Table of Contents

UNITED STATES
SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

FORM 10-K

☒ **ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**
For the fiscal year ended January 3, 2020

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	Trading Symbol(s)	Name of each exchange on which registered
Common Stock $.001 Par Value per Share	**EXEL**	**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 ☒ 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 ☒

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 ☒ 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 (§ 232.405 of this chapter) during the preceding 12 months (or for such shorter period that the registrant was required to submit such files). Yes ☒ No ☐

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	☒	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 ☒

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: $5,731,439,777. Excludes shares of the registrant's common stock held by persons who were directors and/or executive officers of the registrant at June 28, 2019 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.

Number shares of the registrant's common stock outstanding as of February 18, 2020: 305,393,240

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 May 4, 2020, in connection with the registrant's 2020 Annual Meeting of Stockholders are incorporated herein by reference into Part III of this Annual Report on Form 10-K.

EXELIXIS, INC.
ANNUAL REPORT ON FORM 10-K
INDEX

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 ends on the Friday closest to December 31st. Fiscal year 2019, which was a 53-week fiscal year, ended on January 3, 2020, fiscal year 2018, which was a 52-week fiscal year, ended on December 28, 2018 and fiscal year 2017, which was a 52-week fiscal year, ended on December 29, 2017. For convenience, references in this report as of and for the fiscal years ended January 3, 2020, December 28, 2018 and December 29, 2017 are indicated as being as of and for the years ended December 31, 2019, 2018 and 2017, respectively.

Item 1. Business

Overview

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. 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, received regulatory approval and established a commercial presence in various geographies around the world. Two are derived from cabozantinib, our flagship molecule, an inhibitor of multiple tyrosine kinases including MET, AXL, VEGF receptors and RET. Our cabozantinib products 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 these 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). For additional information about these products, see "—Collaborations—Other Collaborations."

Over the course of 2019, revenues from CABOMETYX and COMETRIQ sales and from the royalties and milestone payments we have received pursuant to collaboration agreements with our partners, coupled with disciplined expense management, have fueled the growth of our organization. We believe in our long-term growth prospects, which are supported by a healthy cash position and profitability over the past three fiscal years. We are utilizing our cash and investments to enable potential future success by expanding the development program for cabozantinib and by building a pipeline of new drug candidates through 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.

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 cabozantinib 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 2019, 2018 and 2017, we generated $760.0 million, $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 be approved in Japan, it will be marketed by our collaboration partner Takeda Pharmaceutical Company Limited (Takeda). In 2019, 2018 and 2017, we earned $62.4 million, $32.3 million and $3.8 million, respectively, of royalties on net sales of cabozantinib products 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 a 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. Estimates suggest that approximately 32,000 patients in the U.S. and 71,000 worldwide will require systemic treatment for kidney cancer in 2020. A growing number of these patients with RCC have been or will be treated with CABOMETYX, which has become a standard of care for the treatment of patients suffering from this difficult-to-treat disease.

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 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 2019, we continued to work closely with 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 51 countries outside of the U.S., including the Member States of 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, Takeda achieved an important regulatory milestone in April 2019 with its application to the Japanese Ministry of Health, Labour and Welfare (MHLW) for Manufacturing and Marketing Approval of CABOMETYX as a treatment for patients with unresectable and metastatic RCC in Japan.

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 nearly 43,000 cases of liver cancer estimated to be diagnosed in the U.S. during 2020, this patient population has long been 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, including immune checkpoint inhibitor (ICI) combination therapies if approved, we believe the second- and later-line HCC market has the potential to grow significantly in coming years, as these new treatment options are expected to result in an increasing number of patients receiving multiple lines of therapy. With the 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 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 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, and Health Canada's November 2019 approval brought a much-needed therapy to Canadian patients with HCC. In addition to the Member States of the EU and Canada, CABOMETYX is also approved for previously treated HCC indications in Taiwan, South Korea, Australia and Hong Kong, among other countries. With respect to the Japanese market, in January 2020, Takeda applied to the Japanese MHLW for Manufacturing and Marketing Approval of CABOMETYX as a treatment for patients with unresectable HCC who progressed after prior systemic therapy.

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

Estimates suggest that there will be approximately 900 MTC cases diagnosed in the U.S. in 2020. 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 2019, 2018 and 2017, we generated $26.5 million, $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 ICIs, in a broad development program comprising over 85 ongoing or planned clinical trials across multiple indications. We, along with our 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-funding select trials with us, our collaboration partners Ipsen and Takeda also conduct trials in their territories through similar independently-sponsored programs.

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 other therapies, including 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 pivotal trial (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)
Metastatic Variant Histology RCC	Phase 2* (CABOSUN II)
Locally Advanced Non-Metastatic Clear Cell RCC	Phase 2*
Hepatocellular Carcinoma (HCC)	
Second- and later-line HCC	Approved in U.S. and EU (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	
High-risk prostate cancer	Phase 2* (SPARC)
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.

CLINICAL DEVELOPMENT PROGRAM FOR CABOZANTINIB, IN COMBINATION WITH OTHER THERAPIES		
Indication	**Combination Regimen**	**Status Update**
Genitourinary Cancers		
First-line advanced RCC	+ nivolumab	Phase 3 pivotal trial (CheckMate 9ER)
First-line advanced or metastatic RCC	+ nivolumab + ipilimumab	Phase 3 pivotal trial (COSMIC-313)
First-line metastatic RCC	+ nivolumab vs. nivolumab after 4 cycles of nivolumab + ipilimumab	Phase 3† randomized (PDIGREE)
Advanced or metastatic RCC with a clear-cell component	+ CB-839 (telaglenastat)	Phase 2 pivotal trial (CANTATA)
Advanced or metastatic non-clear cell RCC	+ nivolumab	Phase 2*
Advanced RCC with bone metastasis	+ radium-223 dichloride	Phase 2† (RadiCal)

Cisplatin-Ineligible advanced UC	+ pembrolizumab	Phase 2* (PemCab)
Genitourinary tumors	+ nivolumab ± ipilimumab	Phase 1b†
Genitourinary tumors	+ nivolumab + ipilimumab	Phase 2† (ICONIC)
Gastrointestinal Cancers		
First-line advanced HCC	+ atezolizumab	Phase 3 pivotal trial (COSMIC-312), including a single-agent cabozantinib 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)
Thyroid Cancers		
Advanced DTC	+ nivolumab + ipilimumab	Phase 2†
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*
Neuroendocrine Tumors (NET) and Carcinoid		
Advanced carcinoid tumors	+ nivolumab	Phase 2*
Head and Neck Cancers		
Recurrent, metastatic squamous cell carcinoma	+ cetuximab	Phase 1*
Recurrent, metastatic squamous cell carcinoma	+ pembrolizumab	Phase 2*
Melanoma		
Unresectable, advanced melanoma	+ nivolumab + ipilimumab	Phase 2*
Advanced, metastatic melanoma	+ pembrolizumab	Phase 2*
Sarcoma		
Unresectable or metastatic leiomyosarcoma and other soft tissue sarcomas	+ temozolomide	Phase 1*
Sarcomas of the extremities	+ radiation therapy	Phase 2*
Additional Trials in Multiple Tumor Types		
Advanced solid tumors	+ atezolizumab	Phase 1b with 20 cabozantinib and atezolizumab expansion cohorts, including metastatic castration-resistant prostate cancer (mCRPC) (pivotal cohort), RCC, UC, HCC, colorectal adenocarcinoma, DTC, NSCLC, endometrial cancer, ovarian cancer, breast cancer, gastric or gastroesophageal junction adenocarcinoma and head and neck cancer (COSMIC-021), and three single-agent cabozantinib exploratory cohorts (UC, NSCLC and mCRPC), and one single-agent atezolizumab exploratory cohort (mCRPC)

Advanced CRC, HCC, gastric, gastroesophageal or esophageal adenocarcinoma	+ durvalumab	Phase 1* (CAMILLA)
Advanced non-squamous NSCLC, UC and advanced malignant mesothelioma	+ pemetrexed	Phase 1*

* 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 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 (The Alliance) 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.

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.

CELESTIAL had met its primary endpoint, with cabozantinib providing a statistically significant and clinically meaningful improvement versus placebo in OS, at which time the independent data monitoring committee, 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 0.76; 95% confidence interval 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. ORR was 4% with cabozantinib and 0.4% with placebo. 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. PFS in the subgroup was 5.5 months with cabozantinib versus 1.9 months with placebo. 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 collaboration 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, multicenter, 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 we expect top-line results from the trial in 2020. The study is also comparing COMETRIQ capsules with CABOMETYX tablets and, if positive, could facilitate the transition of metastatic MTC patients being treated with COMETRIQ to CABOMETYX.

Late-Stage Exelixis Sponsored Trial Evaluating Cabozantinib as a Monotherapy

Differentiated Thyroid Cancer (DTC) - COSMIC-311

Published studies indicate that approximately 53,000 new cases of thyroid cancer will be diagnosed in the U.S. in 2020. Differentiated thyroid tumors, which make up about 90% of all thyroid cancers, are typically treated with surgery followed by ablation of the remaining thyroid with radioiodine (RAI). Approximately 5% to 15% of differentiated thyroid tumors are resistant to radioiodine treatment. With limited treatment options, these patients have a life expectancy of only three to six years from the time metastatic lesions are detected. New treatment options are therefore urgently needed.

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 trial aims to enroll approximately 300 patients at approximately 150 sites globally, and patients enrolled in the trial will be randomized in a 2:1 ratio to receive either cabozantinib 60 mg or placebo once daily. We completed enrollment of the first 100 patients in the trial in February 2020 and plan to conduct an analysis in these first 100 patients for the co-primary endpoint of ORR, and an interim analysis of PFS in the second half of 2020. We further expect to reach total enrollment of 300 patients for the trial in the second half of 2020.

COSMIC-311 was informed by cabozantinib's encouraging clinical activity in phase 1 and 2 trials in patients with RAI-refractory DTC, including: an Exelixis-sponsored phase 1 open-label trial assessing the safety, tolerability and antitumor activity of cabozantinib in patients with DTC; a phase 2 single-arm, open-label trial evaluating cabozantinib for the first-line treatment of metastatic RAI-refractory DTC, conducted by the Center for Rare Cancers and Personalized Therapy at the Abramson Cancer Center of the University of Pennsylvania (Abramson Cancer Center); and a phase 2 single-arm trial evaluating cabozantinib in patients with RAI-refractory DTC who had been previously treated with at least one VEGFR-targeted therapy, conducted by the International Thyroid Oncology Group. Among the 15 RAI-refractory DTC patients enrolled in the Exelixis-sponsored phase 1 trial, PR was achieved by 53% of patients, and SD was reported in 40% of patients. Among the 35 patients in the Abramson Cancer Center phase 2 study who were evaluable for response, PR was achieved by 54% of patients, and SD was reported in 43% of patients. All but one evaluated patient in the Abramson Cancer Center trial experienced a decrease in tumor target lesions, and with a median follow up of 35 weeks, the median PFS had not been reached as of the data cut-off date. Among the 25 RAI-refractory DTC patients in the International Thyroid Oncology Group Study, PR was achieved by 40% of patients, and SD was reported in 52% of patients. Median PFS was 12.7 months, and median OS was 34.7 months. The safety profile in all three studies were consistent with the established profile of cabozantinib and other TKIs.

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 late-stage or other potentially label-enabling trials.

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 may also evaluate these combinations in other phase 3 pivotal trials in various other tumor types. 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. In accordance with the terms of the modified CheckMate 9ER protocol, 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, while the primary endpoint for the trial remains PFS, and the secondary endpoint is OS. The triplet combination continues to be evaluated in COSMIC-313, an ongoing phase 3 pivotal trial being conducted pursuant to our clinical collaboration with BMS. CheckMate 9ER completed enrollment in May 2019, and BMS announced that top-line results are expected in the first half of 2020. The trial is supported financially through the co-funding of both of our collaboration partners, Ipsen and Takeda.

RCC - COSMIC-313

In May 2019, we initiated COSMIC-313, a multicenter, randomized, double-blinded, controlled phase 3 pivotal trial evaluating the triplet combination of cabozantinib, nivolumab and ipilimumab versus the combination of nivolumab and ipilimumab in patients with previously untreated advanced intermediate- or poor-risk RCC. The study aims to enroll approximately 676 patients at up to 150 sites globally. Patients are being randomized 1:1 to the experimental arm of the triplet combination of cabozantinib, nivolumab and ipilimumab and to the control arm of nivolumab and ipilimumab in combination with matched placebo. The primary endpoint for the trial is PFS, and the secondary endpoint is OS. We expect to complete enrollment for COSMIC-313 in early 2021 and to report top-line results of the event-driven analyses from the trial in the 2022 timeframe.

We are sponsoring COSMIC-313, and BMS is providing nivolumab and ipilimumab free of charge.

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 was designed to enroll 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/kg of nivolumab every two weeks, and the other group receiving 40 mg of cabozantinib daily, 3 mg/kg of nivolumab every two weeks and 1 mg/kg ipilimumab every six weeks. The primary endpoints for the cohorts are safety and tolerability and ORR; secondary endpoints include duration of response (DOR), PFS and OS.

Results for CheckMate 040 were presented at ASCO's Gastrointestinal Cancers Symposium in January 2020. For the 36 patients treated with the combination of cabozantinib and nivolumab, ORR was 19%, and DCR was 75%. Median PFS was 5.4 months, and median OS was 21.5 months. For the 35 patients treated with the combination of cabozantinib, nivolumab and ipilimumab, ORR was 29%, and DCR was 83%. Median PFS was 6.8 months, and median OS had not yet been reached as of the data cut-off date. The safety profile for the combinations in the trial was consistent with the established profile of each agent, and no new safety signals have emerged.

Combination Studies with F. Hoffmann-La Roche Ltd. (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 clinical supply agreement, 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. Informed by the data generated from the phase 1b trial, COSMIC-021, we also entered into a joint clinical research agreement with Roche in December 2019, pursuant to which we plan to evaluate this combination in various late-stage clinical trials, including in non-small cell lung cancer (NSCLC), metastatic castration-resistant prostate cancer (mCRPC) and

RCC. For additional information on the terms of the master clinical supply agreement and joint clinical research 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 20 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 mCRPC who have previously received enzalutamide and/or abiraterone acetate without prior docetaxel for mCRPC and experienced radiographic disease progression in soft tissue;
- patients with mCRPC who have previously received enzalutamide and/or abiraterone acetate with prior docetaxel therapy for mCRPC;
- patients with mCRPC who have previously received enzalutamide and/or abiraterone acetate without prior docetaxel therapy for mCRPC;
- 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 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 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;
- 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 was designed to initially enroll approximately 30 patients. However, based on continuing encouraging efficacy and safety data, certain cohorts have been or may be further expanded, including the cohorts of patients with NSCLC who have been previously treated with an ICI and mCRPC who have been previously treated with enzalutamide and/or abiraterone acetate and experienced radiographic disease progression in soft tissue. In addition, in order to address the contribution of components, there are three exploratory cohorts that will evaluate cabozantinib as a single-agent therapy in 1) patients with NSCLC without a defined tumor genetic alteration who have progressed following treatment with an ICI, 2) patients with UC who have progressed following treatment with an ICI and 3) patients with mCRPC, as well as a fourth exploratory cohort that will evaluate atezolizumab as a single-agent therapy in patients with mCRPC. We anticipate completing enrollment of up to 1,732 patients in the trial in late 2020, which timing is subject to the initiation of additional cohorts or expansion of selected existing cohorts.

Since its initiation, data from COSMIC-021 have been instrumental in guiding our clinical development strategy for cabozantinib in combination with ICIs, including supporting the initiation of COSMIC-312 and other planned pivotal trials in NSCLC, mCRPC and RCC. In particular, data from the mCRPC cohort of the trial were presented at ASCO's Genitourinary Cancers Symposium in February 2020. Based on an interim analysis of 44 enrolled patients treated with the combination of cabozantinib and atezolizumab, the ORR was 32% (2 CRs and 12 PRs) and the DCR was 80%. Among the 36 patients with high-risk clinical features, the ORR was 33%. The safety profile for the combination was consistent with the established profile of each agent, and no new safety signals have emerged. Based on regulatory feedback from the FDA, and if supported by the clinical data, we intend to file with the FDA for accelerated approval in an mCRPC indication as early as in 2021.

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 trial also includes a third arm evaluating cabozantinib monotherapy in this first-line setting in order to address the contribution of components. The study has a target enrollment of 740 patients at up to 250 sites globally. Patients are being 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. As reflected by the results from completed trials and summaries of ongoing trials below, 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 1b study conducted under our CRADA with NCI-CTEP evaluating cabozantinib in combination with nivolumab with or without ipilimumab in patients with previously treated genitourinary tumors guided the choice of dose for the ongoing CheckMate 9ER trial in previously untreated advanced RCC. The study evaluated 78 patients; 49 were treated with the doublet combination of cabozantinib and nivolumab and 29 were treated with the triplet combination of cabozantinib, nivolumab and ipilimumab. 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. 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 agent, and no new safety signals have emerged.

PDIGREE is a phase 3 trial led by The Alliance which plans to enroll 1,046 intermediate- or poor-risk advanced RCC patients who have a clear cell component in their tumors. All patients are initially treated with up to 4 cycles of induction ipilimumab combined with nivolumab. Subsequently, patients are treated based on their response to the induction therapy. Patients achieving a complete response (CR) continue on maintenance nivolumab, while patients with progressive disease (PD) are switched to cabozantinib monotherapy. Patients who neither achieve a CR nor develop PD during induction are randomized 1:1 to either maintenance nivolumab or nivolumab in combination with cabozantinib 40 mg daily. The primary endpoint is OS, while PFS, CR rate, ORR and safety are among the secondary endpoints.

PAPMET is a 4-arm randomized phase 2 trial being conducted by the Southwest Oncology Group in patients with locally advanced or metastatic papillary RCC. The study was designed to enroll 180 patients with either type I or type II papillary RCC. Patients may have received up to one prior line of therapy. The trial compares a control arm of sunitinib with 3 independent investigational arms of single-agent MET inhibitors: cabozantinib; crizotinib; and savolitinib. The primary endpoint is PFS. An IA led to the closing of accrual to the crizotinib and savolitinib arms due to lack of efficacy. The cabozantinib arm continues as the only remaining investigational arm.

RADICAL is a randomized phase 2 trial being conducted by The Alliance which plans to enroll up to 210 patients with advanced RCC. All patients must have at least 2 sites of bone metastases and may have received up to 2 prior lines of systemic therapy. Patients are randomized 1:1 to be treated with cabozantinib in combination with radium-223 dichloride or cabozantinib as a single agent. The primary endpoint is symptomatic skeletal event-free survival, while secondary endpoints include PFS, OS, ORR and safety.

Neuroendocrine Tumors

The Alliance is leading the CABINET study which treats patients with well- or moderately-differentiated neuroendocrine tumors (NETs). CABINET includes 2 separate randomized studies, one for patients with pancreatic NETs and the other for patients with carcinoid tumors. The planned enrollment for the pancreatic NET study is 185 patients and for the carcinoid study is 210 patients. Both studies randomize previously treated patients 2:1 to cabozantinib 60 mg daily or placebo. The primary endpoint for both studies is PFS per Response Evaluation Criteria in Solid Tumors 1.1 as determined by a blinded IRRC.

Other Cancer Indications

There are 46 ongoing and 28 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 various other anti-cancer therapies, including monoclonal antibodies, chemotherapeutic agents, small molecules which target specific cellular pathways, or radiation. In addition to the various trials described above, our CRADA includes ongoing randomized phase 2 studies in endometrial cancer and NSCLC, both in combination with an ICI.

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

XL092 Development Program

XL092 is the first internally-discovered compound to enter the clinic following our re-initiation of internal 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 is being studied in a multicenter 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 is enrolling patients with advanced solid tumors, with the primary objective of determining a dose for daily oral administration of XL092 suitable for further evaluation. We anticipate that dose expansion cohorts and potential combination cohorts with ICIs will begin to enroll in 2020. Assuming positive data from the initial phase of 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: Internal Drug Discovery and Business Development Programs

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

Internal Drug Discovery

We also remain committed to building our product pipeline by discovering and developing new cancer therapies for patients. From 2000 until 2012, we had an active internal drug 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.

Our current internal drug discovery organization is leveraging that history in a focused and measured manner. Notably, these efforts are led by some of the same experienced scientists that led the efforts to discover cabozantinib, cobimetinib and esaxerenone, which have been approved for commercialization. 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.

Furthest along in these efforts is XL092. For additional information on XL092, see "-XL092 Development Program." We have also advanced an additional compound, XL265, an inhibitor of MET and TAM kinases, into preclinical development, and are conducting multiple additional lead optimization programs for inhibitors of a variety of targets that we believe play significant roles in tumor growth. We anticipate that some of these programs will yield preclinical development candidates during 2020.

Business Development

We augment our internal discovery activities with business development initiatives aimed at identifying and in-licensing promising, early-stage oncology assets and then further develop them utilizing our established clinical development infrastructure. In furtherance of this strategy, we have entered into multiple collaboration and license agreements, including with: Aurigene Discovery Technologies Limited (Aurigene), which is focused on the discovery and development of novel small molecules as therapies for cancer; Iconic Therapeutics, Inc. (Iconic), which is focused on the advancement of a next-generation antibody-drug conjugate (ADC) program targeting tissue factor in solid tumors; Invenra, Inc. (Invenra), which is focused on the discovery and development of multispecific antibodies for the treatment of cancer; and StemSynergy Therapeutics, Inc. (StemSynergy), which is focused on the discovery and development of novel oncology compounds aimed to inhibit tumor growth by targeting Casein Kinase 1 alpha (CK1α). We have already made progress under our collaborations with these partners and believe we will continue to do so in 2020. Both the tissue factor (ADC) program with Iconic and the lead Aurigene program targeting CDK7 are in preclinical development and could result in IND filings in 2020. For additional information on each of these collaborations, see "—Collaborations—In-licensing Collaborations."

We are seeking additional, external collaborative relationships around assets at all stages of development and technologies that complement our internal drug discovery and clinical 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.

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 on three occasions, including 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 in 2016. As of December 31, 2019, we achieved aggregate milestone payments of $330.0 million related to regulatory and commercial progress by Ipsen since the inception of the collaboration agreement, including milestone payments during 2019 of 1) $50.0 million upon Ipsen's achievement of $250.0 million in net sales of cabozantinib in its territories over four consecutive fiscal quarters, 2) $3.0 million upon the approval by Health Canada of cabozantinib for the first-line treatment of adults with advanced RCC, and 3) $2.0 million upon the approval by Health Canada of cabozantinib for the treatment of patients with advanced HCC who have been previously treated with sorafenib.

We are also eligible to receive future development and regulatory milestone payments from Ipsen, totaling an aggregate of $79.0 million upon additional approvals of cabozantinib in future indications and/or jurisdictions, as well as contingent payments of up to $470.4 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. During the year ended December 31, 2019 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 also reset each calendar year. As of December 31, 2019, we have earned royalties of $98.7 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 has opted not to co-fund the triplet arm of the study evaluating cabozantinib with nivolumab and ipilimumab); the dose escalation phase and first 20 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 1) the expiration of patent claims related to cabozantinib, 2) the expiration of regulatory exclusivity covering cabozantinib or 3) 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 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, which was subsequently amended effective March 2018 and May 2019, to, among other things, modify the amount of reimbursements we receive for costs associated with our required pharmacovigilance activities and milestones we are eligible to receive. 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 an upfront payment of $50.0 million from Takeda in 2017. As of December 31, 2019, we have also achieved regulatory and development milestones in the aggregate of $26.0 million since the inception of the collaboration agreement, including a $16.0 million milestone achieved during the year ended December 31, 2019 upon Takeda's submission of a regulatory application to the Japanese MHLW for Manufacturing and Marketing Approval of cabozantinib as a treatment for patients in Japan with unresectable and metastatic RCC. We also earned a $10.0 million milestone in the first quarter of 2020 for the January 2020 submission of a regulatory application to the Japanese MHLW for Manufacturing and Marketing Approval of cabozantinib as a treatment for patients in Japan with unresectable HCC who progressed after prior systemic therapy.

Under the collaboration agreement, as amended, as of December 31, 2019, we are eligible to receive regulatory and development milestone payments from Takeda of up to $20.0 million related to first-line RCC and second-line HCC, including the $10.0 million milestone we earned for the submission of a regulatory application in 2020 described above. We are also eligible to receive additional regulatory and development milestone payments, without limit, for additional potential future indications. We are further eligible to receive commercial milestones, including milestone payments earned for the first commercial sale of a product, of up to $155.0 million. We also receive royalties on the 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 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 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 1) two years after first generic entry with respect to such product in Japan or 2) 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.

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 in the CheckMate 9ER and COSMIC-313 trials and for HCC in the CheckMate 040 trial. We also intend to evaluate these combinations in other phase 3 pivotal trials in various other tumor types. For descriptions of the CheckMate 9ER, COSMIC-313 and CheckMate 040 trials, see "—Cabozantinib Development Program—Trials Conducted Under our Clinical Collaboration Agreements—Combination Studies with Bristol-Myers Squibb Company (BMS)."

Under the terms of the collaboration agreement with BMS, as subsequently amended effective March 2019, May 2019 and November 2019, 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 responsibility for the payment of costs for each such trial will be determined on a trial-by-trial basis. 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 sponsor of both trials, 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 F. Hoffmann-La Roche Ltd. (Roche)."

Building upon encouraging clinical activity observed in COSMIC-021, in December 2019 we entered into a joint clinical research agreement with Roche for the purpose of further evaluating the combination of cabozantinib with

atezolizumab in patients with locally advanced or metastatic solid tumors, including in three planned phase 3 pivotal trials in advanced NSCLC, mCRPC and RCC. If a party to the joint clinical research agreement proposes any additional combined therapy trials beyond the initial three planned phase 3 pivotal trials, the joint clinical research agreement provides that such proposing party must notify the other party and that if agreed to, any such additional combined therapy trial will become part of the collaboration, or if not agreed to, the proposing party may conduct such additional combined therapy trial independently, subject to specified restrictions set forth in the joint clinical research agreement.

