to be reported in accordance with our historic accounting under Topic 840.

In May 2017, we entered into the Lease with Ascentris for office and research facilities located at the Premises in Alameda, California. The Lease was amended in October 2017 and June 2018 to increase the space leased to an aggregate of 134,765 square feet. We have made certain tenant improvements to the space leased on the Premises, for which we received $8.2 million in reimbursements in January 2019. The Lease’s initial term is through January 31, 2028. Rent payments began February 1, 2018, following the conclusion of a partial twelve-month rent abatement period. We have two five-year options to extend the Lease and a one-time option to terminate the Lease without cause on the last day of the 8th year of the initial term; none of these optional periods have been considered in the determination of the right-of-use asset or the lease liability for the Lease as we did not consider it reasonably certain that we would exercise any such options. The Lease further provides that we are obligated to pay to Ascentris certain variable costs, including taxes and operating expenses. We also have a right of first offer to lease certain additional space, in the aggregate of approximately 170,000 square feet of space, as that additional space becomes available at 1601, 1701 and 1751 Harbor Bay Parkway, Alameda, California over the remainder of the initial term of the Lease at a market rate determined pursuant to the Lease.

We had an additional operating lease which expired in July 2018 for two buildings in South San Francisco, California with a total area of 116,063 square feet.

We have performed an evaluation of our other contracts with customers and suppliers in accordance with Topic 842 and have determined that, except for the leases described above, a nominal operating lease for space at a data center to house our data servers and a nominal financing lease for office equipment, none of our contracts contain a lease.

The balance sheet classification of our lease liabilities was as follows (in thousands):

	December 31, 2018	December 31, 2017
Operating lease liabilities:		
Current portion included in Other current liabilities	$ 2,738	$ 540
Long-term portion of lease liabilities	12,099	408
Total operating lease liabilities	14,837	948
Financing lease liabilities:		
Financing obligation for build-to-suit lease	—	14,530
Current portion included in Other current liabilities	49	—
Long-term portion of lease liabilities	79	—
Total financing lease liabilities	128	14,530
Total lease liabilities	$ 14,965	$ 15,478

The components of lease costs, which were included in Operating expenses in our Consolidated Statements of Operations, were as follows (in thousands):

	Year Ended December 31,		
	2018	2017	2016
Operating lease cost	$4,189	$3,944	$8,620
Variable lease cost	1,661	2,216	1,056
Sublease income	—	(1,225)	(3,553)
Total lease costs	$5,850	$4,935	$6,123

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Cash paid for amounts included in the measurement of lease liabilities for the year ended December 31, 2018 was $3.9 million and was included in Net cash provided by operating activities in our Consolidated Statements of Cash Flows. As of December 31, 2018, the maturities of our operating lease liabilities were as follows (in thousands):

	Operating leases
Years ending December 31,	
2019	$2,794
2020	2,823
2021	2,904
2022	3,000
2023	3,082
Thereafter	13,584
Total lease payments	28,187
Less:	
Present value adjustment	(5,180)
Tenant improvement reimbursements	(8,170)
Operating lease liabilities	$14,837

Operating lease liabilities are based on the net present value of the remaining lease payments over the remaining lease term. In determining the present value of lease payments, we use our incremental borrowing rate based on the information available at the lease commencement date. As of December 31, 2018, the weighted average remaining lease term is 9.0 years and the weighted average discount rate used to determine the operating lease liability was 4.50%.

Letters of Credit and Restricted Cash

We have obtained two standby letters of credit related to the Lease with Ascentris with a combined credit limit of $1.0 million as of both December 31, 2018 and 2017. We have also obtained standby letters of credit related to a workers compensation insurance policy with credit limits of $0.1 million and $0.6 million as of December 31, 2018 and 2017, respectively. We had also previously obtained a standby letter of credit related to our South San Francisco lease with a credit limit of $0.5 million as of December 31, 2017 which was released during 2018. As of December 31, 2018, none of our letters of credit have been drawn upon. All of the letters of credit are fully collateralized by certificates of deposit. The certificate of deposits used to collateralize the standby letters of credit were included in short-term and long-term restricted cash and investments.

We were previously required to provide collateral as part of an employee purchasing card program. The collateral requirement for the purchase card program at December 31, 2017 was $3.0 million. During 2018 we were notified that we had been released from this collateral requirement. The collateral was invested in certificates of deposit which were included in long-term restricted cash and investments.

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NOTE 12. QUARTERLY FINANCIAL DATA (UNAUDITED)

The unaudited quarterly financial data for the last two fiscal years was as follows (in thousands, except per share data):

	Quarter Ended			
	December 31,	September 30,	June 30,	March 31,
2018:				
Total revenues [1]	$228,602	$ 225,397	$186,108	$213,719
Gross profit [2]	$168,873	$ 155,586	$139,839	$128,633
Income from operations	$111,602	$ 125,176	$85,770	$116,307
Net income	$360,089	$ 126,630	$87,494	$115,857
Net income per share, basic	$1.20	$ 0.42	$0.29	$0.39
Net income per share, diluted	$1.15	$ 0.41	$0.28	$0.37
2017:				
Total revenues	$120,072	$ 152,510	$99,008	$80,887
Gross profit [2]	$91,520	$ 91,758	$84,990	$65,674
Income from operations	$37,431	$ 81,180	$27,113	$20,186
Net income	$38,489	$ 81,382	$17,656	$16,700
Net income per share, basic	$0.13	$ 0.28	$0.06	$0.06
Net income per share, diluted	$0.12	$ 0.26	$0.06	$0.05

(1) Total revenues for the three months ended March 31, 2018 have been adjusted to reflect the reclassification of the $1.4 million profit related to the profit sharing arrangement with Genentech for the commercialization of COTELLIC. For three months ended March 31, 2018, the net profit had been classified as Selling, general and administrative expenses as we were expecting an overall loss for the year ended December 31, 2018. During the three months ended June 30, 2018, we determined that the U.S. commercialization of COTELLIC would result in a profit for the year ended December 31, 2018 and therefore, we reclassified the profit for the three months ended March 31, 2018 from Selling, general and administrative expenses to Collaboration revenues to be consistent with presentation for the three and six months ended June 30, 2018. See “Note 3. Collaboration Agreements” for more information on our collaboration agreement with Genentech.

(2) Gross profit is computed as Net product revenues less Cost of goods sold.

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Item 9. Changes in and Disagreements With Accountants on Accounting and Financial Disclosure

Not applicable.

Item 9A. Controls and Procedures

Evaluation of Disclosure Controls and Procedures. Based on the evaluation of our disclosure controls and procedures (as defined under Rules 13a-15(e) or 15d-15(e) under the Securities Exchange Act of 1934, as amended) required by Rules 13a-15(b) or 15d-15(b) under the Securities Exchange Act of 1934, as amended, our Chief Executive Officer and our Chief Financial Officer have concluded that as of the end of the period covered by this report, our disclosure controls and procedures were effective.

Limitations on the Effectiveness of Controls. A control system, no matter how well conceived and operated, can provide only reasonable, not absolute, assurance that the objectives of the control system are met. Because of inherent limitations in all control systems, no evaluation of controls can provide absolute assurance that all control issues, if any, within an organization have been detected. Accordingly, our disclosure controls and procedures are designed to provide reasonable, not absolute, assurance that the objectives of our disclosure control system are met and, as set forth above, our principal executive officer and principal financial officer have concluded, based on their evaluation as of the end of the period covered by this report, that our disclosure controls and procedures were effective to provide reasonable assurance that the objectives of our disclosure control system were met.

Management’s Report on Internal Control Over Financial Reporting. Our management is responsible for establishing and maintaining adequate internal control over financial reporting. Our internal control over financial reporting is a process designed under the supervision of our principal executive and principal financial officers to provide reasonable assurance regarding the reliability of financial reporting and the preparation of our financial statements for external reporting purposes in accordance with U.S. generally accepted accounting principles.

As of the end of our 2018 fiscal year, management conducted an assessment of the effectiveness of our internal control over financial reporting based on the framework established in the original Internal Control – Integrated Framework issued by the Committee of Sponsoring Organizations of the Treadway Commission (2013 framework) (COSO). Based on this assessment, management has determined that our internal control over financial reporting as of December 28, 2018 was effective. There were no material weaknesses in internal control over financial reporting identified by management.

The independent registered public accounting firm Ernst & Young LLP has issued an audit report on our internal control over financial reporting, which is included on the following page.

Changes in Internal Control Over Financial Reporting. There were no changes in our internal control over financial reporting that occurred during our most recent fiscal quarter that have materially affected, or are reasonably likely to materially affect, our internal control over financial reporting.

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Report of Independent Registered Public Accounting Firm

To the Stockholders and the Board of Directors of Exelixis, Inc.