Pursuant to the terms of the joint clinical research agreement, each party granted to the other a non-exclusive, worldwide (excluding, in our case, territory already the subject of a license by us to Takeda), non-transferable, royalty-free license, with a right to sublicense (subject to limitations), to use the other party's intellectual property and compounds solely as necessary for the party to perform its obligations under the joint clinical research agreement. The parties' efforts will be governed through a joint steering committee established to guide and oversee the collaboration and the conduct of the combined therapy trials. Each party will be responsible for providing clinical supply for all combined therapy trials, and the cost of the supply will be borne by such party. The clinical trial expenses for each combined therapy trial agreed to be conducted jointly under the joint clinical research agreement will be shared equally between the parties, and the clinical trial expenses for each additional combined therapy trial not agreed to be conducted jointly under the joint clinical research agreement will be borne by the proposing party, except that the cost of clinical supply for all combined therapy trials will be borne by the party that owns the applicable product.

Unless earlier terminated, the joint clinical research agreement provides that it will remain in effect until the completion of all combined therapy trials under the collaboration, the delivery of all related trial data to both parties, and the completion of any then agreed-upon additional analyses. The joint clinical research agreement may be terminated for cause by either party based on any 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 will terminate upon completion of any ongoing activities under the joint clinical research agreement.

In-licensing Collaborations

Aurigene Collaboration

In July 2019, we entered into an exclusive collaboration, option and license agreement with Aurigene to in-license as many as six programs to discover and develop small molecules as therapies for cancer. Under the terms of the agreement, we made aggregate upfront payments of $17.5 million for exclusive options to license up to six programs, including three pre-existing programs. We are also responsible for up to $32.6 million in research funding for the discovery and preclinical development work on these programs. During the year ended December 31, 2019, we incurred $4.0 million in expense for the discovery and preclinical development funding commitment.

For each option we decide to exercise, we will be required to pay an exercise fee of either $10.0 million or $12.0 million, depending on the program, and would then assume responsibilities for all subsequent clinical development, manufacturing and commercialization for that program. Aurigene would then become eligible for up to $148.8 million per program in potential development and regulatory milestone payments, $280.0 million per program in potential commercial milestone payments, as well as royalties on potential sales. Under the terms of the agreement, Aurigene retains limited development and commercial rights for India and Russia.

Iconic Collaboration

In May 2019, we entered into an exclusive option and license agreement with Iconic to advance an innovative next-generation ADC program for cancer, leveraging Iconic's expertise in targeting tissue factor in solid tumors. Tissue factor is highly expressed on tumor cells and in the tumor microenvironment, and tissue factor overexpression, while not oncogenic itself, facilitates angiogenesis, metastasis and other processes important to tumor development and progression. ICON-2, Iconic's lead oncology ADC program, is a rationally designed second-generation ADC with potential for an improved therapeutic index and safety profile. Under the terms of the agreement, we gained an exclusive option to license ICON-2 in exchange for an upfront payment to Iconic of $7.5 million and a commitment for preclinical development funding. During the year ended December 31, 2019, we incurred $9.8 million in expense for the preclinical development funding commitment. If we exercise the option, we will be required to make an option exercise fee payment of $20.0 million to Iconic; we would then assume responsibilities for all subsequent clinical development, manufacturing and commercialization activities, and Iconic would become eligible for up to $190.6 million in potential development, regulatory and first-sale milestone payments, $262.5 million in potential commercial milestone payments, as well as royalties on potential sales.

Invenra Collaboration

In May 2018, we entered into a collaboration and license agreement with Invenra 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 provides that we will receive an exclusive, worldwide license to one preclinical, multispecific antibody 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 October 2019, we expanded our collaboration to include the development of novel binders against six additional targets, which we can use to generate multispecific antibodies based on Invenra's B-Body™ technology platform, or with other platforms and formats at our option. As of December 31, 2019, we have initiated three additional discovery projects and two binder projects, and in total we incurred an aggregate of $7.0 million and $4.0 million in expense during the years ended December 31, 2019 and 2018, respectively, in consideration of the upfront licensing and project initiation fees. Invenra is eligible to receive up to $131.5 million in project initiation fees and milestone payments based on the achievement of specific development and regulatory milestones for a B-Body product in the first indication, or in lieu of such payments, up to $43.4 million in project initiation fees and milestone payments based on the achievement of specific development and regulatory milestones for a non- B-Body product. Upon successful commercialization of a product, Invenra is eligible to receive sales-based milestone payments up to $325.0 million as well as single-digit tiered royalties on net sales of the approved product. We have the right to initiate three additional discovery projects for development subject to an upfront payment of $2.0 million for each B-Body project and four additional binder projects subject to an upfront payment of $1.5 million for each project, as well as additional milestone payments and royalties for any products that arise from these efforts.

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 CK1α, a component of the Wnt signaling pathway implicated in key oncogenic processes. Activation of β-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 β-catenin stabilization are prevalent. Compounds targeting CK1α have also been shown to induce degradation of β-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 CK1α. We paid StemSynergy an upfront payment of $3.0 million in initial research and development funding during the year ended December 31, 2018 and provided $1.9 million and $1.2 million in additional research and development funding during the years ended December 31, 2019 and 2018, respectively. StemSynergy is eligible for up to $0.5 million in additional research and development funding 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.

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 and Daiichi Sankyo 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. 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. 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 in March 2009, granted 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. 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.; however, following a review of the commercial landscape, we and Genentech scaled back the personal promotion of COTELLIC in this indication in the U.S. in January 2018. 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.

Cobimetinib Profit Sharing and Royalty Revenues

Under the terms of the 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 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 2019, we earned royalties of $5.7 million on net sales of COTELLIC outside the U.S. and a $4.6 million profit on the profit and loss sharing of U.S. actual sales which are recorded in Collaboration revenues. Since the inception of the collaboration agreement, we have also received aggregate upfront and milestone payments of $50.0 million and are not eligible for any additional milestone payments.

Cobimetinib Clinical Development Program

In addition to its established commercialization of COTELLIC, Genentech continues to make 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 IST program, including an ongoing phase 3 pivotal trial exploring the combination of cobimetinib with atezolizumab and vemurafenib in BRAF V600 mutant melanoma (IMspire150), which we announced had met its primary endpoint in December 2019, and 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 an additional 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.

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. In December 2019, IMspire150 met its primary endpoint, demonstrating a significant and clinically meaningful improvement in PFS. Results will be presented at an upcoming medical meeting and discussed with healthcare authorities around the world, including the FDA and the EMA.

Daiichi Sankyo - Esaxerenone

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 MHLW in January 2019, and the first commercial sale of the branded esaxerenone product MINNEBRO in Japan in May 2019 triggered the payment of a $20.0 million milestone payment to us. As of December 31, 2019, and after giving effect to the milestone payment associated with the Japanese regulatory application for esaxerenone, we have achieved an aggregate of $65.5 million in development, regulatory and commercialization milestone payments related to MINNEBRO over the life of the collaboration agreement and are eligible to receive commercialization milestone payments of up to $90.0 million. 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. As of December 31, 2019, we have earned royalties of $0.1 million on net sales of MINNEBRO by Daiichi Sankyo since the approval of MINNEBRO in January 2019.

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

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 continue to expand through our clinical development and commercial progress, we continue to appropriately expand our supply chain through secondary third-party contract manufacturers and suppliers. 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 Practice (GMP), 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. In addition, through our third-party contract manufacturers and data service

providers, we continue to provide serialized commercial products as required to comply with the Drug Supply Chain Security Act (DSCSA).

We monitor and evaluate the performance of our third-party contract manufacturers on an ongoing basis for compliance with these requirements and to affirm their continuing capabilities to meet both our commercial and clinical 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 so 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 we 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 will continue to enhance our supply chain by incrementally adding additional suppliers for our drug substance and drug product manufacturers where needed. 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 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 facilitate our marketing efforts in reaching our target audience and our delivery of 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.

Environment, Health and Safety

In support of the development and expansion of our product pipeline, we have resumed and expanded our internal drug 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 maintain compliance with these laws and regulations, we do not expect the cost of complying with these laws and regulations to be material.

Government Regulation

Clinical Development

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 Practice;
- 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 a 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 the 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 GMP and Good Clinical Practice (GCP), respectively;
- 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. In rare cases, a Phase 1 study that is designed to assess effectiveness may serve as the basis for FDA marketing approval of a drug or for a label expansion. For instance, at FDA's discretion, a product may receive approval based on a Phase 1b study if

effectiveness results from the study are extremely compelling, approval of the drug would address a significant unmet patient need, and the drug is being approved through the Accelerated Approval pathway. As discussed below, Accelerated Approval generally requires a post-approval study to confirm clinical benefit.

- 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” 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.

The FDA may require, or companies may pursue, additional clinical trials after a product is approved. These so-called phase 4 studies may be deemed 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.

FDA Review and Approval

For approval of a new drug or changes to an approved drug, 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 late-stage or other potentially label-enabling clinical trials. 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. Thus, we and our third-party contract manufacturing organizations 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 contract manufacturing organizations.

In the U.S., the Orphan Drug Act of 1983, as amended, provides incentives for the development of drugs and biological products for rare diseases or conditions that affect fewer than 200,000 people in the U.S. (or 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.). Certain of the incentives turn on the drug first being designated as an orphan drug. To be eligible for designation as an orphan drug (Orphan Drug Designation), 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 or the sponsor of the subsequent drug must provide a plausible hypothesis of clinical superiority over the previously approved same drug. Upon receipt of Orphan Drug Designation, the sponsor is eligible for tax credits of up to 25% for qualified clinical trial expenses and waiver of the Prescription Drug User Fee Act application fee. In addition, upon marketing approval, an orphan-designated drug could be eligible for seven years of market exclusivity if no drug considered the same drug was previously approved for the same orphan condition (or if the subsequent drug is demonstrated to be clinically superior to any such previously approved same drug). 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 an approved drug's orphan exclusivity through a demonstration of clinical superiority over the previously approved drug.

The FDA has various programs that 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. Examples of such programs included Fast Track designation, breakthrough therapy designation, priority review and accelerated approval, and the eligibility criteria of and benefits for each program vary:

- *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, by providing, among other things, eligibility for accelerated approval if relevant criteria are met, and rolling review, which allows submission of individually completed sections of an NDA or for FDA review before the entire submission is completed.

- *Breakthrough therapy* designation is a process designed to expedite the development and review of 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. 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.

- *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.

- *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 a certain intermediate clinical endpoint, 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.

The Drug Price Competition and Patent Term Restoration Act of 1984 (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 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 Federal

Food, Drug, and Cosmetic Act (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.

In September 2019, we received a Paragraph IV certification notice letter from MSN Pharmaceuticals, Inc. (MSN), that it had filed an ANDA with the FDA for a generic version of CABOMETYX tablets, and we subsequently filed a patent infringement lawsuit against MSN on October 29, 2019. For a more detailed discussion of this litigation matter, see "Legal Proceedings" in Part I, Item 3 of this Annual Report on Form 10-K.

Regulatory Approval 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. Once fully implemented, this regulation will harmonize 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. Although Regulation (EU) 536/2014 was adopted and entered into force in 2014, the timing of its application depends on confirmation of full functionality of the Clinical Trials Information System (CTIS) through an independent audit. Regulation (EU) 536/2014 will then become applicable six months after the EC publishes notice of this confirmation. In December 2015, the EMA's Management Board endorsed a delivery timeframe with a projected application date in September 2018. However, the system's go-live date has been postponed several times due to technical difficulties with the development of the information technology systems. At its meeting in October 2019, the EMA's Management Board

did not provide the firm date for the audit to be carried out in order for Regulation (EU) 536/2014 to be applied. The application of Regulation (EU) 536/2014 will likely be further delayed. Until CTIS is confirmed to be fully functional based on an independent audit, there is uncertainty about the date of application of Regulation 536/2014. In the interim, Directive 2001/20 continues to be applicable for regulating clinical trials conducted in the Member States of the EU.

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 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. 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 and Privacy 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 (AKS), which prohibits, among other things, soliciting, receiving, offering or paying remuneration, directly or indirectly, to induce or reward for, the purchase or recommendation of an item or service reimbursable under a federal healthcare program, such as Medicare and Medicaid; 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; and 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. 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 governmental healthcare program, and many of which differ from each other in significant ways and may not have the same effect, further complicate compliance efforts.

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, the California Consumer Privacy Act of 2018, as amended (CCPA), went into operation on January 1, 2020 and broadly defines personal information, affords California residents expanded privacy rights and protections and provides for civil penalties for violations and a private right of action related to certain data security 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 knowingly encourage, assist or otherwise facilitate a HIPAA-covered entity (or its business associate) to use or disclose individually identifiable health information in a manner 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 laws in all 50 states requiring security breach notification in some circumstances. CCPA, HIPAA, and these other laws could create liability for us or increase our cost of doing business. International laws, such as the EU General Data Protection Regulation 2016/679 (GDPR), could also apply to our operations. Failure to provide adequate privacy protections and maintain compliance with applicable privacy laws could jeopardize business transactions across borders and result in significant penalties.

In addition, the Patient Protection and Affordable Care Act of 2010, as amended (PPACA) created a federal requirement under the federal Open Payments program, that requires certain manufacturers to track and report to the Centers for Medicare & Medicaid Services annually certain payments and other transfers of value provided to physicians (as defined by such law) and teaching hospitals made in the previous calendar year. In addition, there are also an increasing number of state laws that control pharmaceutical product pricing or 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 us to pay substantial rebates or offer our drugs at substantial discounts to certain purchasers (including “covered entities” purchasing under the 340B Drug Discount Program). We are also required to discount our 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 and regulatory guidance, 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. Failure to properly calculate prices, or to offer required discounts or rebates could subject us to substantial penalties.

Coverage and 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. Each third-party payer may have its own policy regarding what products it will cover, the conditions under which it will cover such products, and how much it will pay for such 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 guarantee what reimbursement rate, if any, will be approved. Patients may be less likely to use our products if coverage is not provided and reimbursement may not cover a significant portion of the cost of our products.

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.

Healthcare Reform

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 increasing legislative and enforcement interest in the U.S. with respect to drug pricing practices. In particular, there have been several recent U.S. Congressional inquiries, hearings and proposed and enacted federal legislation designed to, among other things: reduce or limit the prices of drugs and make them more affordable for patients; reform the structure of Medicare Part D pharmaceutical benefits, including through increasing manufacturer contributions to offset Medicare beneficiary costs; bring more transparency to drug pricing rationale and methodologies; and facilitate the importation of certain lower-cost drugs from other countries, expedite the development and approval of generic drugs and biosimilars. At the state level, legislatures have increasingly passed legislation and implemented regulations designed to control pharmaceutical and biological product pricing, including restrictions on pricing or reimbursement at the state government level, limitations on discounts to patients, marketing cost disclosure and transparency measures, and, in some cases, policies to encourage importation from other countries (subject to federal approval) and bulk purchasing, including the National Medicaid Pooling Initiative. For example, in October 2017, California as adopted 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.

The U.S. pharmaceutical industry has already been significantly impacted by major legislative initiatives and related political contests, including, for example, efforts to repeal, substantially modify or invalidate some or all of the provisions of the PPACA. Notably, in December 2018, a Texas U.S. District Court Judge ruled that the PPACA is unconstitutional in its entirety because the penalty enforcing the “individual mandate” was repealed by Congress as part of the Tax Cuts and Jobs Act of 2017. Then, in December 2019, the U.S. Court of Appeals for the 5th Circuit upheld this District Court ruling that the individual mandate was unconstitutional and remanded the case back to the District Court to determine whether the remaining provisions of the PPACA are invalid as well. It is unclear how this decision, future decisions, subsequent appeals and other efforts will impact the PPACA. Additionally, the 2019 year-end federal spending package permanently repealed, effective January 1, 2020, the PPACA-mandated “Cadillac” tax on high-cost employer-sponsored health coverage and medical device taxes, and, effective January 1, 2021, also eliminates the health insurer tax.

In addition, there are pending federal and state-level legislative proposals that would significantly expand government-provided health insurance coverage, ranging from establishing a single-payer, national health insurance system to more limited “buy-in” options to existing public health insurance programs, each of which could have a significant impact on the healthcare industry.

As a result of these developments and trends, third-party payers are increasingly attempting to contain healthcare costs by limiting coverage and the level of reimbursement of new drugs. Insurers are also pursuing means of contracting for pharmaceutical “value” or “outcomes.” These entities could refuse, limit or condition coverage for our products, such as by using tiered reimbursement or pressing for new forms of value-based contracting, which could adversely affect product sales. Due to the volatility in the current regulatory and market dynamics, we are unable to predict the impact of any legislative, regulatory, third-party payer or policy actions, including potential cost containment and healthcare reform measures.

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. Pricing and reimbursement negotiations with governmental authorities or payers in EU member states can take six to 12 months or longer after the initial marketing authorization is granted for a product, or after the marketing authorization for a new indication is granted. To obtain reimbursement and/or pricing approval in some countries, drug manufacturers and collaboration partners may also be required to conduct a study that seeks to establish the cost effectiveness of a new drug compared with other available established therapies. There can be no assurance that any country that has price controls, reimbursement limitations or other requirements 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, including our ability to enforce our intellectual property rights against potential generic competition; and
- the availability of substantial capital resources to fund development and commercialization activities.

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

The markets for which we intend to pursue regulatory approval of cabozantinib are highly competitive. We are aware of products in research or development by our competitors that are intended to treat all of the tumor types we are targeting, and 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 cabozantinib development strategy to address the expanding role of therapies that combine ICIs with other targeted agents in indications for which CABOMETYX is approved or being evaluated in clinical studies, we cannot ensure that our clinical trials will show efficacy in comparison to competing product combinations. Moreover, the complexities of such a development strategy have required and are likely to continue to require collaboration with some of our competitors.

Competition in Approved Cabozantinib Indications

CABOMETYX - RCC: We believe the principal competition for CABOMETYX in advanced RCC includes: the combination of Merck's pembrolizumab and Pfizer's axitinib; the combination of Pfizer's avelumab and axitinib; 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 Amgen's sorafenib; Roche's bevacizumab; the combination of Eisai's lenvatinib and Novartis' everolimus; and generic versions of everolimus and aldesleukin. Additionally, there are a variety of therapies being developed for advanced RCC, including: the combination of Merck's pembrolizumab and Eisai's lenvatinib; the combination of Calithera's CB-839 and Novartis' everolimus; AVEO Pharmaceutical's tivozanib; the combination of BMS' nivolumab and Nektar Therapeutics' NKTR-214; and generic versions of sorafenib and sunitinib.

The competitive landscape for RCC is evolving rapidly, especially given the entrance of ICI and 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 2020 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; Merck's pembrolizumab; and Eli Lilly's ramucirumab. Additionally, there are a variety of therapies being developed for previously treated HCC, including: the combination of BMS's ipilimumab and nivolumab; 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's pralsetinib (for certain subsets of MTC patients); and Loxo Oncology's (a wholly owned subsidiary of Eli Lilly) selpercatinib (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).

Competition in Potential Cabozantinib Indications

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' nivolumab; the combination of Merck's pembrolizumab and Eisai's lenvatinib; BeiGen and Celgene's tislelizumab; the combination of Roche's bevacizumab and atezolizumab; AstraZeneca's durvalumab; the combination of AstraZeneca's durvalumab and tremelimumab; and generic versions of sorafenib.

In addition, we are evaluating the combination of cabozantinib and atezolizumab in COSMIC-021, a phase 1b trial in locally advanced or metastatic solid tumors, including mCRPC. Based on regulatory feedback from the FDA, and if supported by the clinical data, we intend to file with the FDA for accelerated approval in an mCRPC indication as early as 2021. Should the combination of cabozantinib and atezolizumab be approved for the treatment of patients with mCRPC, we believe its principal competition may include: Janssen Biotech's (a wholly owned subsidiary of Johnson & Johnson) abiraterone; Astellas Pharma's and Pfizer's enzalutamide; Janssen Biotech's apalutamide; Bayer's darolutamide; Sanofi's docetaxel; Sanofi's cabazitaxel; Dendreon's Sipuleucel-T; Bayer's radium-223 dichloride; AstraZeneca's and Merck's olaparib; Clovis Oncology's rucaparib; the combination of Merck's pembrolizumab and Sanofi's docetaxel; the combination of Merck's pembrolizumab and Astellas Pharma's and Pfizer's enzalutamide; the combination of BMS' nivolumab and Sanofi's docetaxel; the combination of Merck's pembrolizumab and AstraZeneca's and Merck's olaparib; the combination of AB Science's masitinib and Sanofi's docetaxel; and Novartis' ^{177}Lu-PSMA-617.

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 Takeda's ponatinib, Loxo Oncology's selpercatinib, Blueprint Medicine's pralsetinib, Turning Point Therapeutics' TPX-0046 and Daiichi Sankyo's and Boston Pharmaceuticals' DS 5010 (also known as BOS172738); other MET inhibitors, including AstraZeneca's savolitinib, Pfizer's crizotinib, Mirati's glesatinib and Novartis' and Incyte's capmatinib; other inhibitors of multiple tyrosine kinases, including Eisai's lenvatinib, Mirati's sitravatinib and Boehringer Ingelheim's nintedanib; and ICIs, including BMS' ipilimumab and nivolumab, Merck's pembrolizumab, Roche's atezolizumab, Pfizer's avelumab and AstraZeneca's durvalumab and tremelimumab.

Competition for Cobimetinib

We believe that cobimetinib's principal competition amongst targeted agents includes: the combination of Array's encorafenib and binimetinib; and the combination of Novartis' trametinib and dabrafenib. 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 expected during 2020. Other potential competitors for the treatment of hypertension in Japan, if and when they are approved by the MHLW, include: Janssen Pharmaceuticals' canagliflozin; Reata Pharmaceuticals' bardoxolone methyl; and Gilead Sciences' selonsertib.

We believe that esaxerenone's principal competition for the treatment of diabetic nephropathy in Japan will be finerenone, if and when it is approved by the MHLW.

Significant Customers

We operate as a single business segment and have operations solely in the U.S. During the year ended December 31, 2019, we derived 16% of our revenues from Ipsen, 15% of our revenues from affiliates of CVS Health Corporation, 12% of our revenues from affiliates of McKesson Corporation and 10% of our revenues from affiliates of AmerisourceBergen Corporation. See "Note 2. Revenues" to our "Notes to Consolidated Financial Statements" contained in Part II, Item 8 of this Annual Report on Form 10-K for information about significant customers in prior years.

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 (the '473 Patent) 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.

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
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

To our knowledge after extensive investigation, no other company possesses a portfolio of broad and exclusive rights to the patents and patent applications required for the commercialization of medicines containing cabozantinib. Given the importance of our intellectual property portfolio to our business operations, we intend to vigorously enforce our rights and defend against challenges that have arisen or may arise in this area. For example, in September 2019, we received a notice letter regarding an ANDA submitted to the FDA by MSN, requesting approval to market a generic version of CABOMETYX tablets. The notice letter included a Paragraph IV certification with respect to our U.S. Patent Nos. 8,877,776, 9,724,342, 10,034,873 and 10,039,757, which are listed in the *Orange Book.* MSN's notice letter does not provide a Paragraph IV certification against the '473 Patent, which expires on August 16, 2026, or U.S. Patent No. 8,497,284, which expires on September 24, 2024; therefore, neither the '473 Patent nor U.S. Patent No. 8,497,284 are presently at issue. On October 29, 2019, we filed a complaint for patent infringement against MSN asserting U.S. Patent No. 8,877,776 in the United States District Court for the District of Delaware (the Delaware District Federal Court) arising from MSN's ANDA filing with the FDA. We cannot predict the outcome of this lawsuit or assure you that the lawsuit will prevent the introduction of a generic version of CABOMETYX for any particular length of time, or at all. For a more detailed discussion of this litigation matter, see "Legal Proceedings" in Part I, Item 3 of this Annual Report on Form 10-K.

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, prodrugs, metabolites 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.

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 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, 2019, we had 617 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 risks 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.

We anticipate that for the foreseeable future, our ability to maintain or meaningfully increase cash flow to fund our business operations and growth will depend upon the continued commercial success of CABOMETYX as a treatment for

advanced RCC and previously treated HCC, and possibly for other indications for which cabozantinib is being evaluated in potentially label-enabling clinical trials, if warranted by the data generated from such trials. In this regard, part of our strategy is to pursue additional indications for cabozantinib to increase the number of cancer patients who could benefit from this medicine. However, 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 in the major commercial markets where CABOMETYX is approved. Even if we and our collaboration partners receive the required regulatory approvals to market cabozantinib for additional indications, we and our collaboration partners may not be able to commercialize CABOMETYX effectively and successfully in these additional indications. If revenue from CABOMETYX decreases or remains flat, or if we are unable to expand the labeled indications in major commercial markets where CABOMETYX is approved, 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.

We rely on Ipsen and Takeda for the commercial success of CABOMETYX in its approved indications outside of the U.S., and are unable to control the amount or timing of resources expended by these collaboration partners in the commercialization of CABOMETYX in its approved indications outside of the U.S.

We rely heavily upon the regulatory, commercial, medical affairs, market access and other expertise and resources of our collaboration partners, Ipsen and Takeda, for commercialization of CABOMETYX in their respective territories outside of the U.S. We cannot control the amount and timing of resources that our collaboration partners 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 collaboration partners 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 collaboration partners could be adversely affected by the imposition of governmental price or other controls, political and economic instability, trade restrictions or barriers and changes in tariffs, escalating global trade and political tensions, or otherwise. If our collaboration partners 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.

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 or maintain 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. Market acceptance for CABOMETYX could depend on numerous factors, including the effectiveness and safety profile, or perceived effectiveness and safety profile, of CABOMETYX compared to competing products, the strength of CABOMETYX sales and marketing efforts, and changes in pricing and reimbursement for CABOMETYX. If CABOMETYX does not continue to be prescribed broadly for the treatment of its approved RCC and HCC indications, our product revenues could flatten or decrease, 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 biotechnology, biopharmaceutical and pharmaceutical industries are competitive and are characterized by rapid technological change and diverse offerings of products, particularly in the area of novel oncology therapies. Many of our competitors have greater capital resources, larger research and development staff and facilities, deeper regulatory expertise and more extensive product manufacturing and commercial capabilities than we do, which may afford them a competitive advantage. Further, our competitors may be more effective at in-licensing and developing new commercial products that could render our products, and those of our collaboration partners, obsolete and noncompetitive. 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 scientific and clinical research activities similar to ours.

Furthermore, the specific indications for which CABOMETYX is currently or may be approved, based on the results from clinical trials currently evaluating cabozantinib, 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 the shifting landscape of therapeutic strategy following the advent of ICIs. While we have adapted our cabozantinib development strategy to address the use of therapies that combine ICIs with other targeted agents in indications for which CABOMETYX is approved, we cannot ensure that our clinical trials will show efficacy in comparison to competing product combinations. Moreover, the complexities of such a development strategy have required and are likely to continue to require collaboration with some of our competitors.