Opinion on Internal Control over Financial Reporting

We have audited Exelixis, Inc.'s internal control over financial reporting as of December 28, 2018, based on criteria established in Internal Control-Integrated Framework issued by the Committee of Sponsoring Organizations of the Treadway Commission (2013 framework) (the COSO criteria). In our opinion, Exelixis, Inc. (the Company) maintained, in all material respects, effective internal control over financial reporting as of December 28, 2018, based on the COSO criteria.

We also have audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States) (PCAOB), the consolidated balance sheets of the Company as of December 28, 2018 and December 29, 2017, the related consolidated statements of operations, comprehensive income (loss), stockholders' equity (deficit) and cash flows for each of the three fiscal years in the period ended December 28, 2018, and the related notes and our report dated February 22, 2019 expressed an unqualified opinion thereon.

Basis for Opinion

The Company's management is responsible for maintaining effective internal control over financial reporting and for its assessment of the effectiveness of internal control over financial reporting included in the accompanying Management's Report on Internal Control over Financial Reporting. Our responsibility is to express an opinion on the Company's internal control over financial reporting based on our audit. We are a public accounting firm registered with the PCAOB and are required to be independent with respect to the Company in accordance with the U.S. federal securities laws and the applicable rules and regulations of the Securities and Exchange Commission and the PCAOB.

We conducted our audit in accordance with the standards of the PCAOB. Those standards require that we plan and perform the audit to obtain reasonable assurance about whether effective internal control over financial reporting was maintained in all material respects.

Our audit included obtaining an understanding of internal control over financial reporting, assessing the risk that a material weakness exists, testing and evaluating the design and operating effectiveness of internal control based on the assessed risk, and performing such other procedures as we considered necessary in the circumstances. We believe that our audit provides a reasonable basis for our opinion.

Definition and Limitations of Internal Control Over Financial Reporting

A company's internal control over financial reporting is a process designed to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles. A company's internal control over financial reporting includes those policies and procedures that (1) pertain to the maintenance of records that, in reasonable detail, accurately and fairly reflect the transactions and dispositions of the assets of the company; (2) provide reasonable assurance that transactions are recorded as necessary to permit preparation of financial statements in accordance with generally accepted accounting principles, and that receipts and expenditures of the company are being made only in accordance with authorizations of management and directors of the company; and (3) provide reasonable assurance regarding prevention or timely detection of unauthorized acquisition, use, or disposition of the company's assets that could have a material effect on the financial statements.

Because of its inherent limitations, internal control over financial reporting may not prevent or detect misstatements. Also, projections of any evaluation of effectiveness to future periods are subject to the risk that controls may become inadequate because of changes in conditions, or that the degree of compliance with the policies or procedures may deteriorate.

/s/ Ernst & Young LLP

Redwood City, California

February 22, 2019

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Item 9B. Other Information

Not applicable

PART III

ITEM 10. DIRECTORS, EXECUTIVE OFFICERS AND CORPORATE GOVERNANCE

The information required by this item relating to our directors and nominees, including information with respect to our audit committee, audit committee financial experts and procedures by which stockholders may recommend nominees to our board of directors, is incorporated by reference to the section entitled “Proposal 1 – Election of Class II Directors” appearing in our Proxy Statement for our 2019 Annual Meeting of Stockholders to be filed with the SEC within 120 days after December 28, 2018, which we refer to as our 2019 Proxy Statement. The information required by this item regarding our executive officers is incorporated by reference to the section entitled “Executive Officers” appearing in our 2019 Proxy Statement. The information required by this item regarding compliance with Section 16(a) of the Securities Exchange Act of 1934, as amended, is incorporated by reference to the section entitled “Section 16(a) Beneficial Ownership Reporting Compliance” appearing in our 2018 Proxy Statement.

Code of Ethics

We have adopted a Corporate Code of Conduct that applies to all of our directors, officers and employees, including our principal executive officer, principal financial officer and principal accounting officer. The Corporate Code of Conduct is posted on our website at www.exelixis.com under the caption “Investors & Media—Corporate Governance—Corporate Governance Documents.”

We intend to satisfy the disclosure requirement under Item 5.05 of Form 8-K regarding an amendment to, or waiver from, a provision of this Corporate Code of Conduct by posting such information on our website, at the address and location specified above and, to the extent required by the listing standards of the Nasdaq Stock Market, by filing a Current Report on Form 8-K with the SEC, disclosing such information.

Item 11. Executive Compensation

The information required by this item is incorporated by reference to the sections entitled “Compensation of Executive Officers,” “Compensation of Directors,” “Compensation Committee Interlocks and Insider Participation” and “Compensation Committee Report” appearing in our 2019 Proxy Statement.

Item 12. Security Ownership of Certain Beneficial Owners and Management and Related Stockholder Matters

The information required by this item relating to security ownership of certain beneficial owners and management is incorporated by reference to the section entitled “Security Ownership of Certain Beneficial Owners and Management” appearing in our 2019 Proxy Statement.

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Equity Compensation Plan Information

The following table provides certain information about our common stock that may be issued upon the exercise of stock options and other rights under all of our existing equity compensation plans as of December 31, 2018, which consists of our 2000 Equity Incentive Plan (the 2000 Plan) our 2000 Non-Employee Directors' Stock Option Plan (the Director Plan) our 2000 Employee Stock Purchase Plan (the ESPP) our 2011 Equity Incentive Plan (the 2011 Plan) our 2014 Equity Incentive Plan (the 2014 Plan) our 2016 Inducement Award Plan (the 2016 Plan) our 2017 Equity Incentive Plan (the 2017 Plan) and our 401(k) Plan:

Plan Category	Number of securities to be issued upon exercise of outstanding options, warrants and rights	Weighted-average exercise price of outstanding options, warrants and rights	Number of securities remaining available for future issuance under equity compensation plans (excluding securities reflected in column (a))
	(a)	(b)	(c)
Equity compensation plans approved by stockholders [1]	27,242,369	$ 7.10 [2]	19,415,875
Equity compensation plans not approved by stockholders [3]	289,027	$ 14.34 [4]	571,674
Total	27,531,396	$ 7.17	19,987,549

(1) Equity plans approved by our shareholders are the 2000 Plan, the 2011 Plan, the 2014 Plan, the Director Plan, the 2017 Plan and the ESPP. As of December 31, 2018, a total of 4,722,008 shares of our common stock remained available for issuance under the ESPP, and up to a maximum of 246,410 shares of our common stock may be purchased in the current purchase period. The shares issuable pursuant to our ESPP are not included in the number of shares to be issued pursuant to rights outstanding or and the weighted-average exercise price of such rights as of December 31, 2018, as those numbers are not known.

(2) The weighted-average exercise price takes into account the shares subject to outstanding restricted stock units (RSUs) which have no exercise price. The weighted-average exercise price, excluding such outstanding RSUs, is $8.61.

(3) Represents shares of our common stock issuable pursuant to the 2016 Plan and our 401(k) Plan.

As of December 31, 2018, no shares of our common stock remained available for issuance under the 2016 Plan. In November 2016, the Board adopted the 2016 Plan pursuant to which we reserved 1,500,000 shares of our common stock for issuance under the 2016 Plan. The only persons eligible to receive grants of Awards under the 2016 Plan are individuals who satisfy the standards for inducement grants under Nasdaq Marketplace Rule 5635(c)(4) and the related guidance under Nasdaq IM 5635-1 - that is, generally, a person not previously an employee or director of Exelixis, or following a bona fide period of non-employment, as an inducement material to the individual's entering into employment with Exelixis. An "Award" is any right to receive Exelixis common stock pursuant to the 2016 Plan, consisting of nonstatutory stock options, stock appreciation rights, restricted stock awards, RSUs, or any other stock award.

We sponsor a 401(k) Plan whereby eligible employees may elect to contribute up to the lesser of 50% of their annual compensation or the statutorily prescribed annual limit allowable under Internal Revenue Service regulations. The 401(k) Plan permits us to make matching contributions on behalf of all participants. During the year ended December 31, 2018, we matched 100% of the first $8,500 of participant contributions into our 401(k) Plan in the form of our common stock.

(4) The weighted-average exercise price takes into account the shares subject to outstanding RSUs, which have no exercise price. The weighted-average exercise price, excluding such outstanding RSUs, is $19.49.

Item 13. Certain Relationships and Related Transactions, and Director Independence

The information required by this item is incorporated by reference to the sections entitled “Certain Relationships and Related Party Transactions” and “Proposal 1 – Election of Class II Directors” appearing in our 2019 Proxy Statement.

Item 14. Principal Accounting Fees and Services

The information required by this item is incorporated by reference to the section entitled “Proposal 2 – Ratification of Selection of Independent Registered Public Accounting Firm” appearing in our 2019 Proxy Statement.

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PART IV

Item 15. Exhibits, Financial Statement Schedules

(a) The following documents are being filed as part of this report:

(1) The following financial statements and the Report of Independent Registered Public Accounting Firm are included in Part II, Item 8:

(2) All financial statement schedules are omitted because the information is inapplicable or presented in the Notes to Consolidated Financial Statements.