If we are unable to maintain or increase our internal sales, marketing, market access and product distribution capabilities for our products, 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 maintaining and continuously improving 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- and pre-commercial-stage oncology-focused biotechnology companies seeking to build out and maintain 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. Also, to the extent that the commercial opportunities for CABOMETYX grow over time, we may not properly scale the size and experience of our commercialization teams to market and sell CABOMETYX successfully in an expanded number of indications. If we are unable to maintain or scale our commercial function 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.

If we are unable to enter into or maintain agreements with third parties to store, distribute and commercialize our products, we may be unable 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 for storage and 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).

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 on a timely and competitive basis. These third parties may not provide timely services, and we may be unable to maintain or renew our arrangements with these third parties or enter into new arrangements, on acceptable terms or at all. If we are unable to contract for these third-party services 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 obtain or maintain coverage and reimbursement for our products 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 reimbursement is, and will be, available from third-party payers, including governmental payers, such as Medicare and Medicaid, and private health insurers. Third-party payers continue to scrutinize and manage access to pharmaceutical products and services and may limit reimbursement for newly approved products and indications. Patients are generally not capable of paying for CABOMETYX or COMETRIQ themselves and rely on third-party payers to pay for, or subsidize, the costs of their medications, among other medical costs. Accordingly, market acceptance of CABOMETYX and COMETRIQ is dependent on the extent to which coverage and reimbursement is available from third-party payers. If third-party payers do not provide coverage or 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.

We are subject to 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 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 could impact our operations include, without limitation:

- the federal AKS, which governs our business activities, including our marketing practices, medical educational programs, pricing policies, and relationships with healthcare providers or other entities;
- 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;
- 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;
- the PPACA Open Payments program, 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 (as defined by such law) and teaching hospitals, as well as ownership and investment interests held by physicians and their immediate family members;
- state and local laws and regulations that require drug manufacturers to file reports relating to marketing activities, payments 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; and
- state pharmaceutical price and price reporting laws and regulations that require us to provide notice of price increases or the introduction of new high-cost products, and/or file complex ancillary reports concerning prices and pricing and discount practices.

In addition, we may be subject to the Foreign Corrupt Practices Act, a U.S. law which regulates certain financial relationships with foreign government officials (which could include, for example, medical professionals employed by national healthcare programs) and its foreign equivalents, as well as federal and state consumer protection and unfair competition laws.

These federal and state healthcare laws and regulations govern pharmaceutical marketing practices, including off-label promotion. If our operations are found, or even alleged, to be in violation of the laws described above or any other governmental regulations that apply to us, we, or our officers or employees, may be subject to significant 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, imprisonment, reputational harm, additional reporting requirements and oversight, 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. Under the False Claims Act, these individuals, commonly known as relators or "whistleblowers," may potentially share in amounts paid by the entity to the government in fines or settlement. When an entity is determined to have violated the civil False Claims Act, or settles a lawsuit brought pursuant to the False Claims Act to avoid further prosecution, 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, if any such action is brought against us, our business may be impaired, even if we are ultimately successful in our defense.

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

Federal and state governments in the U.S. are considering legislative and regulatory proposals to change the U.S. healthcare system in ways that could affect our ability to continue to commercialize CABOMETYX and COMETRIQ profitably. Similarly, among policy makers and payers, there is significant interest in promoting such changes with the stated goals of containing healthcare costs, improving quality and expanding patient access. The pharmaceutical industry and specifically the market for the sale, insurance coverage and distribution of pharmaceuticals has been a particular focus of these efforts and would likely be significantly affected by any major legislative or regulatory initiatives.

We face related uncertainties as a result of efforts to repeal, substantially modify or invalidate some or all of the provisions of the PPACA. Notably, in December 2018, a Texas U.S. District Court Judge ruled that the PPACA is unconstitutional in its entirety because the penalty enforcing the “individual mandate” was repealed by Congress as part of the Tax Cuts and Jobs Act of 2017. Then, in December 2019, the U.S. Court of Appeals for the 5th Circuit upheld this District Court ruling that the individual mandate was unconstitutional and remanded the case back to the District Court to determine whether the remaining provisions of the PPACA are invalid as well. It is unclear how this decision, future decisions, subsequent appeals and other efforts will impact the PPACA. Additionally, the 2019 year-end federal spending package permanently repealed, effective January 1, 2020, the PPACA-mandated “Cadillac” tax on high-cost employer-sponsored health coverage and medical device taxes, and, effective January 1, 2021, also eliminates the health insurer tax. There is no assurance that the repeal or modification of some or all of the provisions of the PPACA 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.

In addition, there are pending federal and state-level legislative proposals that would significantly expand government-provided health insurance coverage, ranging from establishing a single-payer, national health insurance system to more limited “buy-in” options to existing public health insurance programs, each of which could have a significant impact on the healthcare industry. While we cannot predict how future legislation (or enacted legislation that has yet to be implemented) will affect our business, such proposals could have the potential to impact access to and sales of our products.

As a result of these developments and trends, third-party payers are increasingly attempting to contain healthcare costs by limiting coverage and the level of reimbursement of new drugs. Insurers are also pursuing means of contracting for pharmaceutical “value” or “outcomes.” These entities could refuse, limit or condition coverage for our products, such as by using tiered reimbursement or pressing for new forms of value-based contracting, which could adversely affect product sales. Furthermore, the expansion of the 340B Drug Discount Program has increased the number of purchasers eligible for significant discounts on branded drugs, including our marketed products. Due to the volatility in the current regulatory and market dynamics, we are unable to predict the impact of any legislative, regulatory, third-party payer or policy actions, including potential cost containment and healthcare reform measures. If enacted, any such measures could have a material adverse impact on our business, financial condition and results of operations.

Pricing for pharmaceutical products in the U.S. has come under increasing attention and scrutiny by federal and state 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.

There have been several recent U.S. Congressional inquiries, hearings and proposed and enacted federal legislation designed to, among other things: reduce or limit the prices of drugs and make them more affordable for patients; reform the structure and financing of Medicare Part D pharmaceutical benefits, including through increasing manufacturer contributions to offset Medicare beneficiary costs; bring more transparency to drug pricing rationale and methodologies; and facilitate the importation of certain lower-cost drugs from other countries. While we cannot know the final form of any such legislative, regulatory and/or administrative measures, some of the pending legislative proposals, such as those incorporating International Pricing Index models, if enacted, would likely have a significant and far-reaching impact on the biopharmaceutical industry and therefore also likely have a material adverse impact on our business, financial condition and results of operations.

In connection with its evaluation of proposals concerning the pricing of, and access to, pharmaceutical products, many companies in our industry have received governmental requests for documents and information relating to drug

pricing and patient support programs. 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.

At the state level, legislatures have increasingly passed legislation and implemented regulations designed to control pharmaceutical and biological product pricing, including restrictions on pricing or reimbursement at the state government level, limitations on discounts to patients, marketing cost disclosure and transparency measures, and, in some cases, policies to encourage importation from other countries (subject to federal approval) and bulk purchasing, including the National Medicaid Pooling Initiative.

For example, California adopted 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. Such obligations to provide notices of price increases to purchasers may influence customer ordering patterns for CABOMETYX and COMETRIQ, which in turn may increase the volatility of our revenues as a reflection of changes in inventory volumes. Furthermore, adoption of drug pricing transparency regulations, and our associated compliance obligations, may increase general and administrative costs and/or diminish our revenues as a result of the imposition of caps on pricing and price increases. Therefore, the implementation of these 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 products.

Lengthy regulatory pricing and reimbursement procedures and cost control initiatives imposed by governments outside the U.S. could delay the marketing of and/or result in downward pressure on the price of our approved products resulting in a decrease in revenue.

Outside the U.S., particularly in the EU, the pricing and reimbursement of prescription pharmaceuticals is generally subject to governmental control. In EU countries, pricing and reimbursement negotiations with governmental authorities or payers can take six to 12 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 also 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 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 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 with affording pharmaceuticals have become the subject of Congressional interest and enhanced government scrutiny. The U.S. Department of Health and Human Services Office of Inspector General established specific guidelines permitting pharmaceutical manufacturers to make donations to charitable organizations that provide co-pay assistance to Medicare patients, provided that manufacturers meet certain specified compliance requirements. If we are deemed not to have complied with these guidelines and other laws or regulations respecting the operation of these programs, we could be subject to damages, fines, penalties or other criminal, civil or administrative sanctions or enforcement actions. A variety of entities, including pharmaceutical manufacturers, but not including our company, have received subpoenas from the U.S. Department of Justice and other enforcement authorities seeking information related to their patient assistance programs and support. Regardless of whether we have complied with the regulations governing patient assistance programs, this type of government investigation could negatively impact our business practices, harm our reputation, divert the attention of management and increase our expenses.

We are subject to laws and regulations relating to privacy, data protection and the collection and processing of personal data. Failure to maintain compliance with these regulations could create additional liabilities for us.

The legislative and regulatory landscape for privacy and data protection continues to evolve globally and in the U.S. For example, the CCPA went into operation on January 1, 2020 and affords California residents expanded privacy rights and protections, including civil penalties for violations and statutory damages under a private right of action for data security

breaches. Similar legislative proposals being advanced in other states and Congress is also considering federal privacy legislation. In addition, most healthcare providers 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 encourage, assist or otherwise facilitate a HIPAA-covered entity (or its business associate) to use or disclose individually identifiable health information in a manner 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 GDPR regulates the processing of personal data of individuals within the EU, even if, under certain circumstances, that processing occurs outside the EU, and also restricts transfers of such data to countries outside of the EU, including the U.S. Should we fail to provide adequate privacy or data security protections or maintain compliance with these laws and regulations, we could be subject to sanctions or other penalties, litigation or an increase in our cost of doing business.

Legislation and regulatory action designed to facilitate the development, approval and adoption of generic drugs in the U.S., and the entrance of generic competitors, could limit the commercial potential of our products, which could have a material adverse impact on our business, financial condition and results of operations.

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 an NDA under section 505(b)(2) of the FDCA 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—FDA Review and Approval." In either case, if an ANDA or 505(b)(2) applicant submits an application referencing one of our marketed products prior to the expiry of one or more our *Orange Book*-listed patents for the applicable product, we may litigate with the potential generic competitor to protect our patent rights, which would result in significant expenses, distraction for our management team, and could have an adverse impact on our stock price. For example, in September 2019, we received a Paragraph IV certification notice letter from MSN that it had filed an ANDA with the FDA for a generic version of CABOMETYX tablets, and we subsequently filed a patent infringement lawsuit against MSN on October 29, 2019. It is possible that MSN or other companies, following FDA approval of an ANDA or 505(b)(2) NDA, could introduce generic versions of our marketed products before our patents expire if they do not infringe our patents or if it is determined that our patents are invalid or unenforceable, and we expect that generic cabozantinib products would be offered at a significantly lower price compared to our marketed cabozantinib products. Therefore, regardless of the regulatory approach, the introduction of a generic version of cabozantinib could significantly decrease our revenues and thereby materially harm our business, financial condition and results of operations.

The U.S. federal government has also taken numerous legislative and regulatory actions to expedite the development and approval of generic drugs and biosimilars. In August 2017, President Trump signed the FDA Reauthorization Act of 2017, which reauthorized the FDA user fee programs for prescription drugs, generic drugs, medical devices, and biosimilars, under which applicants for such products partially pay for the FDA's pre-market review of their product candidates and pay other specified fees. The legislation also 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. In addition, 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 focused on drug competition, including legislation focused on drug patenting and provision of drug to generic applicants for testing. For example, the Creating and Restoring Equal Access To Equivalent Samples (CREATES) Act of 2019, recently signed into law as part of the 2019 year-end federal spending package, purports to promote competition in the market for drugs and biological products by facilitating the timely entry of lower-cost generic and biosimilar versions of those drugs and biological products, including by allowing generic manufacturers access to branded drug samples. While we cannot 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 have a material adverse impact on our business, financial condition and results of operations.

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 late-stage or other potentially label-enabling clinical trials may fail to confirm the results observed in early-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 that require us to conduct further testing or to abandon projects;
- 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;
- lower-than-anticipated patient registration or enrollment in our clinical testing, including in China as a result of the recent coronavirus outbreak;
- failure by our collaboration partners to provide us with an adequate and timely 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
- withholding of authorization from regulators or institutional review boards to commence or conduct clinical trials or delays, suspensions or terminations of clinical research for various reasons, including noncompliance with regulatory requirements or a determination by these regulators and institutional review boards that participating patients are being exposed to unacceptable health risks.

If there are 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 collaboration partners to fund a significant portion of our clinical development programs. Should one or all of our collaboration partners decline to support future planned clinical trials, we will be entirely responsible for financing the further development of cabozantinib or our other product candidates and, as a result, we may be unable to execute our current business plans, which could have a material adverse impact on our business, financial condition and results of operations.

We may not be able to pursue 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 in accordance with our stated timelines or at all. 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 ; the number of clinical sites included in the trials; and the length of time required to enroll eligible patients.

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., as well as by comparable authorities in other countries. The processes 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 they 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. The FDA has substantial discretion in the approval process and may refuse to approve any NDA or sNDA 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, we may encounter delays or rejections based upon changes in policy, which could 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 new indications, such approval may be limited, imposing significant restrictions on the indicated uses, conditions for use, labeling, distribution, and/or production of the product and could impose requirements for post-approval studies, including additional research and clinical trials, all of which may result in significant expense and limit our and our collaboration partners' ability to commercialize cabozantinib in one or more new indications. For example, based on the regulatory feedback from the FDA, and if supported by the clinical data from COSMIC-021, we intend to file with the FDA for accelerated approval of cabozantinib in an mCRPC indication as early as 2021. We expect that as a condition of any potential approval under the FDA's accelerated approval pathway, the FDA will require us to perform confirmatory post-marketing clinical trials to confirm the clinical benefit, if any, of cabozantinib in combination with Roche's atezolizumab in patients with locally advanced or metastatic solid tumors, such as mCRPC. 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 ultimately restrict the commercialization of cabozantinib in any additional indications. Further, these regulatory agencies could also impose various administrative, civil or criminal sanctions for failure to comply successfully with regulatory requirements, including withdrawal of product approval.

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 have invested in substantial technical, financial and human resources toward internal drug discovery activities with the goal of identifying new product candidates to advance into clinical trials. These efforts may initially show promise in identifying product candidates, yet ultimately fail to yield product candidates for multiple reasons. For example, 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 drug 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 capital resources and more extensive clinical development and commercialization capabilities may have a competitive advantage over us. 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 product candidates on acceptable terms that would allow us to realize an appropriate return on our investment. If our internal drug discovery or business development efforts do not result in suitable product candidates, our business 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 financial condition and results of operations.

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 social media communications, there is risk that the unauthorized use of social media by us or our employees to communicate about our products or business, or any inadvertent disclosure of material, nonpublic information through these means, may result in violations 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 material adverse impact on our business, financial condition and results of operations. Furthermore, negative posts or comments about us or our products on social media could seriously damage our reputation, brand image and goodwill.

Risks Related to Our Capital Requirements, Accounting and Financial Results

Our profitability could be negatively impacted by our extensive clinical development, business development and commercialization activities for cabozantinib and pipeline expansion efforts relative to the revenues we generate.

Although we reported net income of $321.0 million and $690.1 million for the years ended December 31, 2019 and 2018, respectively, 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 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, 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 intend to continue to expand our product pipeline through our internal drug discovery efforts and the execution of additional partnerships through business development activities or strategic transactions that align with our oncology drug development, regulatory and commercial expertise, which efforts could involve substantial costs. To offset these costs in the future, we will need to generate substantial revenues. If these costs exceed our current expectations, or we fail to achieve anticipated revenue targets, the market value of our common stock may decline.

Our financial outlook may not be realized.

From time to time, in press releases and otherwise, we may publish estimates, forecasts or other forward-looking statements regarding our future financial or operating results, including estimated revenues, expenses and earnings. Any forecast of our future performance reflects various assumptions. These assumptions are subject to significant risks and uncertainties, and as a matter of course, any number of them may prove to be incorrect. Further, the achievement of any forecast depends on numerous assumptions and other factors (including those described in this discussion), many of which are beyond our control. As a result, we cannot be certain that our performance will be consistent with any management estimates or forecasts or that the variation from such estimates or forecasts will not be material and adverse. Current and potential stockholders are cautioned not to base their entire analysis of our business and prospects upon isolated estimates or forecasts, but instead are encouraged to utilize our entire publicly available mix of historical and forward-looking information, as well as other available information regarding us, our products, the competitive landscape for our products, our commercialization, development and regulatory efforts, as well as those of our collaboration partners, and the biotechnology and pharmaceutical industry generally when evaluating our prospective financial or operating results.

If additional capital is not available to us when we need it, we may be unable to expand our product offerings and maintain business growth.

As of December 31, 2019, we had $1.4 billion in cash and investments. Our business operations grew substantially during 2019. In order to maintain business growth in 2020, we plan to continue to execute on our U.S. commercialization plans for CABOMETYX, while reinvesting in our product pipeline through the continued development of cabozantinib and our other product candidates, internal discovery activities and the execution of strategic transactions. Our ability to achieve 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 internal drug discovery and business development activities;
- 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 internal 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, rising interest rate environments, actual or threatened public health emergencies and outbreak of disease (including for example, the recent coronavirus outbreak), 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 unable to expand our product offerings and maintain business growth, which could have a material adverse impact on our business, financial condition and results of operations.

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. 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. New pronouncements from the Financial Accounting Standards Board 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.

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 stock-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, 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, 2019, we had federal and state net operating loss carryforwards of approximately $675 million. The federal and state net operating loss carryforwards will begin to expire, if not utilized, beginning in 2035 for federal income tax purposes and 2020 for 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, 2019, 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 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 UK's withdrawal from the EU may have a negative effect on global economic conditions, financial markets and our business.

Following the ratification of the Withdrawal Agreement by the European Parliament and UK Parliament, the UK left the EU on January 31, 2020 (commonly referred to as "Brexit"). The Withdrawal Agreement provides for a transition period until December 31, 2020, during which the UK remains in the single market and customs union and the free movement of people will continue, in order to ensure frictionless trade and business continuity until a long-term relationship is agreed. At the end of transition, the UK's relationship with the EU will be determined by the new agreements it has entered into on trade and other areas of cooperation. The new agreements must be reached before the transition period ends. If not, the UK would have to rely on previous international conventions for security cooperation and would trade with the EU on World Trade Organization terms. The exception is Northern Ireland, whose trade in goods with the EU would be covered by the provisions in the Northern Ireland Protocol.

Given the lack of comparable precedent, it is unclear what financial, trade, regulatory and legal implications Brexit will have and how it might affect us. For example, we rely on third-party contract manufacturing organization facilities located in the UK, responsible for packaging, labeling, storing and subsequently distributing supplies of our product to the EU. Any tariffs, differing regulatory requirements and other restrictions on the free movement of goods between the UK and the EU that ultimately result from Brexit may have an adverse impact on this part of our supply chain. Trade restrictions, changes to the regulatory approval or drug cost reimbursement systems, and additional administrative costs may impede the ability of our collaboration partner Ipsen to market our products in Europe. Furthermore, the initial announcement of Brexit caused significant volatility in global stock markets and currency exchange rate fluctuations; therefore, the Brexit transition may continue to 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 could have a material adverse impact on our business, financial condition and results of operations.

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 biotechnology, biopharmaceutical and pharmaceutical companies, including, Ipsen, Takeda, Roche and Genentech, BMS and Daiichi Sankyo, for the development and ultimate commercialization of our products. Our dependence on our relationships with collaboration partners 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 collaboration partners or potential future collaboration partners will devote to the development or commercialization of drug candidates or to their marketing and distribution;
- the possibility that collaboration partners 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 collaboration partners 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;
- the possibility that our collaboration partners may experience financial difficulties;
- our collaboration partners' lack of success in their efforts to obtain regulatory approvals in a timely manner, or at all;
- our collaboration partners' 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 collaboration partners' failure to comply with the terms of our collaboration agreements and related ancillary agreements;
- our collaboration partners' failure to comply with applicable healthcare laws, as well as established guidelines, laws and regulations related to GMP, GCP, GDP and Good Pharmacovigilance Practice;
- the possibility that our collaboration partners 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 third parties in an area or field of exclusivity;
- the possibility that future collaboration partners 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 and our product development efforts could be delayed, all of 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, 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 internal 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 continue to expand through our clinical development and commercial progress, we continue to appropriately expand our supply chain through secondary third-party contract manufacturers and suppliers.

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 fulfill 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. In addition, through our third-party contract manufacturers and data service providers, we continue to provide serialized commercial products as required to comply with the DSCSA. 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 partners' ability to successfully develop and commercialize CABOMETYX and COMETRIQ and generate revenues to which we are entitled under the collaborations.

If third-party scientific advisors and contractors we rely on to assist with our drug discovery efforts do not perform as expected, the expansion of our product pipeline may be delayed.

We work with scientific advisors at academic and other institutions, as well as third-party contractors in various locations throughout the world, that assist us in our research and development efforts, including in internal drug discovery and preclinical development strategy. These third parties are not our employees and may have other commitments or contractual obligations that limit their availability to us. Although these third-party scientific advisors and contractors 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 scientific advisors and contractors or otherwise limit our access to these experts, or that the scientific advisors themselves may now be more reluctant to work with industry partners. Even if these scientific advisors and contractors with whom we have engaged intend to meet their contractual obligations, they may be impacted by external factors, including, without limitation, actual or threatened public health emergencies and outbreak of disease. In fact, certain of our contractors located in China have been affected by the recent coronavirus outbreak, which has restricted their ability to perform their contractually obligated services to us. In any of these circumstances, we have or may continue to experience delays in the receipt of services, lose work performed by these scientific advisors and contractors 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.

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 collaboration partners. We have also outsourced significant elements of our information technology infrastructure to third parties and, as a result, such 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 cybersecurity 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.

Numerous companies have been subject to a wide variety of security incidents, cyber attacks (including through use of ransomware) 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 and our third-party vendors 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 such threats can also vary in motive (including corporate espionage). Cyber attacks continue to become more prevalent and much harder to detect and defend against, and 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 or 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, or 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 cybersecurity systems (including the recruitment and retention of experienced information technology professionals, who are in high demand) 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 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. For example, in September 2019, we received a Paragraph IV certification notice letter from MSN that it has filed an ANDA with the FDA for a generic version of CABOMETYX tablets, and we subsequently filed a patent infringement lawsuit against MSN on October 29, 2019. Should MSN or any other third parties receive FDA approval of an ANDA or a 505(b)(2) NDA with respect to cabozantinib, it is possible that such company or companies could introduce generic versions of our marketed products before our patents expire if they do not infringe our patents or if it is determined that our patents are invalid or unenforceable, and the resulting generic competition could have a material adverse impact on 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, partners and consultants, we cannot provide assurance 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 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 have a material adverse impact on our business, financial condition and results of operations.

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 and resources, and our current and planned personnel and operating practices may not be adequate to support our growth. To effectively manage our growth, we must continue to improve existing, and implement new, facilities, operational and financial systems, and procedures and controls, as well as 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.

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, scientific and pharmaceutical operations personnel will be critical to support activities related to advancing the development program for cabozantinib and our other product candidates, successfully executing upon our commercialization plan for cabozantinib and our internal proprietary research and development efforts. Competition is intense for experienced clinical, commercial, scientific and pharmaceutical operations 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.

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, aircraft disasters (due to the proximity of our headquarters to a major international airport), terrorism and similar events, and any insurance we may maintain may be inadequate to cover our losses. If any disaster were to occur, our ability to operate our business at our facilities could be seriously, or potentially completely, impaired, causing significant delays in our programs and making it difficult for us to recover due to the unique nature of our research activities. Accordingly, an earthquake or other disaster could have a material adverse impact on our business, financial condition and results of operations.

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 or otherwise 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, and our operations can produce hazardous waste products. We cannot eliminate the risk of accidental contamination or discharge, or any resultant injury from these materials, and we may face liability under applicable laws for any injury or contamination that results from our use or the use by our collaboration partners or other third parties of these materials, and such liability may exceed our insurance coverage and our total assets. In addition, we may be required to indemnify our collaboration partners against all damages and other liabilities arising out of our development activities or products produced in connection with our collaborations with them. Moreover, our continued compliance with environmental laws and regulations may be expensive, and current or future environmental regulations may impair our research, development and production efforts.

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 collaboration partners 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 biotechnology, biopharmaceutical and pharmaceutical 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

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:

- the announcement of FDA approval or non-approval, or delays in the FDA review process with respect to cabozantinib, our collaboration partners' product candidates being developed in combination with cabozantinib, or our competitors' product candidates;
- the commercial performance of both CABOMETYX and COMETRIQ and the revenues we generate from those approved products, including royalties paid under our collaboration and license agreements;
- adverse or inconclusive results or announcements related to our or our collaboration partners' clinical trials or delays in those clinical trials;
- the timing of achievement of our clinical, regulatory, partnering, commercial and other milestones for cabozantinib or any of our other programs or product candidates;
- our ability to make future investments in the expansion of our pipeline through internal drug discovery and business development activities;

- our ability to obtain the materials and services, including an adequate product supply for any approved drug product, from our third-party vendors or do so at acceptable prices;
- the timing and amount of expenses incurred for clinical development and manufacturing of cabozantinib;
- 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, such as MSN's ANDA, seeking approval of generic versions of our marketed products;
- quarterly variations in our or our competitors' results of operations;
- changes in our relationships with our collaboration partners, including the termination or modification of our agreements, or other events or conflicts that may affect our collaboration partners' timing and willingness to develop, or if approved, commercialize our products and product candidates out-licensed to them;
- the announcement of an in-licensed product candidate or strategic acquisition;
- litigation, including intellectual property infringement and product liability lawsuits, involving us;
- the impairment of acquired goodwill and other assets;
- changes in earnings estimates or recommendations by securities analysts, or financial guidance from our management team, and any failure to achieve the operating results projected by securities analysts or by our management team;
- 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 disposition of any of our technologies or compounds;
- significant fluctuations in interest rates or foreign currency exchange rates; 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 could have material adverse impact on 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. Likewise, as a result of significant changes in U.S. or global political and economic conditions, actual or threatened public health emergencies and outbreak of disease (including for example, the recent coronavirus outbreak), policies governing foreign trade and health care spending and delivery, 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 prohibition on actions by our stockholders by written consent;
- 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; 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

Our corporate headquarters is located in Alameda, California, where we lease a total of 228,941 square feet of space, including 7,477 square feet of space that we expect to take possession of on or prior to April 30, 2020. The lease expires in October 2031. We have two five-year options to extend the lease. In October 2019, we entered into a build-to-suit lease agreement (the Build-to-Suit Lease) for approximately 220,000 square feet of additional office facilities adjacent to our current corporate headquarters. The term of the Build-to-Suit Lease is for a period of 242 months, which will begin on the substantial completion of the building and tenant improvements by the lessor. We currently anticipate that the term will begin in October 2021. We believe these leased facilities are sufficient to accommodate our current and near-term needs.