(3) The following Exhibits are filed as part of this report.

		Incorporation by Reference				
Exhibit Number	Exhibit Description	Form	File Number	Exhibit/ Appendix Reference	Filing Date	Filed Herewith
3.1	Amended and Restated Certificate of Incorporation of Exelixis, Inc.	10-K	000-30235	3.1	3/10/2010	
3.2	Certificate of Amendment of Amended and Restated Certificate of Incorporation of Exelixis, Inc.	10-K	000-30235	3.2	3/10/2010	
3.3	Certificate of Amendment of Amended and Restated Certificate of Incorporation of Exelixis, Inc.	8-K	000-30235	3.1	5/25/2012	
3.4	Certificate of Ownership and Merger Merging X-Ceptor Therapeutics, Inc. with and into Exelixis, Inc.	8-K	000-30235	3.2	10/15/2014	
3.5	Certificate of Change of Registered Agent and/or Registered Office of Exelixis, Inc.	8-K	000-30235	3.1	10/15/2014	
3.6	Amended and Restated Bylaws of Exelixis, Inc.	8-K	000-30235	3.1	2/21/2019	
4.1	Specimen Common Stock Certificate.	S-1, as amended	333-96335	4.1	4/7/2000	
10.1†	Form of Indemnity Agreement	S-1, as amended	333-96335	10.1	3/17/2000	
10.2†	Exelixis, Inc. 2000 Equity Incentive Plan	10-Q	000-30235	10.1	5/3/2007	
10.3†	Form of Stock Option Agreement under the Exelixis, Inc. 2000 Equity Incentive Plan (early exercise permissible)	10-Q	000-30235	10.2	11/8/2004	
10.4†	Form of Stock Option Agreement under the Exelixis, Inc. 2000 Equity Incentive Plan (early exercise may be restricted)	8-K	000-30235	10.1	12/15/2004	
10.5†	Exelixis, Inc. 2000 Non-Employee Directors' Stock Option Plan	10-K	000-30235	10.6	2/20/2014	

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Exhibit Number	Exhibit Description	Incorporation by Reference				Filed Herewith
		Form	File Number	Exhibit/ Appendix Reference	Filing Date	
10.6†	Form of Stock Option Agreement under the Exelixis, Inc. 2000 Non-Employee Directors' Stock Option Plan	10-K	000-30235	10.7	2/22/2011	
10.7†	Exelixis, Inc. 2000 Employee Stock Purchase Plan	Schedule 14A	000-30235	A	4/13/2016	
10.8†	Exelixis, Inc. 2011 Equity Incentive Plan					X
10.9†	Form of Stock Option Agreement under the Exelixis, Inc. 2011 Equity Incentive Plan	10-Q	000-30235	10.3	8/4/2011	
10.10†	Exelixis, Inc. 2014 Equity Incentive Plan	8-K	000-30235	10.1	5/29/2014	X
10.11†	Form of Stock Option Agreement under the Exelixis, Inc. 2014 Equity Incentive Plan	10-Q	000-30235	10.2	7/31/2014	
10.12†	Form of Stock Option Agreement (Non-Employee Director) under the Exelixis, Inc. 2014 Equity Incentive Plan	10-Q	000-30235	10.4	7/31/2014	
10.13†	Form of Restricted Stock Unit Agreement under the Exelixis, Inc. 2014 Equity Incentive Plan	10-Q	000-30235	10.5	7/31/2014	
10.14†	Form of Restricted Stock Unit Agreement (Non-Employee Director) under the Exelixis, Inc. 2014 Equity Incentive Plan	8-K	000-30235	10.1	10/16/2014	
10.15†	Exelixis, Inc. 2016 Inducement Award Plan					X
10.16†	Form of Stock Option Agreement under the 2016 Inducement Award Plan	8-K	000-30235	10.2	11/22/2016	
10.17†	Form of Restricted Stock Unit Agreement under the 2016 Inducement Award Plan	8-K	000-30235	10.2	11/22/2016	
10.18†	Exelixis, Inc. 2017 Equity Incentive Plan	10-K	000-30235	10.20	2/26/2018	
10.19†	Form of Stock Option Agreement under the Exelixis, Inc. 2017 Equity Incentive Plan	10-K	000-30235	10.21	2/26/2018	
10.20†	Form of Stock Option Agreement (Non-Employee Director) under the Exelixis, Inc. 2017 Equity Incentive Plan	10-K	000-30235	10.22	2/26/2018	
10.21†	Form of Restricted Stock Unit Agreement under the Exelixis, Inc. 2017 Equity Incentive Plan	10-K	000-30235	10.23	2/26/2018	
10.22†	Form of Restricted Stock Unit Agreement (Non-Employee Director) under the Exelixis, Inc. 2017 Equity Incentive Plan	10-K	000-30235	10.24	2/26/2018	
10.23†	Non-Employee Director Equity Compensation Policy	10-K	000-30235	10.25	2/26/2018	
10.24†	Offer Letter Agreement, dated February 3, 2000, between Exelixis, Inc. and Michael Morrissey, Ph.D.	10-Q	000-30235	10.43	8/5/2004	
10.25†	Offer Letter Agreement, dated June 30, 2015, between Exelixis, Inc. and Christopher Senner	10-Q	000-30235	10.5	11/10/2015	

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Exhibit Number	Exhibit Description	Incorporation by Reference				Filed Herewith
		Form	File Number	Exhibit/ Appendix Reference	Filing Date	
10.26†	Offer Letter Agreement, dated June 20, 2006, between Exelixis, Inc. and Gisela M. Schwab, M.D.	8-K	000-30235	10.1	6/26/2006	
10.27†	Offer Letter Agreement, dated February 10, 2014, between Exelixis, Inc. and Jeffrey J. Hessekiel.	10-Q	000-30235	10.4	5/1/2014	
10.28†	Offer Letter Agreement, dated August 11, 2000, between Exelixis, Inc. and Peter Lamb.	10-K	000-30235	10.24	2/29/2016	
10.29†	Offer Letter Agreement, dated August 19, 2010, between Exelixis, Inc. and Patrick J. Haley	10-K	000-30235	10.26	2/27/2017	
10.30†	Resignation Agreement dated July 22, 2010, by and between Exelixis, Inc. and George A. Scangos	10-Q	000-30235	10.1	11/4/2010	
10.31†	Annual Cash Bonus Compensation Plan for Executives	8-K	000-30235	10.1	2/16/2018	
10.32†	Cash Compensation Information for Non-Employee Directors.					X
10.33†	Exelixis, Inc. Change in Control and Severance Benefit Plan, as amended and restated.	10-Q	000-30235	10.5	5/2/2018	
10.34	Lease Agreement dated May 2, 2017, between Ascentris 105, LLC and Exelixis, Inc.	10-Q	000-30235	10.1	8/2/2017	
10.35	First Amendment to Lease Agreement dated October 16, 2017 to Lease Agreement dated May 2, 2017 between Ascentris 105, LLC and Exelixis, Inc.	10-K	000-30235	10.39	2/26/2018	
10.36	Second Amendment to Lease Agreement dated June 13, 2018 to Lease Agreement dated May 2, 2017 between Ascentris 105, LLC and Exelixis, Inc.	10-Q	000-30235	10.2	8/1/2018	
10.37*	Cooperative Research and Development Agreement for Extramural-PHS Clinical Research by and between The U.S. Department of Health and Human Services, as represented by National Cancer Institute, an Institute, Center, or Division of the National Institutes of Health and Exelixis, Inc. dated October 5, 2011	10-K	000-30235	10.45	2/27/2017	
10.38	Amendment #1 dated April 16, 2013, to Cooperative Research and Development Agreement for Extramural-PHS Clinical Research by and between The U.S. Department of Health and Human Services, as represented by National Cancer Institute, an Institute, Center, or Division of the National Institutes of Health and Exelixis, Inc. dated October 5, 2011	10-K	000-30235	10.46	2/27/2017	