Item 3. Legal Proceedings

In September 2019, we received a notice letter regarding an ANDA submitted to the FDA by MSN, requesting approval to market a generic version of CABOMETYX tablets. The notice letter included a Paragraph IV certification with respect to our U.S. Patent Nos. 8,877,776, 9,724,342, 10,034,873 and 10,039,757, which are listed in the *Orange Book.* MSN’s notice letter does not provide a Paragraph IV certification against the ‘473 Patent, which expires on August 16, 2026, or U.S. Patent No. 8,497,284, which expires on September 24, 2024; therefore, neither the ‘473 Patent nor U.S. Patent No. 8,497,284 are presently at issue. On October 29, 2019, we filed a complaint for patent infringement against MSN asserting U.S. Patent No. 8,877,776 in the Delaware District Federal Court arising from MSN’s ANDA filing with the FDA. Based on the information we have received to date, our complaint does not allege infringement of U.S. Patent Nos. 9,724,342, 10,034,873 and 10,039,757. We are seeking, among other relief, an order that the effective date of any FDA approval of the ANDA would be a date no earlier than the expiration of U.S. Patent No. 8,877,776 on October 8, 2030 and equitable relief enjoining MSN from infringing this patent. On November 20, 2019, MSN filed its response to the complaint, alleging that U.S. Patent No. 8,877,776 is invalid and not infringed. A date for a bench trial in this case has been tentatively scheduled for April 2022.

We may also from time to time become a party or subject to various other 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.

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 18, 2020, there were 381 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, 2019.

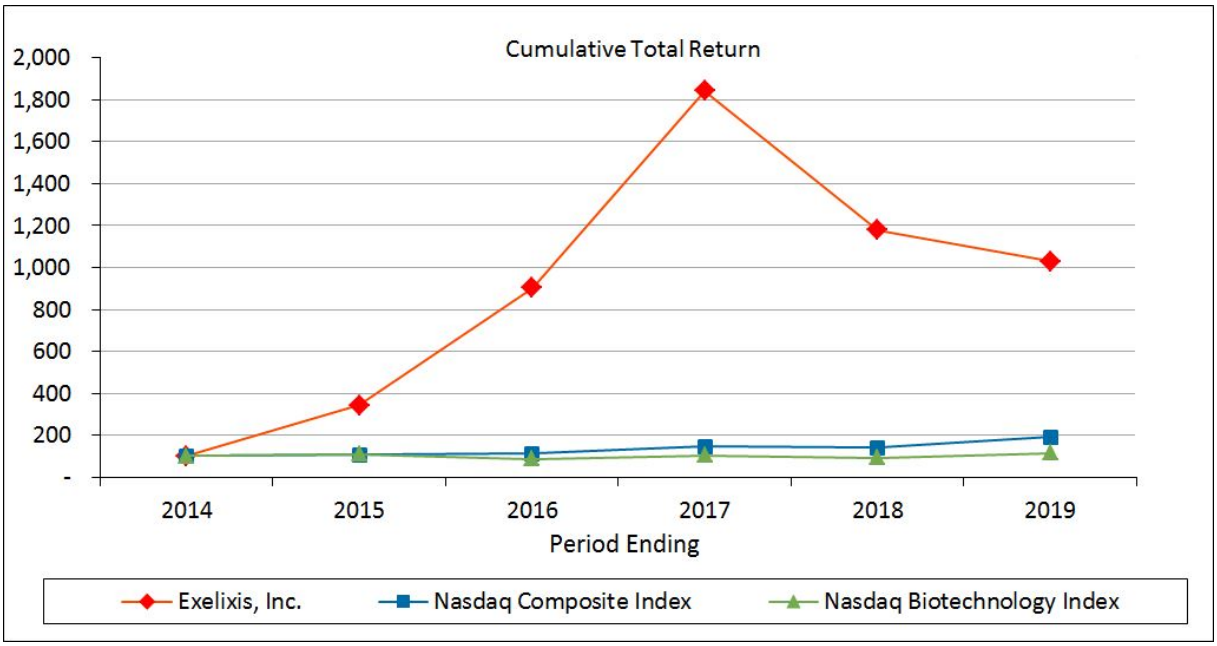
Repurchases of Equity Securities

There were no repurchases of our common stock during the year ended December 31, 2019.

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, 2019, the cumulative total return for our common stock, the Nasdaq Composite Index and the Nasdaq Biotechnology Index. The graph assumes that $100 was invested on December 31, 2014 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,					
	2014	2015	2016	2017	2018	2019
Exelixis, Inc.	100	342	904	1,842	1,178	1,031
Nasdaq Composite Index	100	107	117	151	146	202
Nasdaq Biotechnology Index	100	111	87	106	95	119

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, 2019 and 2018 and for the years ended, December 31, 2019, 2018, and 2017 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, 2017, 2016 and 2015, and for each of the years ended December 31, 2016 and 2015, are derived from audited Consolidated Financial Statements not included in this Annual Report on Form 10-K.

We have adopted a 52- or 53-week fiscal year policy that ends on the Friday closest to December 31st. Fiscal year 2019, which was a 53-week fiscal year, ended on January 3, 2020; fiscal year 2018, which was a 52-week fiscal year, ended on December 28, 2018; fiscal year 2017, which was a 52-week fiscal year, ended on December 29, 2017; fiscal year 2016, which was a 52-week fiscal year, ended on December 30, 2016; and fiscal year 2015, which was a 53-week fiscal year, ended on January 1, 2016.

	Year Ended December 31,				
	2019	2018	2017	2016	2015
	(in thousands, except per share data)				
Consolidated Statements of Income Data:					
Revenues (1)(2)	$ 967,775	$ 853,826	$ 452,477	$ 191,454	$ 37,172
Total operating expenses (2)	$ 598,305	$ 414,971	$ 286,567	$ 219,578	$ 158,593
Income (loss) from operations	$ 369,470	$ 438,855	$ 165,910	$ (28,124)	$ (121,421)
Income tax provision (benefit) (3)	$ 77,097	$ (237,978)	$ 4,350	$ —	$ 55
Net income (loss)	$ 321,012	$ 690,070	$ 154,227	$ (70,222)	$ (161,744)
Net income (loss) per share:					
Basic	$ 1.06	$ 2.32	$ 0.52	$ (0.28)	$ (0.77)
Diluted	$ 1.02	$ 2.21	$ 0.49	$ (0.28)	$ (0.77)
Weighted-average common shares outstanding:					
Basic	302,584	297,892	293,588	250,531	209,227
Diluted	315,009	312,803	312,003	250,531	209,227

	December 31,				
	2019	2018	2017	2016	2015
	(in thousands)				
Consolidated Balance Sheet Data:					
Cash and investments	$ 1,388,628	$ 851,621	$ 457,176	$ 479,554	$ 253,310
Working capital	$ 868,444	$ 791,544	$ 369,704	$ 200,215	$ 126,414
Total assets	$ 1,885,670	$ 1,422,286	$ 655,294	$ 595,739	$ 332,223
Long-term obligations (4)	$ 56,954	$ 29,361	$ 255,163	$ 237,635	$ 420,897
Total stockholders' equity (deficit)	$ 1,685,970	$ 1,287,453	$ 284,961	$ 89,318	$ (140,806)

(1) Revenues for the years ended December 31, 2019 and 2018 are presented under Accounting Standards Update No. 2014-09, *Revenue from Contracts with Customers (Topic 606)*, while revenues for the years ended December 31, 2017, 2016 and 2015 continue to be reported in accordance with our historic accounting under previous revenue recognition guidance, Accounting Standards Codification Topic 605: *Revenue Recognition*.

(2) See "Management's Discussion and Analysis of Financial Condition and Results of Operations" in Part II, Item 7 of this Annual Report on Form 10-K for additional discussion of our operating results.

(3) Net income for the year ended December 31, 2018 included a $244.1 million income tax benefit related to the release of substantially all of the valuation allowance against our deferred tax assets.

(4) The decreases in long-term obligations were primarily due to the repayment of the Secured Convertible Notes due 2018 held by entities associated with Deerfield Management Company, L.P. in 2017, the repayment of the $80.0 million term loan with Silicon Valley Bank in 2017, and the conversions and redemption in 2016 of the 4.25% convertible senior subordinated notes due 2019.

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 ends on the Friday closest to December 31st. Fiscal year 2019, which was a 53-week fiscal year, ended on January 3, 2020, fiscal year 2018, which was a 52-week fiscal year, ended on December 28, 2018 and fiscal year 2017, which was a 52-week fiscal year, ended on December 29, 2017. For convenience, references in this report as of and for the fiscal years ended January 3, 2020, December 28, 2018 and December 29, 2017 are indicated as being as of and for the years ended December 31, 2019, 2018 and 2017, respectively.

This discussion and analysis generally discusses 2019 and 2018 items and year-to-year comparisons between 2019 and 2018. Discussions of 2017 items and year-to-year comparisons between 2018 and 2017 that are not included in this Annual Report on Form 10-K can be found in "Item 7. Management's Discussion and Analysis of Financial Condition and Results of Operations" in our Annual Report on Form 10-K for the fiscal year ended December 31, 2018, filed with the SEC on February 22, 2019.

Overview

We are 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, received regulatory approval and established commercial presence in various geographies around the world. Two are derived from cabozantinib, our flagship molecule, an inhibitor of multiple tyrosine kinases including MET, AXL, VEGF receptors and RET. Our cabozantinib products are: CABOMETYX tablets approved for advanced RCC and previously treated HCC; and COMETRIQ capsules approved for progressive, metastatic MTC. For these types of cancer, cabozantinib has become or is becoming a standard of care. The other two products resulting from our discovery efforts are: COTELLIC, an inhibitor of MEK, approved as part of a combination regimen to treat a specific form of 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.

The FDA first approved CABOMETYX for previously treated patients with advanced RCC in April 2016, and in December 2017 the FDA expanded CABOMETYX's approval 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 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.

To develop and commercialize CABOMETYX and COMETRIQ outside the U.S., we have entered into license agreements with Ipsen and Takeda. We granted to Ipsen rights to cabozantinib outside of the U.S. and Japan, and to Takeda rights to cabozantinib in Japan. Both Ipsen and Takeda 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, Ipsen has continued to execute on its commercialization plans for CABOMETYX, having received regulatory approvals and launched in multiple territories outside of the U.S., including in the EU and Canada, as a treatment for advanced RCC and for HCC in adults who have previously been treated with sorafenib. Additionally, with respect to the Japanese market, Takeda achieved important regulatory milestones with its applications to the Japanese MHLW for Manufacturing and Marketing Approval of CABOMETYX as a treatment for patients with unresectable and metastatic RCC in April 2019, and more recently in January 2020, as a treatment for patients with unresectable HCC who progressed after prior systemic therapy.

In addition to our regulatory and commercialization efforts in the U.S. and the support provided to our collaboration partners for rest of world regulatory and commercialization activities, we are also pursuing other indications for cabozantinib that have the potential to increase 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 therapies, in a broad development program comprising over 85 ongoing or planned clinical trials across multiple indications. We, along with our 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 development program with potentially label-enabling trials. One pivotal trial that has resulted from this effort is COSMIC-311, our ongoing phase 3 pivotal trial evaluating cabozantinib versus placebo in patients with RAI-refractory DTC who have progressed after up to two VEGF receptor-targeted therapies.

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. 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, for which our collaboration partner BMS has announced top-line results are expected in the first half of 2020, 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 previously treated or previously untreated advanced HCC, also in collaboration with BMS and for which initial clinically meaningful results were presented at ASCO's Gastrointestinal Cancers Symposium in January 2020. Additionally in May 2019, as part of our clinical collaboration with BMS, we initiated COSMIC-313, a phase 3 pivotal trial evaluating the triplet combination of cabozantinib, nivolumab and ipilimumab versus the combination of nivolumab and ipilimumab in patients with previously untreated advanced intermediate- or poor-risk RCC. We expect to complete enrollment for COSMIC-313 in early 2021 and to report top-line results of the event-driven analyses from the trial in the 2022 timeframe. We also intend to evaluate the combination of cabozantinib and nivolumab, with or without ipilimumab, in other phase 3 trials in various other tumor types. In an effort to diversify our exploration of combinations with ICIs, we also initiated COSMIC-312, a phase 3 pivotal trial evaluating cabozantinib in combination with the Roche's ICI, atezolizumab, versus sorafenib in previously untreated advanced HCC, and COSMIC-021, a broad phase 1b study evaluating the safety and tolerability of cabozantinib in combination with atezolizumab in patients with locally advanced or metastatic solid tumors. COSMIC-021 is divided into two parts: a dose-escalation phase, which was completed in 2018; and an expansion phase, which is ongoing. Findings from the dose-escalation stage of COSMIC-021 demonstrated that the combination was well-tolerated and showed encouraging anti-tumor activity in patients with advanced RCC. The expansion phase of COSMIC-021 comprises 24 total cohorts, with 20 cohorts evaluating the combination of cabozantinib and atezolizumab and four cohorts evaluating cabozantinib or atezolizumab as single-agent therapies. Based on continuing encouraging efficacy and safety data certain cohorts have been or may be further expanded, including the cohorts of patients with NSCLC who have been previously treated with an ICI and mCRPC who have been previously treated with enzalutamide and/or abiraterone acetate and experienced radiographic disease progression in soft tissue. We anticipate enrolling up to 1,732 patients in the trial in late 2020, which timing is subject to the initiation of additional cohorts or expansion of selected existing cohorts. Since its initiation, data from COSMIC-021 have been instrumental in guiding our clinical development strategy for cabozantinib in combination with ICIs, including supporting planned pivotal trials in NSCLC, mCRPC and RCC. Encouraging results from an interim analysis of the mCRPC cohort of COSMIC-021 were presented at ASCO's Genitourinary Cancer Symposium in February 2020. For additional information on the COSMIC-021 results, see "Business—Cabozantinib Development Program—Trials Conducted under our Clinical Collaboration Agreements—Combination Studies with F. Hoffmann-La Roche Ltd. (Roche)" in Part I, Item 1 of this Annual Report on Form 10-K. Based on regulatory feedback from the FDA, and if supported by the clinical data, we intend to file with the FDA for accelerated approval in an mCRPC indication as early as 2021.

We also remain committed to building our product pipeline by discovering and developing new cancer therapies for patients. Notably, these efforts are led by some of the same experienced scientists that led the efforts to discover cabozantinib, cobimetinib and esaxerenone, which have been approved for commercialization. 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 tyrosine kinase inhibitor that is currently in a phase 1 clinical trial in patients with advanced solid malignancies. We anticipate that dose expansion cohorts and potential combination cohorts with ICIs of this phase 1 trial will begin to enroll in 2020.

We augment these internal drug discovery activities with business development initiatives aimed at identifying and in-licensing promising, early-stage oncology assets and then further develop them utilizing our established clinical

development infrastructure. In furtherance of this strategy, in 2019, we entered into collaboration and license agreements with Aurigene, which is focused on the discovery and development of novel small molecules as therapies for cancer, and Iconic, which is focused on the advancement of a next-generation ADC program targeting the tissue factor in solid tumors. Both the lead Aurigene program targeting CDK7 and tissue factor ADC program with Iconic are in preclinical development and could result in IND filings in 2020. We have also made progress under our 2018 collaborations with Invenra, which is focused on the discovery and development of multispecific antibodies for the treatment of cancer, and StemSynergy, which is focused on the discovery and development of novel oncology compounds aimed to inhibit tumor growth by targeting CK1α. To further enhance our early-stage pipeline, we expect to enter into additional, external collaborative relationships around assets and technologies that complement our internal drug discovery and development efforts.

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

2019 Business Updates and Financial Highlights

During 2019, we continued to execute on our business objectives, generating significant revenue from operations and enabling us to continue to seek to maximize the clinical and commercial potential of our products and expand our product pipeline. Significant business updates and financial highlights for 2019 and subsequent to year end include:

Business Updates

- In January 2019, the FDA approved CABOMETYX as a treatment for patients with HCC who have been previously treated with sorafenib.
- In February 2019, following the FDA’s acceptance of our IND for XL092, a next-generation oral TKI, we initiated a phase 1 dose escalation trial, evaluating the pharmacokinetics, safety and tolerability of XL092 in patients with advanced solid tumors, with the primary objective of determining a dose for daily oral administration suitable for further evaluation.
- In April 2019, Takeda applied to the Japanese MHLW for Manufacturing and Marketing Approval of CABOMETYX as a treatment for patients with unresectable and metastatic RCC.
- In May 2019, we announced the initiation of COSMIC-313, a phase 3 pivotal trial evaluating the triplet combination of cabozantinib, nivolumab and ipilimumab versus the combination of nivolumab and ipilimumab in patients with previously untreated advanced intermediate- or poor-risk RCC, which will be conducted in collaboration with BMS.
- In May 2019, following the Japanese MHLW’s approval, we announced that Daiichi Sankyo launched MINNEBRO as a treatment for patients with hypertension in Japan.
- In May 2019, we announced an exclusive option and license agreement with Iconic to advance an innovative next-generation ADC program for cancer.
- In June 2019, Genentech informed us that IMspire170, Genentech’s phase 3 pivotal trial evaluating the combination of cobimetinib with atezolizumab in patients with previously untreated BRAF V600 wild-type advanced melanoma, did not meet its primary endpoint.
- In July 2019, we announced an amendment 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 expand patient enrollment in certain existing mCRPC and NSCLC cohorts and to add new expansion and exploratory cohorts in mCRPC (an aggregate of 24 total cohorts, with 20 expansion cohorts evaluating the combination of cabozantinib and atezolizumab and four exploratory cohorts evaluating cabozantinib or atezolizumab as single-agent therapies).
- In July 2019, we announced an exclusive collaboration, option and license agreement with Aurigene to in-license as many as six programs to discover and develop small molecules as therapies for cancer.
- In October 2019, Ipsen received regulatory approval from Health Canada for CABOMETYX for the first-line treatment of adults with advanced RCC.
- In October 2019, we expanded our collaboration with Invenra focused on the discovery and development of multispecific antibodies for the treatment of cancer to include the development of novel binders against six additional targets which we can use to generate multispecific antibodies based on Invenra’s B-Body™ technology platform, or with other platforms and formats at our option.
- In October 2019, we filed a patent infringement lawsuit against MSN, following receipt of a Paragraph IV certification notice letter from MSN that it had filed an ANDA with the FDA requesting approval to market a generic version of CABOMETYX tablets, following expiration of the ‘473 Patent, which expires on August 14, 2026. For a

more detailed discussion of this litigation matter, see “Legal Proceedings” in Part I, Item 3 of this Annual Report on Form 10-K.

- In November 2019, Daiichi Sankyo reported positive results from a phase 3 pivotal trial of esaxerenone in patients with diabetic nephropathy.
- In November 2019, Ipsen received regulatory approval from Health Canada for CABOMETYX for treatment of patients with HCC who have been previously treated with sorafenib.
- In December 2019, we announced that IMspire150, the phase 3 pivotal trial evaluating the combination of cobimetinib with atezolizumab and vemurafenib in patients with previously untreated BRAF V600 mutant melanoma, met its primary endpoint. Results will be presented at an upcoming medical meeting and discussed with healthcare authorities around the world, including the FDA and EMA.
- In December 2019, we announced a joint clinical research agreement with Roche for the purpose of further evaluating the combination of cabozantinib with atezolizumab in patients with locally advanced or metastatic solid tumors, including in three planned phase 3 pivotal trials in advanced NSCLC, mCRPC and RCC.
- In January 2020, we announced an amendment to the protocol for COSMIC-021 to further expand patient enrollment in an existing mCRPC cohort to up to 130 patients.
- In January 2020, clinically meaningful data from CheckMate 040, the phase 1/2 trial evaluating cabozantinib in combination with nivolumab and in combination with both nivolumab and ipilimumab in patients with previously treated or previously untreated advanced HCC, were presented at ASCO’s Gastrointestinal Cancers Symposium. For additional information on the CheckMate 040 results, see “Business—Cabozantinib Development Program—Trials Conducted under our Clinical Collaboration Agreements—Combination Studies with Bristol-Myers Squibb Company (BMS)” in Part I, Item 1 of this Annual Report on Form 10-K.
- In January 2020, Takeda applied to the Japanese MHLW for approval to manufacture and sell CABOMETYX as a treatment for patients with unresectable HCC who progressed after prior systemic therapy in Japan.
- In February 2020, we presented clinically meaningful results from the mCRPC cohort of COSMIC-021 at ASCO’s Genitourinary Cancers Symposium. For additional information on the COSMIC-021 results, see “Business—Cabozantinib Development Program—Trials Conducted under our Clinical Collaboration Agreements—Combination Studies with F. Hoffmann-La Roche Ltd. (Roche)” in Part I, Item 1 of this Annual Report on Form 10-K.
- In February 2020, we announced the enrollment of the first 100 patients in COSMIC-311, the phase 3 pivotal trial of cabozantinb versus placebo in patients with RAI-refractory DTC who have progressed after up to two prior VEGF receptor-targeted therapies.

2019 Financial Highlights

- Net product revenues for 2019 increased to $760.0 million, compared to $619.3 million for 2018.
- Total revenues for 2019 increased to $967.8 million, compared to $853.8 million for 2018.
- Research and development expenses for 2019 increased to $337.0 million, compared to $182.3 million for 2018.
- Selling, general and administrative expenses for 2019 increased to $228.2 million, compared to $206.4 million for 2018.
- Provision for income taxes for 2019 was $77.1 million, compared to an income tax benefit of $238.0 million for 2018.
- Net income for 2019 was $321.0 million, or $1.06 per share, basic and $1.02 per share, diluted, compared to $690.1 million, or $2.32 per share, basic and $2.21 per share diluted, for 2018.
- Cash and investments increased to $1.4 billion at December 31, 2019, compared to $0.9 billion at December 31, 2018.

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 challenges and risks that may impact our ability to execute on our 2020 business objectives. In particular, for the foreseeable future, we expect our ability to generate sufficient cash flow to fund our business operations and growth will depend upon the continued commercial success of CABOMETYX as a treatment for advanced RCC and previously treated HCC, and possibly for other indications for which cabozantinib is being evaluated in potentially label-enabling clinical trials, if warranted by the data generated from such trials. However, 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 in the major commercial markets where CABOMETYX is approved. Even if we and our collaboration partners receive the required regulatory approvals to market cabozantinib for additional indications, we and our collaboration partners may not be able to commercialize CABOMETYX effectively and successfully in these additional indications. In addition, CABOMETYX will only continue to be commercially successful if private third-party and government payers continue to provide coverage and reimbursement. However, as is the case for all innovative pharmaceutical therapies, obtaining and maintaining coverage and reimbursement for CABOMETYX is becoming increasingly difficult, both within the U.S. and in foreign markets, because of growing concerns over healthcare cost containment and corresponding policy initiatives and activities aimed at limiting access to, and restricting the prices of, pharmaceuticals.

Achievement of our 2020 business objectives and the continued success of CABOMETYX will also depend on the success of our development and commercialization strategies to navigate increased competition, including that from, but not limited to, the use of therapies that combine an ICI with another targeted agent to treat cancer. In the longer term, we may eventually face competition from potential manufacturers of generic versions of our marketed products, including the proposed generic version of CABOMETYX tablets that is the subject of the ANDA submitted to the FDA by MSN, which if approved following the expiration of our composition of matter patent in 2026, could result in significant decreases in the revenue derived from the U.S. sales of CABOMETYX and thereby materially harm our business and financial condition. Separately, our research and development objectives may be impeded by the challenges of scaling our organization to meet the demands of expanded drug development, unanticipated delays in clinical testing and the inherent risks and uncertainties associated with internal drug discovery operations. In connection with efforts to expand our product pipeline, we may be unsuccessful in discovering new drug candidates or identifying 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 biotechnology, biopharmaceutical and pharmaceutical industries 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

Impact of the Duration of Our Fiscal Year

We have adopted a 52- or 53-week fiscal year policy that ends on the Friday closest to December 31st. Accordingly, 2019 was a 53-week fiscal year and 2018 was a 52-week fiscal year. The 53-week fiscal year in 2019, as compared to the 52-week fiscal year in 2018, contributed to the year-over-year increases in certain revenues and expenses.

Revenues

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

	Year Ended December 31,		Percentage Change
	2019	2018	
Net product revenues	$ 759,950	$ 619,279	23 %
Collaboration revenues	207,825	234,547	(11)%
Total revenues	$ 967,775	$ 853,826	13 %

Net Product Revenues

Gross product revenues, discounts and allowances, and net product revenues were as follows (dollars in thousands):

	Year Ended December 31,		Percentage Change
	2019	2018	
Gross product revenues	$ 957,621	$ 738,529	30%
Discounts and allowances	(197,671)	(119,250)	66%
Net product revenues	$ 759,950	$ 619,279	23%

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

	Year Ended December 31,		Percentage Change
	2019	2018	
CABOMETYX	$ 733,421	$ 599,946	22%
COMETRIQ	26,529	19,333	37%
Net product revenues	$ 759,950	$ 619,279	23%

The increase in product revenues for CABOMETYX for the year ended December 31, 2019, as compared to 2018, was primarily due to a 17% increase in the number of units of CABOMETYX sold and, to a lesser extent, an increase in the average selling price of the product. The increase in CABOMETYX sales volume reflects the continued growth of CABOMETYX for the treatment of patients with advanced RCC as well as the launch of CABOMETYX for the treatment of patients with HCC who have been previously treated with sorafenib, following FDA approval for that indication in January 2019.