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Exhibit Number	Exhibit Description	Incorporation by Reference				Filed Herewith
		Form	File Number	Exhibit/ Appendix Reference	Filing Date	
10.39	Amendment #2 dated July 18, 2016, to Cooperative Research and Development Agreement for Extramural-PHS Clinical Research by and between The U.S. Department of Health and Human Services, as represented by National Cancer Institute, an Institute, Center, or Division of the National Institutes of Health and Exelixis, Inc. dated October 5, 2011	10-K	000-30235	10.47	2/27/2017	
10.40**	Amendment #3 dated May 29, 2018, to Cooperative Research and Development Agreement for Extramural-PHS Clinical Research by and between The U.S. Department of Health and Human Services, as represented by National Cancer Institute, an Institute, Center, or Division of the National Institutes of Health and Exelixis, Inc. dated October 5, 2011					X
10.41*	Collaboration and License Agreement dated February 29, 2016, by and between Exelixis, Inc. and Ipsen Pharma SAS	10-Q/A	000-30235	10.3	9/30/2016	
10.42*	First Amendment dated December 20, 2016, to the Collaboration and License Agreement dated February 29, 2016, by and between Exelixis, Inc. and Ipsen Pharma SAS	10-K	000-30235	10.49	2/27/2017	
10.43*	Second Amendment dated September 14, 2017, to the Collaboration and License Agreement dated February 29, 2016, by and between Exelixis, Inc. and Ipsen Pharma SAS	10-Q	000-30235	10.2	11/1/2017	
10.44*	Third Amendment dated October 26, 2017, to the Collaboration and License Agreement dated February 29, 2016, by and between Exelixis, Inc. and Ipsen Pharma SAS	10-K	000-30235	10.46	2/26/2018	
10.45*	Supply Agreement dated February 29, 2016, by and between Exelixis, Inc. and Ipsen Pharma SAS	10-Q/A	000-30235	10.4	9/30/2016	
10.46*	First Amendment dated October 26, 2017, to the Supply Agreement dated February 29, 2016, by and between Exelixis, Inc. and Ipsen Pharma SAS	10-K	000-30235	10.48	2/26/2018	
10.47*	Collaboration Agreement dated December 22, 2006, by and between Exelixis, Inc. and Genentech, Inc.	10-K	000-30235	10.51	2/27/2017	
10.48*	First Amendment, dated March 13, 2008, to the Collaboration Agreement dated December 22, 2006, by and between Exelixis, Inc. and Genentech, Inc.	10-K	000-30235	10.52	2/27/2017	

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Exhibit Number	Exhibit Description	Incorporation by Reference				Filed Herewith
		Form	File Number	Exhibit/ Appendix Reference	Filing Date	
10.49	Second Amendment, dated April 30, 2010, to the Collaboration Agreement dated December 22, 2006, by and between Exelixis, Inc. and Genentech, Inc.	10-Q	000-30235	10.5	8/5/2010	
10.50 *	Third Amendment, dated July 19, 2017, to the Collaboration Agreement dated December 22, 2006, by and between Exelixis, Inc. and Genentech, Inc.	10-Q	000-30235	10.5	8/2/2017	
10.51*	Collaboration and License Agreement dated January 30, 2017, by and between Exelixis, Inc. and Takeda Pharmaceutical Company Limited	10-Q/A	000-30235	10.1	7/14/2017	
10.52*	First Amendment dated March 22, 2018, to the Collaboration and License Agreement dated January 30, 2017, by and between Exelixis, Inc. and Takeda Pharmaceutical Company Limited	10-Q	000-30235	10.1	8/1/2018	
10.53*	Clinical Trial Collaboration Agreement dated February 24, 2017, by and between Exelixis, Inc. and Bristol-Meyers Squibb Company	10-Q	000-30235	10.2	5/1/2017	
10.54*	Supplement to the Clinical Trial Collaboration Agreement dated February 24, 2017, by and among Exelixis, Inc., Bristol-Meyers Squibb Company and Ipsen Pharma SAS	10-Q	000-30235	10.3	5/1/2017	
10.55*	First Amendment dated July 6, 2018, to the Supplement to the Clinical Trial Collaboration Agreement dated February 24, 2017, by and among Exelixis, Inc., Bristol-Meyers Squibb Company and Ipsen Pharma SAS	10-Q	000-30235	10.1	11/1/2018	
10.56*	Supplement dated July 6, 2018, to the Clinical Trial Collaboration Agreement dated February 24, 2017, by and among Exelixis, Inc., Bristol-Meyers Squibb Company and Takeda Pharmaceutical Company Limited	10-Q	000-30235	10.2	11/1/2018	
10.57*	Ono Territorial Supplemental Agreement dated July 6, 2018, to the Clinical Trial Collaboration Agreement dated February 24, 2017, by and among Exelixis, Inc., Ono Pharmaceutical Co., Ltd. and Bristol-Meyers Squibb Company	10-Q	000-30235	10.3	11/1/2018	
21.1	Subsidiaries of Exelixis, Inc.					X
23.1	Consent of Independent Registered Public Accounting Firm					X
24.1	Power of Attorney (contained on signature page)					X
31.1	Certification of Principal Executive Officer Pursuant to Exchange Act Rules 13a-14(a) and Rule 15d-14(a)					X