The increase in product revenues for COMETRIQ for the year ended December 31, 2019, as compared to 2018, was primarily due to a 24% increase in the number of units of COMETRIQ sold and, to a lesser extent, an increase in the average selling price of the product. The increase in COMETRIQ sales volume was entirely due to a comparator purchase of the product for use in a clinical trial. Excluding the comparator purchase, COMETRIQ sales volume has continued to decrease since the launch of CABOMETYX in April 2016.

We expect our 2020 net product revenues to remain in-line with 2019, reflecting the continued evolution of the metastatic RCC and HCC treatment landscapes.

We recognize product revenues net of discounts and allowances as 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 discounts and allowances for the year ended December 31, 2019, as compared to 2018, was primarily the result of the overall increase in product sales volume and increases in Public Health Service hospital utilization and the dollar amount of the related chargebacks, and, to a lesser extent, increases in utilization and the dollar amount of chargebacks associated with Veterans Affairs hospitals and Group Purchasing Organizations, as well as increases to other government and commercial rebates. We expect a moderate increase in our discounts and allowances as a percentage of gross product revenues during 2020 as the number of patients participating in government programs continues to increase, and as the discounts given and rebates paid to government payers also increase.

Collaboration Revenues

Collaboration revenues were as follows (dollars in thousands):

	Year Ended December 31,		Percentage Change
	2019	2018	
Collaboration revenues:			
License revenues	$ 161,299	$ 192,188	(16)%
Research and development services revenues	49,965	39,501	26 %
Other collaboration revenues	(3,439)	2,858	n/m
Total collaboration revenues	$ 207,825	$ 234,547	(11)%

License Revenues

License revenues include the recognition of the portion of milestone payments allocated to the transfer of intellectual property licenses for which it had become probable in the related period that the milestone would be achieved and a significant reversal of revenues would not occur, as well as royalty revenues.

Milestone revenues, which are allocated between license revenues and research and development services revenues, were $96.2 million for the year ended December 31, 2019, as compared to $164.4 million for the comparable periods in 2018. Due to the nature and timing of milestone events, their achievement can vary significantly from year to year. Milestone revenues by period primarily included the following:

- Milestone revenues for the year ended December 31, 2019 primarily included: 1) recognition of a $50.0 million milestone from Ipsen upon their achievement of $250.0 million in net sales of cabozantinib in their territories over four consecutive quarters; 2) recognition of a $20.0 million milestone from Daiichi Sankyo for the first commercial sale of MINNEBRO tablets as a treatment for patients with hypertension in Japan; 3) recognition of $9.9 million in revenues related to a $16.0 million milestone from Takeda for the submission of a regulatory application for cabozantinib as a treatment for patients with advanced RCC to the Japanese MHLW; 4) recognition of $9.1 million in revenues related to a $10.0 million milestone from Takeda for the submission of a regulatory application in January 2020 for cabozantinib as a treatment for patients with advanced HCC to the Japanese MHLW; and 5) recognition of two milestones totaling $5.0 million from Ipsen on the approvals by Health Canada of cabozantinib for the treatment of adults with first-line RCC and for the treatment of adults with advanced HCC who have been previously treated with sorafenib.
- Milestone revenues for the year ended December 31, 2018 primarily included: 1) recognition of $46.5 million in revenue related to a $50.0 million milestone from Ipsen for the approval of cabozantinib for the first-line treatment of adults with intermediate- or poor-risk advanced RCC by the EC; 2) recognition of $37.2 million in revenue related to a $40.0 million milestone from Ipsen for the approval by the EC of cabozantinib for previously-treated HCC; 3) recognition of a $25.0 million milestone from Ipsen upon their achievement of $100.0 million in net sales of cabozantinib in their territories over four consecutive quarters; 4) recognition of a $20.0 million milestone upon Daiichi Sankyo's submission to the Japanese MHLW of a regulatory application for esaxerenone as a treatment for patients with hypertension; 5) recognition of $18.6 million of a $20.0 million milestone from Ipsen for the initiation of COSMIC-312; and 6) recognition of a $5.0 million milestone from Ipsen on the approval by Health Canada of cabozantinib for the treatment of adults with advanced RCC.

Royalties increased primarily as a result of an increase in royalties on Ipsen's net sales of cabozantinib outside of the U.S. and Japan. Ipsen royalties were $62.4 million for the year ended December 31, 2019, as compared to $32.3 million in 2018. 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 of CABOMETYX, which, as of December 31, 2019, is approved and commercially available in 51 and 48 countries outside of the U.S., respectively.

In addition, we earned royalties on ex-U.S. net sales of COTELLIC by Genentech of $5.7 million for the year ended December 31, 2019, as compared to $5.6 million in 2018. We also earned $0.1 million in royalties on the sale of MINNEBRO by Daiichi Sankyo for the year ended December 31, 2019.

Research and Development Services Revenues

Research and development services revenues include the recognition of deferred revenue for the portion of upfront and milestone payments that have been allocated to research and development services performance obligations, as well as development cost reimbursements earned under our collaboration agreements.

Development cost reimbursements increased in 2019, as compared to 2018, primarily as a result of reimbursements from Ipsen for their share of the increase in spending on the COSMIC-312 and COSMIC-021 studies.

Other Collaboration Revenues

Other collaboration revenues include royalties earned by GSK related to Ipsen's sales of products containing cabozantinib, the profit on the U.S. commercialization of COTELLIC from Genentech and product supply revenues, net of product supply costs.

Profits on the U.S. commercialization of COTELLIC under our collaboration agreement with Genentech were $4.6 million for the year ended December 31, 2019, as compared to $8.1 million in 2018. Sales of COTELLIC in the U.S. have declined following Genentech's decision to scale back the personal promotion of COTELLIC commencing in January 2018.

For year ended December 31, 2019, other collaboration revenues were reduced by $8.4 million for the 3% royalty we are required to pay GSK on the net sales by Ipsen of any product incorporating cabozantinib, as compared to $5.4 million in 2018. As royalty generating sales of cabozantinib by Ipsen have increased as described above, our royalty payments to GSK have also increased. In addition, pursuant to a license agreement we entered into with Ligand, we are required to pay a royalty of 0.5% to Ligand on net sales of MINNEBRO; such amounts were either not significant or zero for the years ended December 31, 2019 and 2018.

2020 Expectations

We expect our collaboration revenues to decrease in 2020 as a result of a decrease in milestones expected to be achieved during the year.

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
	2019	2018	
Cost of goods sold	$ 33,097	$ 26,348	26%
Gross margin	96%	96%	

Cost of goods sold consists primarily of a 3% royalty payable to GSK on U.S. net sales of any product incorporating cabozantinib, as well as the cost of inventory sold, indirect labor costs, write-downs related to expiring and excess inventory, and other third-party logistics costs. The increase in cost of goods sold for the year ended December 31, 2019, as compared to 2018, was primarily the result of the increases in product sales volume described above. We expect the cost of goods sold and our gross margin to remain flat during 2020.

Research and Development Expenses

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

	Year Ended December 31,		Percentage Change
	2019	2018	
Research and development expenses	$ 336,964	$ 182,257	85%

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

The increase in research and development expenses for the year ended December 31, 2019, as compared to 2018, was primarily related to increases in clinical trial costs, license and other collaboration costs, personnel expenses, consulting and outside services, the allocation of general corporate 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, and comparator drug purchases, increased $70.3 million for the year ended December 31, 2019, as compared to 2018. The increase in clinical trial costs was primarily due to costs associated with the expanding clinical trial program for cabozantinib which includes COSMIC-311, COSMIC-312, COSMIC-313, COSMIC-021 and CheckMate 9ER. License and other collaboration costs increased $39.4 million for the year ended December 31, 2019, as compared to 2018, primarily as a result of the collaboration agreements we entered into with Aurigene in July 2019 and Iconic in May 2019. Personnel expenses increased $17.9 million for the year ended December 31, 2019, respectively, as compared to 2018, primarily due to increases in headcount to support our expanded discovery and development efforts. Consulting and outside services increased $7.5 million for the year ended December 31, 2019, as compared to 2018, primarily in support of our expanded discovery and development efforts. Stock-based compensation increased $6.3 million for the year ended December 31, 2019, as compared to 2018, primarily due to the increase in headcount, as well as the expense recognition for restricted stock units that were granted in September 2018 that either have vested or are expected to vest upon the achievement of specific performance targets (the 2018 PSUs). General corporate costs, which include our costs for facilities, information technology, human resources, financial planning and analysis and purchasing, are allocated to cost of goods sold, research and development and selling general and administrative expenses based on headcount. The allocation of general corporate costs to research and development expenses increased $7.1 million for the year ended December 31, 2019, as compared to 2018, primarily due to increases in headcount to support our expanded discovery and development efforts.

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: 1) development; 2) drug discovery; and 3) 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,	
	2019	2018
Research and development expenses:		
Development:		
Clinical trial costs	$ 136,763	$ 66,434
Personnel expenses	61,433	48,114
Consulting and outside services	14,531	9,693
Other development costs	15,034	13,505
Total development	227,761	137,746
Drug discovery:		
License and other collaboration costs	47,691	8,245
Other drug discovery (1)	25,610	13,699
Total drug discovery	73,301	21,944
Other (2)	35,902	22,567
Total research and development expenses	$ 336,964	$ 182,257

(1) Primarily includes personnel expenses, consulting and outside services and laboratory supplies.
(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 continued 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 85 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; company-sponsored COSMIC-313, for which BMS is providing nivolumab and ipilimumab 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.

We are also committed to building our product pipeline by discovering and developing new cancer therapies for patients. In this regard, we are conducting internal drug discovery activities with the goal of identifying new product candidates to advance into clinical trials. We augment these internal drug discovery activities with business development initiatives aimed at identifying and in-licensing promising, early-stage oncology assets and then further develop them utilizing our established clinical development infrastructure.

We expect our research and development expenses to continue to increase in 2020 as a result of the expected initiation and completion of numerous late-stage and other potentially label-enabling cabozantinib trials.

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 our ability to expand the labeled indications of use for CABOMETYX and 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
	2019	2018	
Selling, general and administrative expenses	$ 228,244	$ 206,366	11%

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

The increase in selling, general and administrative expenses for the year ended December 31, 2019, as compared to 2018, was primarily related to increases in personnel expenses, stock-based compensation, consulting and outside services and marketing costs, and were partially offset by a decrease in corporate giving. Personnel expenses increased $11.5 million for the year ended December 31, 2019, as compared to 2018, primarily due to an increase in administrative headcount to support the company’s commercial and research and development organizations. Stock-based compensation increased $9.7 million for the year ended December 31, 2019, as compared to 2018, primarily due to an increase in headcount as well as the expense recognition for certain of the 2018 PSUs. Consulting and outside services increased $4.2 million and marketing costs increased $3.2 million for the year ended December 31, 2019, as compared to 2018, primarily due to increased marketing activities in support of the launch of CABOMETYX for the treatment of patients with HCC who have been previously treated with sorafenib and continued support of the product in an increasingly competitive RCC market. Corporate giving, consisting predominantly of donations to independent patient support foundations, decreased $6.5 million for the year ended December 31, 2019, as compared to 2018.

We expect our selling, general and administrative expenses to continue to increase in 2020 in support of our continued commercial investment in CABOMETYX and the growth in the broader organization.

Other Income (Expenses), Net

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

	Year Ended December 31,		Percentage Change
	2019	2018	
Interest income	$ 27,959	$ 12,840	118%
Other, net	680	397	71%
Total other income (expenses), net	$ 28,639	$ 13,237	116%

The increase in interest income for the year ended December 31, 2019, as compared to 2018, was the result of increase in our investment balance as well as an increase in the yield earned on those investments.

Income Tax Provision (Benefit)

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

	Year Ended December 31,	
	2019	2018
Income tax provision (benefit)	$ 77,097	$ (237,978)

Our effective income tax rate was 19.4% during the year ended December 31, 2019. During the year ended December 31, 2018, we recorded 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. Other than the benefit we recorded for the release of our valuation allowance, income taxes for the year ended December 31, 2018 primarily related to a provision for taxes in states for which we do not have net operating loss carryforwards due to a limited operating history. We expect that our effective tax rate will be between 20 percent and 22 percent in 2020.

Liquidity and Capital Resources

As of December 31, 2019, we had $1.4 billion in cash and investments. 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.

We expect to continue to spend significant amounts to fund the continued development and commercialization of cabozantinib. In addition, we intend to continue to expand our product pipeline through our internal 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 though 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

Cash flow activities were as follows (in thousands):

	Year Ended December 31,	
	2019	2018
Net cash provided by operating activities	$ 526,956	$ 415,720
Net cash used in investing activities	$ (587,247)	$ (297,850)
Net cash provided by financing activities	$ 12,553	$ 9,691

Operating Activities

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 deferred taxes, stock-based compensation, depreciation, non-cash lease expense 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 Statements of Income.

The most significant factors that contributed to the increase in cash provided by operating activities for the year ended December 31, 2019, as compared to 2018, were the increase in cash received on sales of our products and the changes in operating assets and liabilities described above, which were partially offset by an increase in cash paid for operating expenses.

Investing Activities

Cash used in investing activities for the year ended December 31, 2019 was primarily due to investment purchases of $1.2 billion, and purchases of property, equipment and other of $12.8 million, less cash provided by the maturity and sale of investments of $608.3 million.

Cash used in investing activities for the year ended December 31, 2018 was primarily due to investment purchases of $557.8 million and purchases of property and equipment of $33.3 million, less cash provided by the maturity and sale of investments of $293.0 million.

Financing Activities

Cash provided by financing activities for the year ended December 31, 2019 was primarily a result of $22.5 million in proceeds from the issuance of common stock under our equity incentive plans, partially offset by $9.9 million of taxes paid related to net share settlements.

Cash provided by financing activities for the year ended December 31, 2018 was primarily a result of $17.3 million in proceeds from the issuance of common stock under our equity incentive plans, partially offset by $7.6 million of taxes paid related to net share settlements.

Contractual Obligations

Contractual obligations as of December 31, 2019 were as follows (in thousands):

	Payments Due by Period				
Contractual Obligations (1)	**Total**	**Less than 1 Year**	**1-3 Years**	**3-5 Years**	**More than 5 Years**
Leases (2)	$ 302,737	$ 4,641	$ 19,289	$ 29,194	$ 249,613
Purchase obligations (3)	33,344	29,335	2,913	1,096	—
Other long-term obligations	1,626	—	1,626	—	—
Total contractual cash obligations	$ 337,707	$ 33,976	$ 23,828	$ 30,290	$ 249,613

(1) In addition to the amounts presented, we have committed to make payments for potential future milestones, research funding commitments and royalties to certain collaboration partners as part of our agreements with those parties. Because the amount and timing of those payments is uncertain they 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) We entered into the build-to-suit lease agreement in October 2019, which is expected to commence in October 2021. The amounts presented include the estimated lease commitment payments at the estimated commencement of the lease, subject to adjustment dependent upon the actual total development costs of the premises but do not include the impact of a tenant improvement allowance of approximately $16.5 million. For more information about our lease obligations, see “Note 11. Commitments” in our “Notes to Consolidated Financial Statements” contained in Part II, Item 8 of this Annual Report on Form 10-K.

(3) Purchase obligations include firm purchase commitments related to manufacturing and maintenance of inventory, software services and other facilities and equipment.

Off-Balance Sheet Arrangements

As of December 31, 2019, we did not have any material off-balance-sheet arrangements, as defined by applicable SEC regulations.

Critical Accounting Policies and 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; 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-based compensation 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.

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, distributors and commercial payors; and (d) returns. Discounts and allowances are complex and require significant judgment by management. Management assesses estimates each period and updates them to reflect current information.

We initially record estimates for these deductions at the time we recognize the related gross product revenue. We base our estimates for the expected utilization 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 obligations, 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. We base the relevant period estimates of sales 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. We generally consider such increases or decreases to be changes in estimates and they 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

We execute all of our clinical trials with support from contract research organizations and other vendors and we accrue costs for clinical trial activities performed by these third parties 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 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-based Compensation

Stock-based compensation expense requires us to estimate the fair value of stock options, including PSOs, and the estimate the number of shares subject to PSUs that will ultimately vest.

Fair value models require a number of complex and subjective assumptions including our stock price volatility, employee exercise patterns and risk-free interest rates. 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 consider 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 take advantage of 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.

We recognize stock-based compensation for PSUs over the requisite service period only for awards which we estimate will ultimately vest, which requires judgment as to the probability and timing of the achievement of the underlying performance goals. Significant factors we consider in making those judgments include forecasts of our product revenues and those of our collaboration partners, estimates regarding the operational progress of late-stage clinical development programs and discovery pipeline expansion performance targets. To the extent actual results, or updated estimates, differ from current estimates, such amounts are recorded as a cumulative adjustment in the period estimates are revised.

For additional description of our stock-based compensation, see "Note 8. Employee Benefit Plans" to our "Notes to Consolidated Financial Statements" contained in Part II, Item 8 of this Annual Report on Form 10-K.

Income Taxes

We compute our income tax provision or benefit under the asset and liability method. Significant estimates are required in determining our income tax provision or benefit. We base some of these estimates 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 we deem a reversal of any portion of our valuation allowance against our deferred tax assets to be appropriate, we recognize a tax benefit 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 9. 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.

Item 7A. Quantitative and Qualitative Disclosures About Market Risk

We are exposed to cash flow and earnings fluctuations as a result of certain market risks. These market risks primarily relate to credit risk, changes in interest rates and foreign exchange rates. Our investment portfolio is used to preserve our capital until it is required to fund operations, including our research and development activities. None of these market risk-sensitive instruments are held for trading purposes. We do not have derivative financial instruments in our investment portfolio.

Credit Risk

We manage credit risk associated with our investment portfolio through our investment policy, which limits purchases to high-quality issuers and limits the amount of our portfolio that can be invested in a single issuer.

Interest Rate Risk

We invest our cash in a variety of financial instruments, principally securities issued by the U.S. government and its agencies, investment-grade corporate bonds and commercial paper, and money market funds. These investments are denominated in U.S. Dollars. All of our interest-bearing securities are subject to interest rate risk and could decline in value if interest rates fluctuate. Substantially all of our investment portfolio consists of marketable securities with active secondary or resale markets to help ensure portfolio liquidity, and we have implemented guidelines limiting the term-to-maturity of our investment instruments. Due to the conservative and short-term nature of these instruments, we do not believe that we have a material exposure to interest rate risk. If market interest rates were to increase or decrease by one percentage point, the fair value of our investment portfolio would increase or decrease by an immaterial amount.

Foreign Exchange Rate Risk

Fluctuations in the exchange rates of the U.S. dollar and foreign currencies may have the effect of increasing or decreasing our revenues and expenses. 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 collaboration 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. Research and development expenses include clinical trial services performed by third-party contract research organizations and other vendors located outside the U.S. that may bill us in currencies where their services are provided,

which is also predominantly the Euro. 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 certain sales-based milestones may also be delayed. Similarly, if the U.S. dollar weakens against a foreign currency, then our research and development expenses would increase. However, we believe that we are not subject to material risks arising from changes in foreign exchange rates and that a hypothetical 10% increase or decrease in foreign exchange rates would not have a material adverse impact on our financial condition, results of operations or cash flows.

Item 8. Financial Statements and Supplementary Data

EXELIXIS, INC.
INDEX TO CONSOLIDATED FINANCIAL STATEMENTS

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 January 3, 2020 and December 28, 2018, the related consolidated statements of income, comprehensive income, stockholders' equity and cash flows for each of the three fiscal years in the period ended January 3, 2020, 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 January 3, 2020 and December 28, 2018, and the results of its operations and its cash flows for each of the three fiscal years in the period ended January 3, 2020, 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 January 3, 2020, 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 25, 2020 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.

Critical Audit Matter

The critical audit matter communicated below is a matter arising from the current period audit of the financial statements that was communicated or required to be communicated to the audit committee and that: (1) relates to accounts or disclosures that are material to the financial statements and (2) involved our especially challenging, subjective or complex judgments. The communication of the critical audit matter does not alter in any way our opinion on the consolidated financial statements, taken as a whole and we are not, by communicating the critical audit matter below, providing a separate opinion on the critical audit matter or on the accounts or disclosures to which it relates.

	Revenue recognition - Product sales
Description of the Matter	During the year ended January 3, 2020, the Company's gross product revenues were $957.6 million. As discussed in Note 1 of the financial statements, the Company sells its products principally to specialty distributors and specialty pharmacy providers, or collectively, Customers. These Customers subsequently resell the products to health care providers and patients. Revenues from product sales are recognized when control is transferred to the Customer.

Auditing the Company's product sales was challenging, specifically related to the effort required to audit Customer sales activity to assess whether incentives resulted in orders in excess of demand (i.e., channel stuffing) and whether any such transactions meet the criteria for revenue recognition. This involved judgmentally assessing factors including market demand, Customer ordering patterns, Customer inventory levels, contractual terms and incentives offered.

How We Addressed the Matter in Our Audit

We obtained an understanding, evaluated the design and tested the operating effectiveness of controls designed to monitor and review inventory levels in the channel and sales under Customer incentive programs. This includes testing relevant controls over the information systems that are important to the initiation, recording and billing of revenue transactions as well as controls over the completeness and accuracy of the data used.

Our audit procedures over the Company's product sales included, among others, examination of inventory channel reports for unusual trends or transactions as well as performing analytical procedures to detect and investigate anomalies within the data. Procedures included those to detect sales of short dated product near year end as well as testing the completeness and accuracy of the underlying data. We also examined the terms and conditions of any new or amended contracts with Customers and its impact on the Company's returns reserve. We also confirmed the terms and conditions of contracts directly with a selection of Customers, including whether there are side agreements and terms not formally included in the contract that may impact the Company's returns reserve. In addition, we obtained written representations from members of the commercial function and the market access group regarding changes to Customer incentives and the completeness of the terms and conditions reported to the legal and accounting departments.

/s/ Ernst & Young LLP

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

Redwood City, California
February 25, 2020

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

	December 31,	
	2019	**2018**
ASSETS		
Current assets:		
Cash and cash equivalents	$ 266,501	$ 314,775
Short-term investments	585,742	378,559
Trade receivables, net	119,073	162,771
Inventory	12,886	9,838
Prepaid expenses and other current assets	26,988	31,073
Total current assets	1,011,190	897,016
Long-term investments	536,385	158,287
Property and equipment, net	48,892	50,897
Deferred tax assets, net	172,374	244,111
Goodwill	63,684	63,684
Other long-term assets	53,145	8,291
Total assets	$ 1,885,670	$ 1,422,286
LIABILITIES AND STOCKHOLDERS' EQUITY		
Current liabilities:		
Accounts payable	$ 11,581	$ 10,901
Accrued compensation and benefits	37,364	32,142
Accrued clinical trial liabilities	38,777	18,231
Rebates and fees due to customers	18,719	14,954
Accrued collaboration liabilities	11,856	7,419
Other current liabilities	24,449	21,825
Total current liabilities	142,746	105,472
Long-term portion of deferred revenue	6,596	15,897
Long-term portion of operating lease liabilities	48,011	12,178
Other long-term liabilities	2,347	1,286
Total liabilities	199,700	134,833
Commitments		
Stockholders' equity:		
Preferred stock, $0.001 par value, 10,000 shares authorized and no shares issued	—	—
Common stock, $0.001 par value; 400,000 shares authorized; issued and outstanding: 304,831 and 299,876 at December 31, 2019 and 2018, respectively	305	300
Additional paid-in capital	2,241,947	2,168,217
Accumulated other comprehensive income (loss)	3,069	(701)
Accumulated deficit	(559,351)	(880,363)
Total stockholders' equity	1,685,970	1,287,453
Total liabilities and stockholders' equity	$ 1,885,670	$ 1,422,286

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

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

	Year Ended December 31,		
	2019	**2018**	**2017**
Revenues:			
Net product revenues	$ 759,950	$ 619,279	$ 349,008
Collaboration revenues	207,825	234,547	103,469
Total revenues	967,775	853,826	452,477
Operating expenses:			
Cost of goods sold	33,097	26,348	15,066
Research and development	336,964	182,257	112,171
Selling, general and administrative	228,244	206,366	159,330
Total operating expenses	598,305	414,971	286,567
Income from operations	369,470	438,855	165,910
Other income (expense), net:			
Interest income	27,959	12,840	4,883
Interest expense	—	—	(8,679)
Other, net	680	397	(3,537)
Total other income (expense), net	28,639	13,237	(7,333)
Income before income taxes	398,109	452,092	158,577
Income tax provision (benefit)	77,097	(237,978)	4,350
Net income	$ 321,012	$ 690,070	$ 154,227
Net income per share:			
Basic	$ 1.06	$ 2.32	$ 0.52
Diluted	$ 1.02	$ 2.21	$ 0.49
Weighted-average common shares outstanding:			
Basic	302,584	297,892	293,588
Diluted	315,009	312,803	312,003

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

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

	Year Ended December 31,		
	2019	**2018**	**2017**
Net income	$ 321,012	$ 690,070	$ 154,227
Other comprehensive income (loss):			
Net unrealized gains (losses) on available-for-sale securities, net of tax impact of $(1,049), $156, and $0, respectively	3,770	(354)	69
Comprehensive income	$ 324,782	$ 689,716	$ 154,296

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

EXELIXIS, INC.
CONSOLIDATED STATEMENTS OF STOCKHOLDERS' EQUITY
(in thousands)

	Common Stock		Additional Paid-in Capital	Accumulated Other Comprehensive Income (Loss)	Accumulated Deficit	Total Stockholders' Equity
	Shares	Amount				
Balance at December 31, 2016	289,924	$ 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	5	17,404	—	—	17,409
Issuance of common stock on exercise of warrants	877	1	(1)	—	—	—
Stock-based compensation	—	—	23,938	—	—	23,938
Balance at December 31, 2017	296,209	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	3,667	4	13,407	—	—	13,411
Stock-based compensation	—	—	40,626	—	—	40,626
Balance at December 31, 2018	299,876	300	2,168,217	(701)	(880,363)	1,287,453
Net income	—	—	—	—	321,012	321,012
Other comprehensive income	—	—	—	3,770	—	3,770
Issuance of common stock under equity incentive and stock purchase plans	4,955	5	17,128	—	—	17,133
Stock-based compensation	—	—	56,602	—	—	56,602
Balance at December 31, 2019	304,831	$ 305	$2,241,947	$ 3,069	$ (559,351)	$ 1,685,970

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

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

	Year Ended December 31,		
	2019	2018	2017
Net income	$ 321,012	$ 690,070	$ 154,227
Adjustments to reconcile net income to net cash provided by operating activities:			
Depreciation	8,348	4,915	1,187
Stock-based compensation	56,602	40,626	23,938
Non-cash lease expense	2,819	2,854	—
Deferred taxes	71,002	(244,111)	—
Other, net	88	1,129	(6,795)
Changes in operating assets and liabilities:			
Trade receivables, net	43,716	(85,471)	(43,299)
Inventory	(5,731)	(3,181)	(3,319)
Prepaid expenses and other assets	(5,723)	(8,525)	(378)
Deferred revenue	(9,301)	271	13,745
Accounts payable and other liabilities	44,124	17,143	26,305
Net cash provided by operating activities	526,956	415,720	165,611
Cash flows from investing activities:			
Purchases of property, equipment and other	(12,834)	(33,297)	(21,143)
Proceeds from sale of property and equipment	—	308	164
Purchases of investments	(1,182,682)	(557,832)	(319,090)
Proceeds from sales and maturities of investments	608,269	292,971	376,864
Net cash (used in) provided by investing activities	(587,247)	(297,850)	36,795
Cash flows from financing activities:			
Proceeds from issuance of common stock under equity incentive and stock purchase plans	22,499	17,278	22,423
Taxes paid related to net share settlement of equity awards	(9,904)	(7,574)	(6,563)
Principal repayments of debt	—	—	(185,788)
Other, net	(42)	(13)	—
Net cash provided by (used in) financing activities	12,553	9,691	(169,928)
Net (decrease) increase in cash, cash equivalents and restricted cash equivalents	(47,738)	127,561	32,478
Cash, cash equivalents and restricted cash equivalents at beginning of period	315,875	188,314	155,836
Cash, cash equivalents and restricted cash equivalents at end of period	$ 268,137	$ 315,875	$ 188,314
Supplemental cash flow disclosure:			
Cash paid for interest	$ —	$ —	$ 20,460
Cash paid for taxes	$ 7,873	$ 10,677	$ 538
Non-cash activities:			
Right-of-use assets obtained in exchange for lease obligations	$ 29,562	17,180	$ —
Property and equipment deemed to have been acquired in build-to-suit lease	$ —	$ —	$ 14,530
Unpaid liabilities incurred for purchases of property and equipment	$ 26	$ 802	$ 524

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

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. 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, received regulatory approval and established a commercial presence in various geographies around the world. Two are derived from cabozantinib, our flagship molecule, an inhibitor of multiple tyrosine kinases including MET, AXL, VEGF receptors and RET. Our cabozantinib products 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. For these types of cancer, cabozantinib has become or is becoming a standard of care. Beyond these 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 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).

Basis of Presentation

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.

We have made reclassifications to our prior years' Consolidated Balance Sheet and Consolidated Statements of Cash Flows to conform to the current year's presentation. These reclassifications had no effect on total current assets, total assets, total operating cash flows, total investing cash flows or total financing cash flows.

We have adopted a 52- or 53-week fiscal year policy that ends on the Friday closest to December 31st. Fiscal year 2019, which was a 53-week fiscal year, ended on January 3, 2020, fiscal year 2018, which was a 52-week fiscal year, ended on December 28, 2018 and fiscal year 2017, which was a 52-week fiscal year, ended on December 29, 2017. For convenience, references in this report as of and for the fiscal years ended January 3, 2020, December 28, 2018 and December 29, 2017 are indicated as being as of and for the years ended December 31, 2019, 2018 and 2017, respectively.

Segment Information

We operate in one business segment that focuses on the discovery, development and commercialization of new medicines for difficult-to-treat cancers. 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, we

evaluate our significant estimates. 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. Actual results could differ materially from those estimates.

Recently Adopted Accounting Pronouncements

In the third quarter of 2019, we adopted 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 requires a customer in a hosting arrangement that is a service contract to follow the guidance in Accounting Standards Codification (ASC) 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 requires capitalized implementation costs to be expensed over the term of the hosting arrangement, which includes reasonably certain renewals. We adopted ASU 2018-15 using the prospective transition method in the accompanying Consolidated Financial Statements. The adoption of ASU 2018-15 did not have a material impact on our Consolidated Financial Statements.

In the first quarter of 2019, we adopted ASU 2018-02, *Income Statement—Reporting Comprehensive Income (Topic 220)* (ASU 2018-02). There was no financial impact from the adoption of ASU 2018-02 and we did not make an election to reclassify the income tax effects of the Tax Cuts and Jobs Act of 2017 from accumulated other comprehensive income (loss) to accumulated deficit. In connection with the adoption of ASU 2018-02, we adopted the individual unit of account approach for releasing income tax effects from accumulated other comprehensive income (loss).

In the first quarter of 2019, we also adopted ASU 2017-08, *Receivables—Nonrefundable Fees and Other Costs (Subtopic 310-20)* (ASU 2017-08). ASU 2017-08 shortens the amortization period for certain callable debt securities held at a premium. Specifically, ASU 2017-08 requires the premium to be amortized to the earliest call date. ASU 2017-08 does not require an accounting change for securities held at a discount; the discount continues to be amortized to maturity. The adoption of ASU 2017-08 did not have a material impact on our Consolidated Financial Statements.

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, certificates of deposit and marketable debt securities which are subject to minimal credit and market risk.

We designate all investments in marketable debt securities as available-for-sale and therefore, report such investments at fair value, with unrealized gains and losses recorded in accumulated other comprehensive income (loss). For securities sold prior to maturity, the cost of securities sold is based on the specific identification method. We include realized gains and losses on the sale of investments in other income (expense), net in the accompanying Consolidated Statements of Income.

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. The classification of restricted cash equivalents as short-term or long-term is dependent upon the longer of the remaining term to maturity of the investment or the remaining term of the related restriction.

We subject all of our investments 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.

Fair Value Measurements

We define fair value as 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). When determining the fair value measurements for assets and liabilities which are required to be recorded at fair value, we consider the principal or most advantageous market in which we would transact and the market-based risk measurements or assumptions that

market participants would use in pricing the asset or liability, such as risks inherent in valuation techniques, transfer restrictions and credit risks.

Accounts Receivable

We record trade accounts receivable 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 have been insignificant.

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 write downs are charged to either cost of goods sold or the cost of supplied product included in collaboration revenues in the accompanying Consolidated Statements of Income. 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

We record property and equipment at cost, net of depreciation. We compute depreciation using the straight-line method based on estimated useful lives of the assets, which ranges up to 15 years and depreciate leasehold improvements over the lesser of their estimated useful lives or the remainder of the lease term. We charge repairs and maintenance costs to expense as incurred. We periodically review property and equipment for impairment whenever events or changes in circumstances indicate that the carrying amount of an asset may not be recoverable. We did not recognize impairment charges in any of the periods presented.

Goodwill

We recorded goodwill amounts as the excess purchase price over tangible assets, liabilities and intangible assets acquired based on their estimated fair value. We periodically review the carrying amount of goodwill for impairment (at least annually) and whenever events or changes in circumstance indicate that the carrying value may not be recoverable. Historically, we assessed the recoverability of our goodwill on the last day of our third quarter. Beginning in 2019, we changed the date of our annual goodwill impairment assessment to the first day of our fourth quarter to allow for operational expediency. The change in goodwill impairment testing date does not represent a significant change to our accounting for goodwill. 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. We perform a quantitative assessment if the qualitative assessment results in a more-likely-than-not determination or if a qualitative assessment is not performed. The quantitative 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 fair value. We continue to operate in one segment, which is also considered to be our sole reporting unit and therefore, goodwill is tested for impairment at the enterprise level. We did not recognize any impairment charges in any of the periods presented.

Collaboration Agreements

We assess whether our collaboration agreements are subject to ASC 808: *Collaborative Arrangements* (Topic 808) based on whether they involve joint operating activities and whether both parties have active participation in the arrangement and are exposed to significant risks and rewards. To the extent that the arrangement falls within the scope of Topic 808, we assess whether the payments between us and our collaboration partner are subject to other accounting literature. If we conclude that payments from the collaboration partner to us represent consideration from a customer, then we account for those payments within the scope of Topic 606. However, if we conclude that our collaboration partner is not a customer for certain activities, such as for certain collaborative research and development activities, we present such payments as a reduction of research and development expense.

Revenue

In the first quarter of 2018, we adopted Topic 606 using the modified retrospective method applied to those contracts that were not completed as of the adoption date. Results for the years ended December 31, 2019 and 2018 are presented under Topic 606, while results for the year ended December 31, 2017 have not been adjusted and continue to be reported in accordance with our historic accounting under previous revenue recognition guidance, ASC Topic 605: *Revenue Recognition* (Topic 605). 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 are within the scope of Topic 606, we perform the following five steps: 1) identify the contract(s) with a customer; 2) identify the performance obligations in the contract; 3) determine the transaction price; 4) allocate the transaction price to the performance obligations in the contract; and 5) 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

We record revenues from product sales 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, Federal government entities purchasing via the Federal Supply Schedule, 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 specialty distributor by the Customer. The allowance for chargebacks is based on actual chargebacks received and 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. during 2018 and 2017, the Medicare Part D prescription drug benefit mandated participating manufacturers to fund 50% of the Medicare Part D insurance coverage gap for prescription drugs sold to eligible patients. This amount increased to 70% in 2019. 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, we classify these payments in selling, general and administrative expenses in our Consolidated Statements of Income.

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 sales-based milestone payments; product supply services; development cost reimbursements; profit sharing arrangements; and royalties on net sales of licensed products. Except for profit sharing arrangements, payments for product supply services and certain development cost reimbursements, each of these payment types were within the scope of Topic 606 during the years ended December 31, 2019 and 2018. As part of the accounting for these arrangements, we 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.

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.

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.

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 collaboration arrangements may include promises of future clinical development and drug safety services, as well as participation on certain joint committees. When such services are provided to a customer, and they are distinct from the licenses provided to our collaboration partners, these promises are accounted for as a separate performance obligation which we estimate using internal development costs incurred and projections through the term of the arrangements. We record revenue for these services as the performance obligations are satisfied over time.

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 account for such arrangements in accordance with 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 years ending December 31, 2019 and 2018 and accordingly, those profits are recognized as collaboration revenues in the accompanying Consolidated Statements of Income. 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 Income.

Royalty and Sales-based Milestone Payments: For arrangements that include royalties and sales-based milestone payments, including milestone payments earned for the first commercial sale of a product, the license is deemed to be the predominant item to which such payments relate and we recognize revenue at the later of when the related sales occur or when the performance obligation to which the royalty has been allocated has been 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, the cost of manufacturing, indirect labor costs, 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 and 2017 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, 2019 or 2018.

Research and Development Expenses

Research and development costs are expensed as incurred and primarily include: (1) direct and indirect internal costs for drug discovery; (2) upfront license and project initiation fees, license option fees, funded research and milestone payments incurred for our in-licensing arrangements with our collaboration partners; and (3) development costs associated with our clinical trial projects, which include fees paid to Contract Research Organizations (CRO) performing work on our behalf.

Our clinical trial projects have been executed with support from third-party CROs, who specialize in conducting and managing global clinical trials. We accrue expenses for clinical trial activities performed by the CROs based upon the estimated amount of work completed on each trial. For clinical trial expenses, the significant factors used in estimating accruals include direct CRO costs, the number of patients enrolled, the number of active clinical sites involved, the duration for which the patients will be enrolled in the trial and patient out of pocket costs. We monitor patient enrollment levels and related activities to the extent possible through CRO meetings and correspondence, internal reviews 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. As described further above, certain payments made to us from our collaboration partners may be presented as a reduction of research and development expense.

Development, regulatory or commercial milestone payments to collaboration partners are recorded as research and development costs when we determine such payments become probable.

Leases

We determine if an arrangement includes a lease at the inception of the agreement. For each of our lease arrangements, we record a right-of-use asset representing our right to use an underlying asset for the lease term and a lease liability representing our obligation to make lease payments. Operating lease right-of-use assets and liabilities are recognized at the lease commencement date based on the net present value of lease payments over the lease term. In determining the weighted average discount rate used to calculate the net present value of lease payments, we use our incremental borrowing rate based on the information available at the lease commencement date. 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 for our operating leases is recognized on a straight-line basis over the lease term. We have elected not to apply the recognition requirements of Topic 842 for short-term leases.

Advertising

Advertising expenses were $17.9 million, $14.8 million and $8.6 million for the years ended December 31, 2019, 2018 and 2017, respectively. We expense the costs of advertising, including promotional expenses, as incurred. Advertising expenses are recorded in sales, general and administrative expenses.

Stock-Based Compensation

We account for stock-based payments to employees, including grants of service-based restricted stock awards, performance-based restricted stock awards (PSUs), service-based stock options, performance-based stock options (PSOs), and purchases under our 2000 Employee Stock Purchase Plan (ESPP) in accordance with ASC 718, *Compensation-Stock Compensation*, which requires that stock-based payments (to the extent they are compensatory) be recognized in our Consolidated Statements of Income based on their fair values. We account for forfeitures of stock-based awards as they occur. 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) and PSUs are estimated as the value of the underlying shares of our common stock. The grant date fair values are estimated using a Monte Carlo simulation pricing model for PSOs with market vesting conditions and a Black-Scholes Merton option pricing model for other stock options. Both option pricing models require the input of subjective assumptions. These variables include, but are not limited to, the expected volatility of our stock price and the expected term of the awards. We consider both implied and historical volatilities when developing an estimate of expected volatility. We estimate the term using historical data. We recognize compensation expense over the requisite service period on an accelerated basis for awards with a market or performance condition and on a straight-line basis for service-based stock options and awards. Compensation expense relating to PSUs is recognized when we determine that it is probable that the performance goals will be achieved, which we assess on a quarterly basis.

Income Taxes

Our income tax provision or benefit is computed under the asset and liability method. Significant estimates are required in determining our income tax provision or benefit. 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 9. 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.

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 income (expense), net in the accompanying Consolidated Statements of Income. Net foreign currency translational gains and losses were not material for the years ended December 31, 2019, 2018 and 2017.

Recent Accounting Pronouncements Not Yet Adopted

In December 2019, the Financial Accounting Standards Board (FASB) issued ASU 2019-12, *Income Taxes (Topic 740)-Simplifying the Accounting for Income Taxes* (ASU 2019-12). ASU 2019-12 simplifies the accounting for income taxes by removing certain exceptions to the general principles in Topic 740 and clarifying and amending existing guidance. ASU 2019-12 will be effective for us in the first quarter of 2021 with early adoption permitted. We are currently assessing the impact of ASU 2019-12 on our Consolidated Financial Statements.

In November 2018, 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 ASC Topic 808, *Collaborative Arrangements* (Topic 808) to the unit of account guidance in Topic 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 in the first quarter of 2020. We are currently assessing the impact of ASU 2018-18 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 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 us in the first quarter of 2020. We do not expect the adoption of ASU 2017-04 to have a material impact on our Consolidated Financial Statements.

In June 2016, the FASB issued ASU No. 2016-13, *Financial Instruments—Credit Losses (Topic 326)* (ASU 2016-13). ASU 2016-13 implements an impairment model, known as the current expected credit loss model that is based on expected losses rather than incurred losses. Under the new guidance, an entity will recognize as an allowance its estimate of expected credit losses. ASU 2016-13 is effective for us in the first quarter of 2020. We are currently assessing the impact of ASU 2016-13 on our Consolidated Financial Statements.

NOTE 2. REVENUES

Revenues consisted of the following (in thousands):

	Year Ended December 31,		
	2019	2018	2017
Product revenues:			
Gross product revenues	$ 957,621	$ 738,529	$ 402,569
Discounts and allowances	(197,671)	(119,250)	(53,561)
Net product revenues	759,950	619,279	349,008
Collaboration revenues:			
License revenues	161,299	192,188	96,637
Research and development service revenues	49,965	39,501	8,737
Other collaboration revenues	(3,439)	2,858	(1,905)
Total collaboration revenues	207,825	234,547	103,469
Total revenues	$ 967,775	$ 853,826	$ 452,477

Net product revenues, license revenues and research and development services revenues were recorded in accordance with Topic 606 during the years ended December 31, 2019 and 2018 and Topic 605 during the year ended December 31, 2017. During the periods presented in accordance with Topic 606, 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 includes the recognition of the portion of upfront payment milestones allocated to the transfer of intellectual property licenses for which it had become probable in the current period that the milestone would be achieved and a significant reversal of revenues would not occur, as well as royalty revenues. Research and development services revenues includes the recognition of deferred revenue for the portion of upfront and milestone payments that have been allocated to research and development services performance obligations, as well as development cost reimbursements earned under our collaboration agreements. Other collaboration revenues were recorded in accordance with Topic 808 for all periods presented and includes product supply revenues, net of product supply costs and the royalties we paid to GSK on sales by Ipsen Pharma SAS (Ipsen) of products containing cabozantinib. Profits on the U.S. commercialization of COTELLIC for the years ended December 31, 2019 and 2018 were also included other collaboration revenues, and losses on the U.S. commercialization of COTELLIC for the year ended December 31, 2017 were included in selling, general and administrative expenses

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

	Year Ended December 31,		
	2019	2018	2017
CABOMETYX	$ 733,421	$ 599,946	$ 324,000
COMETRIQ	26,529	19,333	25,008
Net product revenues	$ 759,950	$ 619,279	$ 349,008

The percentage of total revenues by customer who individually accounted for 10% or more of our total revenues were as follows:

	Year Ended December 31,		
	2019	2018	2017
Ipsen	16%	21%	15%
Affiliates of CVS Health Corporation	15%	13%	16%
Affiliates of McKesson Corporation	12%	12%	11%
Affiliates of AmerisourceBergen Corporation	10%	8%	8%
Accredo Health, Incorporated	9%	9%	11%
Diplomat Specialty Pharmacy	5%	9%	18%

Revenues by geographic region were as follows (in thousands):

	Year Ended December 31,		
	2019	2018	2017
U.S.	$ 770,244	$ 632,927	$ 367,906
Europe	152,771	182,879	69,792
Japan	44,760	38,020	14,779
Total revenues	$ 967,775	$ 853,826	$ 452,477

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

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	Total
Balance at December 31, 2017	$ 1,928	$ 1,795	$ 5,770	$ 9,493
Provision related to sales made in:				
Current period	75,543	13,017	31,040	119,600
Prior periods	(403)	206	(153)	(350)
Payments and customer credits issued	(74,746)	(11,980)	(24,741)	(111,467)
Balance at December 31, 2018	2,322	3,038	11,916	17,276
Provision related to sales made in:				
Current period	129,936	15,605	48,250	193,791
Prior periods	3,989	(111)	2	3,880
Payments and customer credits issued	(128,733)	(15,035)	(44,946)	(188,714)
Balance at December 31, 2019	$ 7,514	$ 3,497	$ 15,222	$ 26,233

The reserves for chargebacks and discounts for prompt payment are recorded as a reduction of trade receivables, net and the remaining reserves are recorded as rebates and fees due to customers in the accompanying Consolidated Balance Sheets.

Contract Assets and Liabilities

We receive payments from our collaboration partners based on billing schedules established in each contract. Amounts are recorded as accounts receivable when our right to consideration is unconditional. We may also recognize revenue in advance of the contractual billing schedule and such amounts are recorded as a contract asset when recognized. Contract assets were $1.1 million and $0 as of December 31, 2019 and 2018, respectively, and are presented in prepaid expenses and other current assets in the accompanying Consolidated Balance Statements. We may be required to defer recognition of revenue for upfront and milestone payments until we perform our obligations under these arrangements, and such amounts are recorded as deferred revenue upon receipt or when due. Contract liabilities were $6.6 million and $15.9 million as of December 31, 2019 and 2018, respectively, and are presented in long-term portion of deferred revenue in the accompanying Consolidated Balance Sheets. For those contracts that have multiple performance obligations, contract assets and liabilities are reported on a net basis at the contract level. Significant changes in contract assets during the year ended December 31, 2019, as compared to 2018, were a result of the determination that it is probable that we will earn a $10.0 million milestone from Takeda Pharmaceutical Company Limited (Takeda) for the submission of a regulatory application in 2020 for cabozantinib as a treatment for patients with second-line HCC in Japan. This contract asset was recorded in prepaid expenses and other current assets in the accompanying Consolidated Balance Sheets, offset by the effect of reporting the Takeda contract asset and liability on a net basis.

During the years ended December 31, 2019 and 2018, we recognized $6.5 million and $8.7 million, respectively, in revenues that were included in the beginning deferred revenue balance for those years.

During the years ended December 31, 2019 and 2018, we recognized $161.2 million and $198.1 million, respectively, in revenues 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, Takeda and Daiichi Sankyo.

As of December 31, 2019, $63.1 million of the transaction price allocated to our performance obligations had not been satisfied. See “Note 3. Collaboration Agreements - Cabozantinib Commercial Collaborations - Performance Obligations and Transaction Prices for our Ipsen and Takeda Collaborations” for additional information about our performance obligations.

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 and Daiichi Sankyo 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 the amount of collaboration revenues recognized during the years ended December 31, 2019, 2018 and 2017.

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 on three occasions, including 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.

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 1) the expiration of patent claims related to cabozantinib, 2) the expiration of regulatory exclusivity covering cabozantinib or 3) 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. We may terminate the collaboration agreement if Ipsen challenges or opposes any patent covered by the collaboration agreement. Ipsen may terminate the collaboration agreement if the U.S. Food and Drug Administration (FDA) or European Medicines Agency 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.

Consideration under the Collaboration

In consideration for the exclusive license and other rights contained in the collaboration agreement, including commercialization rights in Canada, we received aggregate upfront payments of $210.0 million from Ipsen in 2016. As of December 31, 2019, we have achieved aggregate milestones of $330.0 million related to regulatory, development and sales-based progress by Ipsen since the inception of the collaboration agreement, including $55.0 million and $140.0 million in milestones achieved during the years ended December 31, 2019 and 2018, respectively.

As of December 31, 2019, we are eligible to receive additional regulatory and development milestone payments from Ipsen totaling an aggregate of $79.0 million, as well as sales-based milestones, including milestone payments earned for the first commercial sale of a product, of up to $470.4 million. We also receive royalties on the net sales of cabozantinib by Ipsen outside of the U.S. and Japan. During the year ended December 31, 2019 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 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 royalty tiers for Canada also reset each calendar year.

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. Ipsen has opted into and is co-funding: CheckMate 9ER; CheckMate 040 (though Ipsen has opted not to co-fund the triplet arm of the study evaluating cabozantinib with nivolumab and ipilimumab); the dose escalation phase and first 20 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, 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 is supplied at our cost, as defined in the agreement.

Revenues from the Collaboration

Collaboration revenues under the collaboration agreement with Ipsen were $152.8 million, $182.9 million and $69.8 million during the years ended December 31, 2019, 2018 and 2017, respectively. As of December 31, 2019, $45.0 million of the transaction price allocated to our research and development services performance obligation had not been satisfied. 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, which was subsequently amended effective March 2018 and May 2019, to, among other things, modify the amount of reimbursements we receive for costs associated with our required pharmacovigilance activities and milestones we are eligible to receive. 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.

Unless earlier terminated, the collaboration agreement has a term that continues, on a product-by-product basis, until the earlier of 1) two years after first generic entry with respect to such product in Japan or 2) 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 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 an upfront payment of $50.0 million from Takeda in 2017. As of December 31, 2019, we have also achieved regulatory and development milestones in the aggregate of $26.0 million since the inception of the collaboration agreement, including $16.0 million and $10.0 million in milestones achieved during the years ended December 31, 2019 and 2018, respectively. As of December 31, 2019, we had also determined that it was probable that we will earn a $10.0 million milestone in the first quarter of 2020 for the anticipated January 2020 submission of a regulatory application to the Japanese MHLW for Manufacturing and Marketing Approval of cabozantinib as a treatment for patients in Japan with unresectable HCC who progressed after prior systemic therapy.

Under the collaboration agreement, as amended, as of December 31, 2019, we are eligible to receive regulatory and development milestone payments from Takeda of up to $20.0 million related to first-line RCC and second-line HCC, including the $10.0 million milestone we expect to earn for the submission of a regulatory application in the first quarter of 2020 described above. We are also eligible to receive additional regulatory and development milestone payments, without limit, for additional potential future indications. We are further eligible to receive sales-based milestones, including milestone payments earned for the first commercial sale of a product, of up to $155.0 million. We also receive royalties on the 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 reset each calendar year.

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 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. 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.

Revenues from the Collaboration

Collaboration revenues under the collaboration agreement with Takeda were $24.6 million, $18.0 million and $14.8 million during the years ended December 31, 2019, 2018 and 2017, respectively. As of December 31, 2019, $18.1 million of the transaction price allocated to our research and development services performance obligation had not been satisfied.

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 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. 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 is 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 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 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 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 the $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 royalties and sales-based milestones 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 years ended December 31, 2019 and 2018, the transaction price increased as a result of the achievement of various milestones. We further updated the transaction price based upon the actual 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, 2019, 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

Bristol-Myers Squibb Company (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 in the CheckMate 9ER and COSMIC-313 trials and for HCC in the CheckMate 040 trial. Under the terms of the collaboration agreement with BMS, we may also evaluate these combinations in other phase 3 pivotal trials in various other tumor types.

Under the terms of the collaboration agreement with BMS, as subsequently amended effective March 2019, May 2019 and November 2019, 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 Investigational New Drug application, unless otherwise required by a regulatory authority. Each party will be responsible for supplying finished drug product for the applicable clinical trial, and we are sponsoring the COSMIC-313 trial and BMS is sponsoring the CheckMate 9ER and CheckMate 040 trials. The responsibility for the payment of costs for any further trials will be determined on a trial-by-trial basis. 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.

F. Hoffmann-La Roche Ltd. (Roche) Collaboration

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, 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, and 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. We are the sponsor of both trials, and Roche is providing atezolizumab free of charge.

In December 2019, we entered into a joint clinical research agreement with Roche for the purpose of further evaluating the combination of cabozantinib with atezolizumab in patients with locally advanced or metastatic solid tumors, including in three planned phase 3 pivotal trials in advanced non-small cell lung cancer, metastatic castration-resistant prostate cancer and RCC. If a party to the joint clinical research agreement proposes any additional combined therapy trials beyond the initial three planned phase 3 pivotal trials, the joint clinical research agreement provides that such proposing party must notify the other party and that if agreed to, any such additional combined therapy trial will become part of the collaboration, or if not agreed to, the proposing party may conduct such additional combined therapy trial independently, subject to specified restrictions set forth in the joint clinical research agreement.