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Exhibit Number	Exhibit Description	Incorporation by Reference				Filed Herewith
		Form	File Number	Exhibit/ Appendix Reference	Filing Date	
31.2	Certification of Principal Financial Officer Pursuant to Exchange Act Rules 13a-14(a) and Rule 15d-14(a)					X
32.1‡	Certifications of Principal Executive Officer and Principal Financial Officer Pursuant to 18 U.S.C. Section 1350					X
101.INS	XBRL Instance Document					X
101.SCH	XBRL Taxonomy Extension Schema Document					X
101.CAL	XBRL Taxonomy Extension Calculation Linkbase Document					X
101.DEF	XBRL Taxonomy Extension Definition Linkbase					X
101.LAB	XBRL Taxonomy Extension Labels Linkbase Document					X
101.PRE	XBRL Taxonomy Extension Presentation Linkbase Document					X

† Management contract or compensatory plan.

* Confidential treatment granted for certain portions of this exhibit.

** Confidential treatment requested for certain portions of this exhibit.

‡ This certification accompanies this Annual Report on Form 10-K, is not deemed filed with the SEC and is not to be incorporated by reference into any filing of the Company under the Securities Act of 1933, as amended, or the Securities Exchange Act of 1934, as amended (whether made before or after the date of this Annual Report on Form 10-K), irrespective of any general incorporation language contained in such filing.

ITEM 16. FORM 10-K SUMMARY

None provided.

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SIGNATURES

Pursuant to the requirements of Section 13 or 15(d) of the Securities Exchange Act of 1934, the Registrant has duly caused this report to be signed on its behalf by the undersigned, thereunto duly authorized

EXELIXIS, INC.

February 22, 2019 By: /s/ MICHAEL M. MORRISSEY
Date Michael M. Morrissey, Ph.D.
President and Chief Executive Officer

POWER OF ATTORNEY

KNOW ALL PERSONS BY THESE PRESENTS, that each person whose signature appears below constitutes and appoints MICHAEL M. MORRISSEY, CHRISTOPHER J. SENNER and JEFFREY J. HESSEKIEL and each or any one of them, his or her true and lawful attorney-in-fact and agent, with full power of substitution and resubstitution, for him or her and in his or her name, place and stead, in any and all capacities, to sign any and all amendments (including post-effective amendments) to this report on Form 10-K, and to file the same, with all exhibits thereto, and other documents in connection therewith, with the Securities and Exchange Commission, granting unto said attorneys-in-fact and agents, and each of them, full power and authority to do and perform each and every act and thing requisite and necessary to be done in connection therewith, as fully to all intents and purposes as he or she might or could do in person, hereby ratifying and confirming all that said attorneys-in-fact and agents, or any of them, or their or his or her substitutes or substitute, may lawfully do or cause to be done by virtue hereof.

Pursuant to the requirements of the Securities Exchange Act of 1934, this report has been signed by the following persons on behalf of the Registrant and in the capacities and on the dates indicated.

Signatures	Title	Date
/s/ MICHAEL M. MORRISSEY Michael M. Morrissey, Ph.D.	Director, President and Chief Executive Officer (Principal Executive Officer)	February 22, 2019
/s/ CHRISTOPHER J. SENNER Christopher J. Senner	Executive Vice President and Chief Financial Officer (Principal Financial and Accounting Officer)	February 22, 2019
/s/ STELIOS PAPADOPOULOS Stelios Papadopoulos, Ph.D.	Chairman of the Board	February 22, 2019
/s/ CHARLES COHEN Charles Cohen, Ph.D.	Director	February 22, 2019
/s/ CARL B. FELDBAUM Carl B. Feldbaum, Esq.	Director	February 22, 2019
/s/ MARIA C. FREIRE Maria C. Freire, Ph.D.	Director	February 22, 2019

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Signatures	Title	Date
/s/ ALAN M. GARBER Alan M. Garber, M.D., Ph.D.	Director	February 22, 2019
/s/ VINCENT T. MARCHESI Vincent T. Marchesi, M.D., Ph.D.	Director	February 22, 2019
/s/ GEORGE POSTE George Poste, DVM, Ph.D., FRS	Director	February 22, 2019
/s/ GEORGE A. SCANGOS George A. Scangos, Ph.D.	Director	February 22, 2019
/s/ JULIE A. SMITH Julie A. Smith	Director	February 22, 2019
/s/ LANCE WILLSEY Lance Willsey, M.D.	Director	February 22, 2019
/s/ JACK L. WYSZOMIERSKI Jack L. Wyszomierski	Director	February 22, 2019