Pursuant to the terms of the joint clinical research agreement, each party granted to the other a non-exclusive, worldwide (excluding, in our case, territory already the subject of a license by us to Takeda), non-transferable, royalty-free license, with a right to sublicense (subject to limitations), to use the other party's intellectual property and compounds solely as necessary for the party to perform its obligations under the joint clinical research agreement. The parties' efforts will be governed through a joint steering committee established to guide and oversee the collaboration and the conduct of the combined therapy trials. Each party will be responsible for providing clinical supply for all combined therapy trials, and the cost of the supply will be borne by such party. The clinical trial expenses for each combined therapy trial agreed to be conducted jointly under the joint clinical research agreement will be shared equally between the parties, and the clinical trial expenses for each additional combined therapy trial not agreed to be conducted jointly under the joint clinical research agreement will be borne by the proposing party, except that the cost of clinical supply for all combined therapy trials will be borne by the party that owns the applicable product.

We determined the contract is within the scope of Topic 808 as it involves joint operating activities where both parties have active participation in the arrangement and are exposed to significant risks and rewards. Payments between us and Roche under this arrangement are not subject to other accounting literature. Payments due to Roche for our share of clinical trial costs incurred by Roche will be recorded as research and development expense and payments due from Roche for their share of clinical trial costs incurred by us will be recorded as a reduction of research and development expense.

Unless earlier terminated, the joint clinical research agreement provides that it will remain in effect until the completion of all combined therapy trials under the collaboration, the delivery of all related trial data to both parties, and the completion of any then agreed-upon additional analyses. The joint clinical research agreement may be terminated for cause by either party based on any 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 will terminate upon completion of any ongoing activities under the joint clinical research agreement.

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, we continue to be required to pay a 3% royalty to GSK on the net sales of any product incorporating cabozantinib by us and our collaboration partners. Royalties earned by GSK in connection with the sales of cabozantinib are included in cost of goods sold for sales by us and as a reduction of other collaboration revenues for sales by our collaboration partners. Such royalties were $31.3 million, $24.0 million and $12.4 million during the years ended December 31, 2019, 2018 and 2017, respectively.

In-Licensing Collaborations

Aurigene Discovery Technologies Limited (Aurigene) Collaboration

In July 2019, we entered into an exclusive collaboration, option and license agreement with Aurigene to in-license as many as six programs to discover and develop small molecules as therapies for cancer. Under the terms of the agreement, we made aggregate upfront payments of $17.5 million for exclusive options to license up to six programs, including three pre-existing programs. We are also responsible for up to $32.6 million in research funding for the discovery and preclinical development work on these programs. During the year ended December 31, 2019, we incurred $4.0 million in expense for the discovery and preclinical development funding commitment.

For each option we decide to exercise, we will be required to pay an exercise fee of either $10.0 million or $12.0 million, depending on the program, and would then assume responsibilities for all subsequent clinical development, manufacturing and commercialization for that program. Aurigene would then become eligible for up to $148.8 million per program in potential development and regulatory milestone payments, $280.0 million per program in potential commercial milestone payments, as well as royalties on potential sales. Under the terms of the agreement, Aurigene retains limited development and commercial rights for India and Russia.

Iconic Therapeutics, Inc. (Iconic) Collaboration

In May 2019, we entered into an exclusive option and license agreement with Iconic to advance an innovative next-generation antibody-drug conjugate (ADC) program for cancer, leveraging Iconic's expertise in targeting tissue factor in solid tumors. Under the terms of the agreement, we gained an exclusive option to license ICON-2, Iconic's lead oncology ADC program, in exchange for an upfront payment to Iconic of $7.5 million and a commitment for preclinical development funding. During the year ended December 31, 2019, we incurred $9.8 million in expense for the preclinical development funding commitment. Both the upfront payment and the accrual for the preclinical development funding commitment were included in research and development expenses in the accompanying Consolidated Statements of Income. If we exercise the option, we will be required to make an option exercise fee payment of $20.0 million to Iconic; we would then assume responsibilities for all subsequent clinical development, manufacturing and commercialization activities, and Iconic would become eligible for up to $190.6 million in potential development, regulatory and first-sale milestone payments, $262.5 million in potential commercial milestone payments, as well as royalties on potential sales.

Invenra, Inc. (Invenra) Collaboration

In May 2018, we entered into a collaboration and license agreement with Invenra 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 provides that we will receive an exclusive, worldwide license to one preclinical, multispecific antibody 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 October 2019, we expanded our collaboration to include the development of novel binders against six additional targets, which we can use to generate multispecific antibodies based on Invenra's B-Body™ technology platform, or with other platforms and formats at our option. As of December 31, 2019, we have initiated three additional discovery projects and two binder projects, and in total we incurred an aggregate of $7.0 million and $4.0 million in expense during the years ended December 31, 2019 and 2018, respectively, in consideration of the upfront licensing and project initiation fees. Invenra is eligible to receive up to $131.5 million in project initiation fees and milestone payments based on the achievement of specific development and regulatory milestones for a B-Body product in the first indication, or in lieu of such payments, up to $43.4 million in project initiation fees and milestone payments based on the achievement of specific development and regulatory milestones for a non- B-Body product. Upon successful commercialization of a product, Invenra is eligible to receive sales-based milestone payments up to $325.0 million as well as single-digit tiered royalties on net sales of the approved product. We have the right to initiate three additional discovery projects for development subject to an upfront payment of $2.0 million for each B-Body project and four additional binder projects subject to an upfront payment of $1.5 million for each project, as well as additional milestone payments and royalties for any products that arise from these efforts.

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 (CK1α), 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 CK1α. We paid StemSynergy an upfront payment of $3.0 million in initial research and development funding during the year ended December 31, 2018 and provided $1.9 million and $1.2 million in additional research and development funding during the years ended December 31, 2019 and 2018, respectively. StemSynergy is eligible for up to $0.5 million in additional research and development funding 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, 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.

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,		
	2019	2018	2017
Profits and losses on U.S. commercialization	$ 4,615	$ 8,084	$ (2,140)
Royalty revenues on ex-U.S. sales	$ 5,679	$ 5,564	$ 6,398

Profits on the U.S. commercialization of COTELLIC for the years ended December 31, 2019 and 2018 were included collaboration revenues and losses on the U.S. commercialization of COTELLIC for the year ended December 31, 2017 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.

Cobimetinib Profit Sharing and Royalty Revenues

In December 2006, we out-licensed the development and commercialization of cobimetinib to Genentech pursuant to a worldwide collaboration agreement. In November 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. 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 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 candidates. The collaboration agreement may be terminated for cause by either party based on uncured material breach by the other party.

Daiichi Sankyo

In March 2006, we entered into a collaboration agreement with Daiichi Sankyo pursuant to which 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 was responsible for all further preclinical and clinical development, regulatory, manufacturing and commercialization activities for the compounds.

In January 2019, the Japanese Ministry of Health, Labour and Welfare approved esaxerenone, under the brand name MINNEBRO, as a treatment for patients with hypertension and in May 2019, Daiichi Sankyo had its first commercial sale of MINNEBRO.

We have achieved milestones of $20.0 million each during the years ended December 31, 2019 and 2018 for the approval and first commercial sale of MINNEBRO. We are eligible to receive additional sales-based milestone payments of up to $90.0 million under this collaboration agreement. In addition, we are entitled to receive low double-digit royalties on sales of MINNEBRO. Such revenues were $0.1 million during the year ended December 31, 2019. 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.

Collaboration revenues under the collaboration agreement with Daiichi Sankyo were $20.1 million and $20.0 million and zero during the years ended December 31, 2019, 2018 and 2017, respectively.

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

Performance Obligations and Transaction Prices for our Other Collaborations

We have evaluated our collaborations agreements with Genentech and Daiichi Sankyo 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.

NOTE 4. CASH AND INVESTMENTS

Cash, Cash Equivalents and Restricted Cash Equivalents

A reconciliation of cash, cash equivalents, and restricted cash equivalents 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,		
	2019	2018	2017
Cash and cash equivalents	$ 266,501	$ 314,775	$ 183,164
Short-term restricted cash equivalents	—	—	504
Restricted cash equivalents included in long-term investments	1,636	1,100	4,646
Cash, cash equivalents, and restricted cash equivalents as reported within the accompanying Consolidated Statements of Cash Flows	$ 268,137	$ 315,875	$ 188,314

Restricted cash equivalents consisted of certificates of deposit with original maturities of 90 days or less used to collateralize letters of credit and, during prior periods, a purchasing card program. The classification of restricted cash

equivalents as short-term or long-term is dependent upon the longer of the remaining term to maturity of the investment or the remaining term of the related restriction.

Cash and Investments

Cash and investments consisted of the following (in thousands):

	December 31, 2019			
	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Fair Value
Investment securities available-for-sale:				
Commercial paper	$ 389,573	$ —	$ —	$ 389,573
Corporate bonds	752,295	3,934	(3)	756,226
U.S. Treasury and government sponsored enterprises	166,483	187	(5)	166,665
Total investment securities available-for-sale	1,308,351	4,121	(8)	1,312,464
Cash	40,964	—	—	40,964
Money market funds	2,467	—	—	2,467
Certificates of deposit	32,728	5	—	32,733
Total cash and investments	$ 1,384,510	$ 4,126	$ (8)	$ 1,388,628

	December 31, 2018			
	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Fair Value
Investment securities available-for-sale:				
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 investment securities available-for-sale	781,099	182	(883)	780,398
Cash	6,883	—	—	6,883
Money market funds	47,744	—	—	47,744
Certificates of deposit	16,596	—	—	16,596
Total cash and investments	$ 852,322	$ 182	$ (883)	$ 851,621

Gains and losses on the sales of investment securities available-for-sale were insignificant during the years ended December 31, 2019, 2018 and 2017.

We manage credit risk associated with our investment portfolio through our investment policy, which limits purchases to high-quality issuers and limits the amount of our portfolio that can be invested in a single issuer. The fair value and gross unrealized losses on investment securities available-for-sale in an unrealized loss position were as follows (in thousands):

	December 31, 2019					
	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	$ 14,529	$ (3)	$ —	$ —	$ 14,529	$ (3)
U.S. Treasury and government sponsored enterprises	2,848	(5)	—	—	2,848	(5)
Total	$ 17,377	$ (8)	$ —	$ —	$ 17,377	$ (8)

	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)

There were 9 and 199 investment securities in an unrealized loss position as of December 31, 2019 and 2018, respectively. During the years ended December 31, 2019, 2018 and 2017 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, we determined 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.

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

	December 31,	
	2019	2018
Maturing in one year or less	$ 789,913	$ 626,711
Maturing after one year through five years	522,551	153,687
Total investment securities available-for-sale	$ 1,312,464	$ 780,398

NOTE 5. 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. The fair value hierarchy has the following three levels:

- Level 1 - quoted prices (unadjusted) in active markets for identical assets and liabilities;
- Level 2 - inputs other than level 1 that are observable either directly or indirectly, such as 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 - unobservable inputs that are supported by little or no market activity that are significant to the fair value measurement

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

	December 31, 2019		
	Level 1	Level 2	Total
Commercial paper	$ —	$ 389,573	$ 389,573
Corporate bonds	—	756,226	756,226
U.S. Treasury and government sponsored enterprises	—	166,665	166,665
Total investment securities available-for-sale	—	1,312,464	1,312,464
Money market funds	2,467	—	2,467
Certificates of deposit	—	32,733	32,733
Total financial assets carried at fair value	$ 2,467	$ 1,345,197	$ 1,347,664

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

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.

The carrying amount of our remaining financial assets and liabilities, which include cash and restricted cash, receivables and payables approximate their fair values due to the short-term nature.

NOTE 6. INVENTORY

Inventory consisted of the following (in thousands):

	December 31,	
	2019	2018
Raw materials	$ 2,709	$ 1,922
Work in process	9,447	6,170
Finished goods	4,367	3,836
Total	$ 16,523	$ 11,928
Balance Sheet classification:		
Current portion included in inventory	$ 12,886	$ 9,838
Long-term portion included in other long-term assets	3,637	2,090
Total	$ 16,523	$ 11,928

Write-downs related to excess and expiring inventory were $1.3 million, $1.1 million and $1.2 million for the years ended December 31, 2019, 2018 and 2017, respectively.

NOTE 7. PROPERTY AND EQUIPMENT

Property and equipment consisted of the following (in thousands):

		December 31,	
	Estimated Useful Lives	2019	2018
Leasehold improvements	up to 15 years	$ 33,904	$ 33,941
Computer equipment and software	3 years	17,338	15,022
Furniture and fixtures	5 to 7 years	13,053	12,709
Laboratory equipment	5 years	8,904	5,668
Construction in progress		1,253	866
		74,452	68,206
Less: accumulated depreciation		(25,560)	(17,309)
Property and equipment, net		$ 48,892	$ 50,897

Depreciation and amortization expenses were $8.3 million, $4.9 million and $1.2 million during the years ended December 31, 2019, 2018 and 2017, respectively.

NOTE 8. EMPLOYEE BENEFIT PLANS

Equity Incentive Plans and ESPP

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

	Year Ended December 31,		
	2019	2018	2017
Research and development	$ 19,374	$ 13,115	$ 7,569
Selling, general and administrative	37,228	27,511	16,369
Total stock-based compensation	$ 56,602	$ 40,626	$ 23,938

We have several equity incentive plans under which we granted stock options and RSUs, including PSOs and PSUs, to employees and directors. At December 31, 2019, 6,258,319 shares were available for grant under our equity incentive plans.

The Board of Directors (the Board) delegated responsibility for administration of our equity incentive plans to the Compensation Committee of the Board, including the authority to determine the term, exercise price and vesting requirements of each grant. Stock options granted to our employees and directors generally have a four-year vesting term and a one-year vesting term, respectively, 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 and directors generally have a four-year vesting term and a one-year vesting term, respectively. PSUs and PSOs granted pursuant to our equity incentive plans vest upon the achievement of a performance target or market condition, respectively.

We have adopted a Change in Control and Severance Benefit Plan for certain executive officers. 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 their outstanding equity awards accelerated and the exercise period for their stock options 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, $2.2 million, and $1.6 million for the years ended December 31, 2019, 2018 and 2017, respectively. As of December 31, 2019, we had 4,238,999 shares available for issuance under our ESPP. Pursuant to the ESPP, we issued 483,009, 330,492 and 434,523 shares of common stock at an average price per share of $12.60, $15.74 and $11.20 during the years ended December 31, 2019, 2018 and 2017, respectively. Cash received from purchases under the ESPP for the years ended December 31, 2019, 2018 and 2017 was $6.1 million, $5.2 million and $4.9 million, respectively.

We used a Monte Carlo simulation pricing model to value PSOs 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 were as follows:

	Year Ended December 31,		
	2019	2018	2017
Stock options, including PSOs	$ 8.19	$ 9.07	$ 11.42
ESPP	$ 4.85	$ 6.40	$ 6.00

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

	Year Ended December 31,		
	2019	2018	2017
Stock options, including PSOs:			
Risk-free interest rate	1.77%	2.81%	1.98%
Dividend yield	—%	—%	—%
Volatility	48%	55%	59%
Expected life	4.3 years	4.4 years	4.5 years
ESPP:			
Risk-free interest rate	2.16%	1.93%	1.09%
Dividend yield	—%	—%	—%
Volatility	50%	53%	58%
Expected life	6 months	6 months	6 months

We considered both implied and historical volatilities in developing our estimate of expected volatility. The assumption for the expected life of stock options is 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, including the PSUs, was based on the closing price of the underlying common stock on the date of grant.

Activity for stock options, including PSOs, during the year ended December 31, 2019 was as follows (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, 2018	22,674	$ 8.71		
Granted	1,311	$ 20.08		
Exercised	(3,274)	$ 5.01		
Forfeited	(217)	$ 16.89		
Expired	(51)	$ 22.98		
Stock options outstanding at December 31, 2019	20,443	$ 9.91	3.2 years	$ 169,299
Stock options exercisable at December 31, 2019	16,216	$ 7.36	2.6 years	$ 167,449

As of December 31, 2019, there was $33.7 million of unrecognized compensation expense related to our unvested stock options, including PSOs. The compensation expense for the unvested stock options will be recognized over a weighted-average period of 2.2 years.

During the year ended December 31, 2018, in connection with our long-term incentive compensation program, we granted 308,365 PSOs to our President and Chief Executive Officer. 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 on an accelerated basis over the service period of the award, which commenced on the date of grant.

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 2019 and the exercise prices, multiplied by the number of in-the-money stock options) that would have been received by the stock option holders had all stock option holders exercised their stock options on December 31, 2019. The total intrinsic value of stock options exercised during the years ended December 31,

2019, 2018 and 2017 was $54.1 million, $39.1 million and $85.2 million, respectively. Cash received from stock option exercises during the years ended December 31, 2019, 2018 and 2017 was $16.4 million, $12.1 million and $17.6 million, respectively. The total estimated fair value of stock options vested and recorded as expense during the years ended December 31, 2019, 2018 and 2017 was $23.4 million, $18.9 million and $13.1 million, respectively.

Activity for RSUs, including PSUs, during the year ended December 31, 2019 was as follows (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, 2018	4,857	$ 18.42		
Awarded	5,842	$ 19.46		
Vested and released	(1,541)	$ 17.23		
Forfeited	(357)	$ 18.66		
RSUs outstanding at December 31, 2019	8,801	$ 19.31	2.2 years	$ 149,701

As of December 31, 2019, there was $158.0 million of unrecognized compensation expense related to our unvested RSUs, including PSUs. The compensation expense for the unvested RSUs will be recognized over a weighted-average period of 2.7 years.

During 2019, in connection with our long-term incentive compensation program, we awarded 1,926,605 PSUs (the target amount) that will vest upon the achievement of a performance target related to a product approval by the FDA (the 2019 PSUs); employees may earn 150% of the target amount, or an additional 963,136 shares relative to the target amount, if the performance target is achieved before December 31, 2020 and may earn 200% of the target amount, or up to an additional 1,926,605 shares relative to the target amount, if we receive a second product approval by December 31, 2021. During 2018 we awarded 693,131 PSUs that will vest upon the achievement of certain product revenue, late-stage clinical development programs and discovery pipeline expansion performance targets (the 2018 PSUs). The 2018 PSUs and 2019 PSUs were designed to drive the performance of our management team and employees 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 it is determined that attainment of the performance target is probable. During the year ended December 31, 2019, we achieved two of the performance targets for 281,238 of the 2018 PSUs and determined that it was probable that we would achieve one additional performance target for 99,281 additional 2018 PSUs. As a result, 141,004 of the 2018 PSUs have vested as of December 31, 2019 and the remainder are expected to vest over various dates through November 2021. We recognized $4.9 million in compensation expense related to those 2018 PSUs during the year ended December 31, 2019; the remaining unrecognized compensation expense for those 2018 PSUs was $2.1 million as of December 31, 2019. The total unrecognized compensation expense for both the 2019 PSUs and the remaining 2018 PSUs for which we have not yet determined that attainment of the performance target is probable was $80.2 million as of December 31, 2019.

Exelixis, Inc. 401(k) Plan (the 401(k) Plan)

We sponsor the 401(k) Plan under which we historically made matching contributions to our employees' 401(k) accounts in the form of our common stock. We recorded compensation expense related to the stock match of $4.6 million, $3.6 million, and $1.7 million for the years ended December 31, 2019, 2018 and 2017, respectively. Beginning in 2020, we will make matching contributions to our employees' 401(k) accounts in cash.

NOTE 9. INCOME TAXES

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

	Year Ended December 31,		
	2019	2018	2017
Current:			
Federal	$ —	$ —	$ —
State	6,095	6,133	4,350
Total current tax expense	6,095	6,133	4,350
Deferred:			
Federal	71,580	(238,675)	—
State	(578)	(5,436)	—
Total deferred tax expense	71,002	(244,111)	—
Income tax provision (benefit)	$ 77,097	$ (237,978)	$ 4,350

The income tax provision for the year ended December 31, 2019 primarily relates to the utilization of federal net operating loss and state taxes in jurisdictions outside of California, for which we do not have net operating loss carryforwards due to a limited operating history. 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. The income tax provision for the year ended December 31, 2017 primarily related to state taxes in jurisdictions outside of California. Our historical net operating losses were sufficient to fully offset any federal taxable income for the years ended December 31, 2019, 2018 and 2017.

The reconciliation of the U.S. federal income tax provision (benefit) at the statutory federal income tax rates of 21%, 21% and 34% for the years ended December 31, 2019, 2018 and 2017, respectively, to our income tax provision (benefit) was as follows (in thousands):

	Year Ended December 31,		
	2019	2018	2017
U.S. federal income tax provision at statutory rate	$ 83,603	$ 94,939	$ 53,916
State tax expense	1,148	4,690	8,282
Change in valuation allowance	3,208	(315,394)	(34,266)
Research credits	(8,299)	(18,308)	—
Stock-based compensation	(9,177)	(5,998)	(20,548)
Non-deductible executive compensation	4,228	1,111	1,239
Non-deductible interest	—	—	1,367
Other	2,386	982	(5,640)
Income tax provision (benefit)	$ 77,097	$ (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.

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

	December 31,	
	2019	2018
Deferred tax assets:		
Net operating loss carryforwards	$ 65,131	$ 146,701
Tax credit carryforwards	110,037	98,467
Depreciation and amortization	26,792	29,929
Stock-based compensation	14,966	11,366
Lease liabilities	11,211	3,265
Accruals and reserves not currently deductible	8,248	7,160
Deferred revenue	6,547	5,474
Other assets	345	1,140
Total deferred tax assets	243,277	303,502
Valuation allowance	(61,659)	(58,112)
Net deferred tax assets	181,618	245,390
Deferred tax liabilities:		
Lease right-of-use assets	(9,244)	(1,279)
Total deferred tax liabilities	(9,244)	(1,279)
Net deferred taxes	$ 172,374	$ 244,111

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, 2019, 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, 2019 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 are realizable. As of December 31, 2019 and 2018, we continue to carry a valuation allowance of $61.7 million and $58.1 million, respectively, 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 increased by $3.5 million and decreased by $360.8 million during the years ended December 31, 2019 and 2018, respectively.

At December 31, 2019, we had federal net operating loss carryforwards of approximately $225 million, of which approximately $203 million will expire in the years 2035 through 2036, and federal business tax credits of approximately $112 million which expire in the years 2020 through 2039. We also had state net operating loss carryforwards of approximately $450 million, which expire in the years 2020 through 2036, and California research and development tax credits of approximately $38 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 analysis through December 31, 2019, and concluded that an ownership change, as defined under Section 382, had not occurred.

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

	Year Ended December 31,		
	2019	2018	2017
Beginning balance	$ 76,060	$ 79,342	$ 61,809
Change relating to prior year provision	589	(4,254)	247
Change relating to current year provision	2,429	1,083	17,378
Reductions based on the lapse of the applicable statutes of limitations	—	(111)	(92)
Ending balance	$ 79,078	$ 76,060	$ 79,342

We do not anticipate that the amount of unrecognized tax benefits existing as of December 31, 2019 will significantly change over the next 12 months. As of December 31, 2019, we had $79.1 million in unrecognized tax benefits, of which $48.1 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 Income 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 2019 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 10. NET INCOME PER SHARE

Net income per share - basic and diluted, were computed as follows (in thousands, except per share amounts):

	Year Ended December 31,		
	2019	2018	2017
Numerator:			
Net income	$ 321,012	$ 690,070	$ 154,227
Net income allocated to participating securities	—	—	(367)
Net income allocable to common stock - basic	321,012	690,070	153,860
Adjustment to net income allocated to participating securities	—	—	22
Net income allocable to common stock - diluted	$ 321,012	$ 690,070	$ 153,882
Denominator:			
Weighted-average common shares outstanding - basic	302,584	297,892	293,588
Dilutive effect of employee stock plans	12,425	14,911	18,415
Weighted-average common shares outstanding - diluted	315,009	312,803	312,003
Net income per share - basic	$ 1.06	$ 2.32	$ 0.52
Net income per share - diluted	$ 1.02	$ 2.21	$ 0.49

Participating securities included warrants issued in January 2014 to purchase an aggregate of 1.0 million shares of our common stock that were fully exercised in September 2017.

Dilutive securities included outstanding stock options, unvested RSUs and ESPP contributions. Certain potential common shares were excluded from our calculation of weighted-average common shares outstanding - diluted because either they would have had an anti-dilutive effect on net income per share or they are related to shares from PSOs and PSUs that were contingently issuable and the contingency had not been satisfied. See to “Note 8. Employee Benefit Plans” for a further description of our equity awards. These potential common shares were as follows (in thousands):

	Year Ended December 31,		
	2019	2018	2017
Anti-dilutive securities and contingently issuable shares excluded	9,111	3,968	1,645

NOTE 11. COMMITMENTS

Leases

Headquarters Lease

In May 2017, we entered into a Lease Agreement (the Lease) for our corporate headquarters located in Alameda, California (the Initial Premises). The Lease was subsequently amended in October 2017, June 2018, April 2019 and August 2019, resulting in, among other things, an increase to the amount of space leased and changes to the lease term. Our right-of-use asset, lease liability and the related lease costs reflect the 221,464 square feet of space we have taken possession of as of December 31, 2019 (the Current Premises) under the amended Lease. We expect to take possession of the remainder of the space provided for under the August 2019 amendment on or prior to April 30, 2020, which will increase the space leased to 228,941 square feet.

The term of the Lease continues through October 31, 2031 (the Lease Term). We have two five-year options to extend the Lease; these optional periods have not 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.

We have made certain tenant improvements on the Initial Premises, for which we received $8.2 million in reimbursements in January 2019. We were also provided an allowance of up to $1.7 million for tenant improvements to the space we obtained under the April 2019 amendment which is expected to be received in 2020.

The balance sheet classification of our operating lease assets and liabilities were as follows (in thousands):

	December 31,	
	2019	2018
Assets:		
Right-of-use assets included in other long-term assets	$ 41,835	$ 5,867
Liabilities:		
Current portion included in other current liabilities	$ 2,728	$ 2,738
Long-term portion of operating lease liabilities	48,011	12,099
Total operating lease liabilities	$ 50,739	$ 14,837

The components of operating lease costs, which are included in selling, general and administrative expenses in our Consolidated Statements of Income, were as follows (in thousands):

	Year Ended December 31,		
	2019	2018	2017 (1)
Operating lease cost	$ 2,844	$ 4,189	$ 3,944
Variable lease cost	1,024	1,661	2,216
Sublease income	—	—	(1,225)
Total operating lease costs	$ 3,868	$ 5,850	$ 4,935

(1) The 2017 amounts have not been adjusted for the adoption of Topic 842 and continue to be reported in accordance with the previous lease guidance, ASC Topic 840: *Leases*.

Cash paid for amounts included in the measurement of lease liabilities for the year ended December 31, 2019 was $2.9 million and was included in net cash provided by operating activities in our Consolidated Statements of Cash Flows.

As of December 31, 2019, the maturities of our operating lease liabilities were as follows (in thousands):

Year Ending December 31,	Amount
2020	$ 4,538
2021	4,669
2022	4,820
2023	5,147
2024	5,407
Thereafter	41,585
Total lease payments	66,166
Less:	
Imputed interest	(13,685)
Future tenant improvement reimbursements	(1,742)
Operating lease liabilities	$ 50,739

As of December 31, 2019, the weighted average discount rate used to determine the operating lease liability was 3.9% and the weighted average remaining lease term is 11.8 years.

Build-to-Suit Lease

In October 2019, we entered into a build-to-suit Lease Agreement (the Build-to-Suit Lease) for approximately 220,000 square feet of office space located in Alameda, California (the New Premises), adjacent to the Current Premises.

The term of the Build-to-Suit Lease is for a period of 242 months (the Term), which will begin upon the substantial completion of the building and tenant improvements by the lessor. We currently anticipate that the Term will begin in October 2021 (the Lease Commencement Date). The monthly base rent under the Build-to-Suit Lease will equal a percentage of the total development costs incurred in connection with the development of the New Premises (excluding the cost of the tenant improvements in excess of the allowance provided by the lessor and any development costs we pay) and is currently estimated to be about $0.7 million, subject to an annual increase of 3% during the Term. We will also be responsible for paying operating expenses related to the New Premises. The rent payments will begin sixty days following commencement of the Term. We have been provided a tenant improvement allowance for the New Premises of approximately $16.5 million. To the extent that the total development costs of the New Premises exceeds $525 per square foot, we will also pay 50% of such excess costs prior to the commencement of the Term, and may be required to secure such amount and the cost of the tenant improvements in excess of the allowance by providing a letter of credit or depositing such amounts in an account with the lessor's lender prior to the start of construction.

The Build-to-Suit Lease includes two five-year options to extend the term of the Build-to-Suit Lease, exercisable under certain conditions and at a market rate determined in accordance with the Build-to-Suit Lease. We have a one-time option to terminate the Build-to-Suit Lease without cause after the 180th month of the Term, exercisable under certain conditions as described in the Build-to-Suit Lease and subject to a termination payment calculated in accordance with the Build-to-Suit Lease. In addition, we have a right of first offer to purchase the New Premises, subject to certain procedures and exclusions set forth in the Build-to-Suit Lease.

We have determined that, under the guidance provided in Topic 842, we do not have control of the New Premises during the construction period. Therefore, we will not record a right-of-use asset or lease liability for the Build-to-Suit Lease until the Lease Commencement Date. We will evaluate the classification the Build-to-Suit Lease as an operating lease or financing lease at the Lease Commencement Date.

Letters of Credit

We have obtained standby letters of credit related to our lease obligations and certain other obligations with combined credit limits of $1.6 million and $1.1 million as of December 31, 2019 and 2018, respectively. None of our letters of credit have been drawn upon. All of the letters of credit are fully collateralized by certificates of deposit.

NOTE 12. QUARTERLY FINANCIAL DATA (UNAUDITED)

Selected unaudited quarterly financial data was as follows (in thousands, except per share data):

	Fiscal 2019 Quarter Ended			
	March 31,	June 30,	September 30,	December 31, (4)
Total revenues (1)	$ 215,487	$ 240,275	$ 271,703	$ 240,310
Gross profit (2)	$ 172,080	$ 186,136	$ 184,231	$ 184,406
Income from operations	$ 84,559	$ 91,989	$ 115,606	$ 77,316
Net income	$ 75,775	$ 79,042	$ 97,452	$ 68,743
Net income per share:				
Basic	$ 0.25	$ 0.26	$ 0.32	$ 0.23
Diluted	$ 0.24	$ 0.25	$ 0.31	$ 0.22

	Fiscal 2018 Quarter Ended			
	March 31,	June 30,	September 30,	December 31,
Total revenues (1)	$ 213,719	$ 186,108	$ 225,397	$ 228,602
Gross profit (2)	$ 128,633	$ 139,839	$ 155,586	$ 168,873
Income from operations	$ 116,307	$ 85,770	$ 125,176	$ 111,602
Net income (3)	$ 115,857	$ 87,494	$ 126,630	$ 360,089
Net income per share:				
Basic	$ 0.39	$ 0.29	$ 0.42	$ 1.20
Diluted	$ 0.37	$ 0.28	$ 0.41	$ 1.15

(1) Total revenues for the quarters ended March 31, 2019, June 30, 2019, September 30, 2019 and December 31, 2019 included $10.0 million, $20.4 million, $50.6 million and $15.1 million in milestone revenue, respectively, as compared to $66.5 million, $25.8 million, $42.6 million and $29.6 million during the comparable periods in 2018. 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 period to period.

(2) Gross profit is computed as net product revenues less cost of goods sold.

(3) Net income for the quarter ended December 31, 2018 included a $244.1 million income tax benefit related to the release of substantially all of the valuation allowance against our deferred tax assets.

(4) The fiscal quarter ended December 31, 2019 is a 14-week fiscal period. All other quarters presented are 13-week fiscal periods.

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. 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.

Management's Report on Internal Control Over Financial Reporting. Our management is responsible for establishing and maintaining adequate internal control over financial reporting, as such term is defined in Exchange Act Rules 13a-15(f) and 15(d)-15(f). 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 2019 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 January 3, 2020 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.

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 January 3, 2020, 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 January 3, 2020, 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 January 3, 2020 and December 28, 2018 and, the related consolidated statements of income, comprehensive income, stockholders' equity and cash flows for each of the three fiscal years in the period ended January 3, 2020, and the related notes and our report dated February 25, 2020 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 25, 2020

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 Directors” appearing in our Proxy Statement for our 2020 Annual Meeting of Stockholders to be filed with the SEC within 120 days after January 3, 2020, which we refer to as our 2020 Proxy Statement. The information required by this item regarding our executive officers is incorporated by reference to the section entitled “Information about our Executive Officers” appearing in our 2020 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 2020 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 2020 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 2020 Proxy Statement.

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, 2019, which consists of 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) and our 2017 Equity Incentive Plan (the 2017 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)	29,030,468	$ 6.86 (2)	10,497,315
Equity compensation plans not approved by stockholders (3)	213,014	$ 15.76 (4)	—
Total	29,243,482	$ 6.93	10,497,315

(1) Equity plans approved by our shareholders include the Director Plan, the 2011 Plan, the 2014 Plan, the 2017 Plan and the ESPP. As of December 31, 2019, a total of 4,238,999 shares of our common stock remained available for issuance under the ESPP, and up to a maximum of 465,480 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, 2019, as those numbers are not known.

(2) The weighted-average exercise price takes into account the shares subject to outstanding restricted stock units, including such awards with performance conditions (RSUs) which have no exercise price. The weighted-average exercise price, excluding such outstanding RSUs, is $9.83.

(3) Represents shares of our common stock issuable pursuant to the 2016 Plan. As of December 31, 2019, no shares of our common stock remained available for additional grants 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.

(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 $19.41.

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 Directors” appearing in our 2020 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 2020 Proxy Statement.

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	Certificate of Amendment of Amended and Restated Certificate of Incorporation of Exelixis, Inc.	8-K	000-30235	3.1	5/23/2019	
3.7	Amended and Restated Bylaws of Exelixis, Inc.	8-K	000-30235	3.1	2/20/2020	
4.1	Specimen Common Stock Certificate.	S-1, as amended	333-96335	4.1	4/7/2000	
4.2	Description of the Common Stock of Exelixis, Inc. Registered Pursuant to Section 12 of the Securities Exchange Act of 1934, as amended					X
10.1†	Form of Indemnity Agreement	S-1, as amended	333-96335	10.1	3/17/2000	
10.2†	Exelixis, Inc. 2000 Non-Employee Directors' Stock Option Plan	10-K	000-30235	10.6	2/20/2014	

Exhibit Number	Exhibit Description	Incorporation by Reference				Filed Herewith
		Form	File Number	Exhibit/ Appendix Reference	Filing Date	
10.3†	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	
10.4†	Exelixis, Inc. 2000 Employee Stock Purchase Plan	Schedule 14A	000-30235	A	4/13/2016	
10.5†	Exelixis, Inc. 2011 Equity Incentive Plan	10-K	000-30235	10.8	2/22/2019	
10.6†	Form of Stock Option Agreement under the Exelixis, Inc. 2011 Equity Incentive Plan	10-Q	000-30235	10.3	8/4/2011	
10.7†	Exelixis, Inc. 2014 Equity Incentive Plan	8-K	000-30235	10.10	2/22/2019	
10.8†	Form of Stock Option Agreement under the Exelixis, Inc. 2014 Equity Incentive Plan	10-Q	000-30235	10.2	7/31/2014	
10.9†	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	
10.10†	Form of Restricted Stock Unit Agreement under the Exelixis, Inc. 2014 Equity Incentive Plan	10-Q	000-30235	10.5	7/31/2014	
10.11†	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	
10.12†	Exelixis, Inc. 2016 Inducement Award Plan	10-K	000-30235	10.15	2/22/2019	
10.13†	Form of Stock Option Agreement under the 2016 Inducement Award Plan	8-K	000-30235	10.2	11/22/2016	
10.14†	Form of Restricted Stock Unit Agreement under the 2016 Inducement Award Plan	8-K	000-30235	10.2	11/22/2016	
10.15†	Exelixis, Inc. 2017 Equity Incentive Plan	10-K	000-30235	10.20	2/26/2018	
10.16†	Form of Stock Option Agreement under the Exelixis, Inc. 2017 Equity Incentive Plan	10-Q	000-30235	10.5	5/1/2019	
10.17†	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	
10.18†	Form of Restricted Stock Unit Agreement under the Exelixis, Inc. 2017 Equity Incentive Plan	10-Q	000-30235	10.6	5/1/2019	
10.19†	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	
10.20†	Non-Employee Director Equity Compensation Policy	10-Q	000-30235	10.2	5/1/2019	
10.21†	Offer Letter Agreement, dated February 3, 2000, between Exelixis, Inc. and Michael Morrissey, Ph.D.	10-Q	000-30235	10.43	8/5/2004	
10.22†	Offer Letter Agreement, dated June 30, 2015, between Exelixis, Inc. and Christopher Senner	10-Q	000-30235	10.5	11/10/2015	

Exhibit Number	Exhibit Description	Incorporation by Reference				Filed Herewith
		Form	File Number	Exhibit/ Appendix Reference	Filing Date	
10.23†	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	
10.24†	Offer Letter Agreement, dated February 10, 2014, between Exelixis, Inc. and Jeffrey J. Hessekiel.	10-Q	000-30235	10.4	5/1/2014	
10.25†	Offer Letter Agreement, dated August 11, 2000, between Exelixis, Inc. and Peter Lamb.	10-K	000-30235	10.24	2/29/2016	
10.26†	Offer Letter Agreement, dated August 19, 2010, between Exelixis, Inc. and Patrick J. Haley	10-K	000-30235	10.26	2/27/2017	
10.27†	Resignation Agreement dated July 22, 2010, by and between Exelixis, Inc. and George A. Scangos	10-Q	000-30235	10.1	11/4/2010	
10.28†	Annual Cash Bonus Compensation Plan for Executives	8-K	000-30235	10.1	2/16/2018	
10.29†	Cash Compensation Information for Non-Employee Directors.					X
10.30†	Exelixis, Inc. Change in Control and Severance Benefit Plan, as amended and restated.	10-Q	000-30235	10.5	5/2/2018	
10.31†	Policy for Recoupment of Variable Compensation	10-Q	000-30235	10.4	5/1/2019	
10.32	Lease Agreement dated May 2, 2017, between Ascentris 105, LLC and Exelixis, Inc.	10-Q	000-30235	10.1	8/2/2017	
10.33	First Amendment 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	
10.34	Second Amendment 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	
10.35	Third Amendment dated April 1, 2019, to Lease Agreement dated May 2, 2017, between Ascentris 105, LLC and Exelixis, Inc.	8-K	000-30235	10.1	4/5/2019	
10.36	Fourth Amendment dated August 30, 2019, to Lease Agreement dated May 2, 2017, between Hillwood Enterprises, L.P. (as successor in interest to Ascentris 105, LLC) and Exelixis, Inc.	10-Q	000-30235	10.3	10/30/2019	
10.37	Fifth Amendment dated January 16, 2020, to Lease Agreement dated May 2, 2017, between Waterfront EDP, LLC (as successor in interest to Hillwood Enterprises, L.P.) and Exelixis, Inc.					X
10.38	Lease Agreement dated October 25, 2019, between Ernst Development Partners, Inc. and Exelixis, Inc.	10-Q	000-30235	10.2	10/30/2019	

Exhibit Number	Exhibit Description	Incorporation by Reference				Filed Herewith
		Form	File Number	Exhibit/ Appendix Reference	Filing Date	
10.39	First Amendment dated January 16, 2020, to Lease Agreement dated May 2, 2017, between Alameda BTS EDP, LLC (as successor in interest to Ernst Development Partners, Inc.) and Exelixis, Inc.					X
10.40*	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	
10.41	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	
10.42	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	
10.43*	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	10-K	000-30235	10.40	2/22/2019	
10.44*	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	
10.45*	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	

Exhibit Number	Exhibit Description	Incorporation by Reference				Filed Herewith
		Form	File Number	Exhibit/ Appendix Reference	Filing Date	
10.46*	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	
10.47*	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	
10.48*	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	
10.49*	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	
10.50**	Second Amendment dated May 17, 2019, to the Supply Agreement dated February 29, 2016, by and between Exelixis, Inc. and Ipsen Pharma SAS	10-Q	000-30235	10.2	7/31/2019	
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**	Second Amendment dated May 17, 2019, to the Collaboration and License Agreement dated January 30, 2017, by and between Exelixis, Inc. and Takeda Pharmaceutical Company Limited	10-Q	000-30235	10.3	7/31/2019	
10.54*	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	
10.55**	Amendment No. 1 dated March 18, 2019, to the Clinical Trial Collaboration Agreement dated February 24, 2017, by and between Exelixis, Inc. and Bristol-Meyers Squibb Company	10-Q	000-30235	10.1	5/1/2019	
10.56**	Amendment No. 2 dated August 15, 2019, to the Clinical Trial Collaboration Agreement dated February 24, 2017, by and between Exelixis, Inc. and Bristol-Meyers Squibb Company	10-Q	000-30235	10.1	10/30/2019	
10.57	Amendment No. 3 dated November 22, 2019, to the Clinical Trial Collaboration Agreement dated February 24, 2017, by and between Exelixis, Inc. and Bristol-Meyers Squibb Company					X

Exhibit Number	Exhibit Description	Incorporation by Reference				Filed Herewith
		Form	File Number	Exhibit/ Appendix Reference	Filing Date	
10.58*	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	
10.59*	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	
10.60*	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	
10.61*	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	
10.62**	Joint Clinical Research Agreement dated December 18, 2019, by and between Exelixis, Inc. and F. Hoffmann-La Roche Ltd					X
10.63**	Supplement dated December 18, 2019, to the Joint Clinical Research Agreement dated December 18, 2019, by and among Exelixis, Inc., F. Hoffmann-La Roche Ltd and Ipsen Pharma SAS					X
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
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

Exhibit Number	Exhibit Description	Incorporation by Reference				Filed Herewith
		Form	File Number	Exhibit/ Appendix Reference	Filing Date	
101.INS	XBRL Instance Document	The XBRL instance document does not appear in the Interactive Data File because its XBRL tags are embedded within the Inline XBRL document.				
101.SCH	Inline XBRL Taxonomy Extension Schema Document					X
101.CAL	Inline XBRL Taxonomy Extension Calculation Linkbase Document					X
101.DEF	Inline XBRL Taxonomy Extension Definition Linkbase Document					X
101.LAB	Inline XBRL Taxonomy Extension Labels Linkbase Document					X
101.PRE	Inline XBRL Taxonomy Extension Presentation Linkbase Document					X
104	Cover Page Interactive Data File	Formatted as Inline XBRL and contained in Exhibit 101.				

† Management contract or compensatory plan.

* Confidential treatment granted for certain portions of this exhibit.

** Portions of this exhibit have been omitted as being immaterial and would be competitively harmful if publicly disclosed.

‡ 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.

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 25, 2020
Date

By: /s/ MICHAEL M. MORRISSEY
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 25, 2020
/s/ CHRISTOPHER J. SENNER **Christopher J. Senner**	Executive Vice President and Chief Financial Officer (Principal Financial and Accounting Officer)	February 25, 2020
/s/ STELIOS PAPADOPOULOS **Stelios Papadopoulos, Ph.D.**	Chairman of the Board	February 25, 2020
/s/ CHARLES COHEN **Charles Cohen, Ph.D.**	Director	February 25, 2020
/s/ CARL B. FELDBAUM **Carl B. Feldbaum, Esq.**	Director	February 25, 2020
/s/ MARIA C. FREIRE **Maria C. Freire, Ph.D.**	Director	February 25, 2020

Signatures	Title	Date
/s/ ALAN M. GARBER **Alan M. Garber, M.D., Ph.D.**	Director	February 25, 2020
/s/ VINCENT T. MARCHESI **Vincent T. Marchesi, M.D., Ph.D.**	Director	February 25, 2020
/s/ GEORGE POSTE **George Poste, DVM, Ph.D., FRS**	Director	February 25, 2020
/s/ GEORGE A. SCANGOS **George A. Scangos, Ph.D.**	Director	February 25, 2020
/s/ JULIE A. SMITH **Julie A. Smith**	Director	February 25, 2020
/s/ LANCE WILLSEY **Lance Willsey, M.D.**	Director	February 25, 2020
/s/ JACK L. WYSZOMIERSKI **Jack L. Wyszomierski**	Director	February 25, 2020

Exhibit 4.2

DESCRIPTION OF THE COMMON STOCK OF EXELIXIS, INC.
REGISTERED PURSUANT TO SECTION 12 OF THE
SECURITIES EXCHANGE ACT OF 1934, AS AMENDED

Description of Capital Stock

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

Common stock

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

Voting rights. Each holder of common stock is entitled to one vote for each share of common stock held on all matters submitted to a vote of stockholders. Our certificate of incorporation does not provide for the right of stockholders to cumulate votes for the election of directors. Our certificate of incorporation provides that all directors are elected at each annual meeting of our stockholders for one-year terms.

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

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

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

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

Certificate of incorporation and bylaws. The holders of our common stock do not have cumulative voting rights in the election of directors. Because holders of our common stock do not have cumulative voting rights, stockholders holding a majority of the shares of common stock outstanding are able to elect all of the directors to be elected at each annual meeting of our stockholders. Our board of directors is able to elect a director to fill a vacancy created by the expansion of the board of directors or due to the resignation or departure of an existing board member. Our certificate of incorporation and bylaws also provide that all stockholder actions must be effected at a duly called meeting of stockholders and not by a consent in writing, and our bylaws require the consent of stockholders holding at least 25% of our outstanding common stock in order for stockholders to call a special meeting of stockholders; otherwise, only the chairman of the board of directors, the president or the board of directors (pursuant to a resolution adopted by a majority of the total number of authorized directors) may call a special meeting of stockholders. In addition, our bylaws include a requirement for the advance notice of nominations for election to the board of directors or for proposing matters that can be acted upon at a stockholders' meeting. Our certificate of incorporation provides for the ability of the board of directors to issue, without stockholder approval, up to 10,000,000 shares of preferred stock with terms set by the board of directors, which rights could

be senior to those of our common stock. Our certificate of incorporation and bylaws also provides that approval of at least 66 2/3% of the shares entitled to vote at an election of directors will be required to adopt, amend or repeal our bylaws, or repeal the provisions of our certificate of incorporation regarding the election of directors and the inability of stockholders to take action by written consent in lieu of a meeting.

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

Section 203 of the Delaware General Corporation Law

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

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

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

Forum Selection Bylaw

Unless we consent in writing to the selection of an alternative forum, the Court of Chancery of the State of Delaware shall, to the fullest extent permitted by law, be the sole and exclusive forum for (1) any derivative action or proceeding brought on behalf of Exelixis, (2) any action asserting a claim of breach of a fiduciary duty owed by any current or former director, officer, other employee or stockholder of Exelixis to Exelixis or to our stockholders, (3) any action asserting a claim arising pursuant to any provision of the Delaware General Corporation Law, the certificate of incorporation or the bylaws or as to which the Delaware General Corporation Law confers jurisdiction on the Court of Chancery of the State of Delaware, or (4) any action asserting a claim governed by the internal affairs doctrine. Any person or entity purchasing or otherwise acquiring or holding any interest in shares of capital stock of Exelixis is deemed to have notice of and consented to the forum selection provisions of the bylaws. This provision does not apply to actions arising under the Securities Act of 1933, as amended, or the Securities Exchange Act of 1934, as amended, or any claim for which the federal courts have exclusive jurisdiction.

Exhibit 10.29

CASH COMPENSATION INFORMATION FOR NON-EMPLOYEE DIRECTORS

Exelixis, Inc.
Cash Compensation for Non-Employee Directors

Board of Directors	Retainer Fee	$50,000
	Additional Chair Retainer Fee	$31,000
	Meeting Fee[1][2]	$2,500
Audit Committee	Retainer Fee	$12,000
	Additional Chair Retainer Fee	$13,000
	Meeting Fee[1][3]	$1,000
Compensation Committee	Retainer Fee	$10,000
	Additional Chair Retainer Fee	$10,000
	Meeting Fee[1][3]	$1,000
Nominating and Corporate Governance Committee	Retainer Fee	$5,000
	Additional Chair Retainer Fee	$10,000
	Meeting Fee[1][4]	$1,000
Research & Development Committee	Retainer Fee	$5,000
	Additional Chair Retainer Fee	$10,000
	Meeting Fee[1][4]	$1,000
Risk Committee	Retainer Fee	$5,000
	Additional Chair Retainer Fee	$10,000
	Meeting Fee[1][4]	$1,000

1 Meetings for which minutes are generated count toward the meeting threshold to determine when Meeting Fees are to be paid.
2 Meeting Fee paid for all meetings in excess of eight meetings.
3 Meeting Fee paid for all meetings in excess of seven meetings.
4 Meeting Fee paid for all meetings in excess of four meetings.

Exhibit 10.37

FIFTH AMENDMENT TO LEASE AGREEMENT

THIS FIFTH AMENDMENT TO LEASE AGREEMENT (this “Amendment”) is made and entered into on January 16, 2020 (the "Execution Date") by and between ALAMEDA WATERFRONT EDP, LLC, a California limited liability company (“Landlord”), and EXELIXIS, INC., a Delaware corporation (“Tenant”).

RECITALS

A. Ascentris 105, LLC, a Colorado limited liability company (“Ascentris”), and Tenant entered into that certain Lease Agreement dated May 2, 2017, as amended by that certain First Amendment to Lease Agreement dated October 16, 2017, that certain Second Amendment to Lease Agreement dated June 13, 2018, and that certain Third Amendment to Lease Agreement dated April 1, 2019 (the “Third Amendment”, and that lease, as amended through and including the Third Amendment, the “Original Lease”) with respect to premises in the multiple building project known as 1750 North Loop Road and 1601, 1701, 1751, 1801 and 1851 Harbor Bay Parkway, Alameda, California. Hillwood Enterprises, L.P. (“Hillwood”), a Texas limited partnership, and Tenant entered into that certain Fourth Amendment to Lease Agreement dated August 30, 2019 (the “Fourth Amendment”), which amended the Original Lease effective upon the Closing (as defined in the Fourth Amendment). Upon the Closing, Ascentris assigned the Original Lease to Landlord pursuant to an Assignment and Assumption of Leases dated as of October 31, 2019 and Hillwood assigned the Fourth Amendment to Landlord pursuant to an Assignment and Assumption of Fourth Amendment to Lease Agreement dated October 31, 2019. The Original Lease (as assigned to Landlord), as amended by the Fourth Amendment (as assigned to Landlord), is referred to herein as the “Lease”.

B. Landlord and Tenant desire to amend Tenant’s parking allocation on the terms and conditions of this Amendment.

AMENDMENT

NOW THEREFORE, in consideration of good and valuable consideration and the mutual agreements herein contained, and other good and valuable consideration, the receipt and sufficiency of which is hereby acknowledged, the parties do hereby agree as follows:

1. Defined Terms. All capitalized terms used but not defined in this Amendment will have the meanings set forth for such terms in the Lease. All terms that are defined in this Amendment and used in any provisions that are added to the Lease pursuant to this Amendment will have the meanings in the Lease set forth for such terms in this Amendment.

2. Parking Allocation. Section 10 of the Third Amendment is hereby deleted. Section 10 of the Fourth Amendment is replaced in its entirety with the following:

“**Parking; Signage**. Section 19 of the Lease is hereby amended so that Tenant may utilize up to 396 unassigned parking spaces within the Project at no charge. Effective as of the 1601 Space Commencement Date, Section 19 of the Lease is hereby amended so that Tenant may utilize up to 509 unassigned parking spaces within the Project at no charge. Effective as of the “Start Date” for Suite 100 of the 1701 Space, Section 19 of the Lease is hereby amended so that Tenant may utilize up to 12 additional unassigned parking spaces within the Project at no charge. Effective as of the “Start Date” for Suite 125 of the 1701 Space, Section 19 of the Lease is hereby amended so that Tenant may utilize up to 7 additional unassigned parking spaces within the Project at no charge. Effective as of the “Start Date” for Suite 150 of the 1701 Space, Section 19 of the Lease is hereby amended so that Tenant may utilize up to 3 additional unassigned parking spaces within the Project at no charge. Effective as of the “Start Date” for Suites 115 and 200 of the 1701 Space, Section 19 of the Lease is hereby amended so that Tenant may utilize up to 156 additional unassigned parking spaces within the Project at no charge. Accordingly, following the “Start Dates” for all 1701 Space and 1601 Space, Tenant may utilize up to 687 unassigned parking spaces within the Project at no charge. Notwithstanding anything in the Lease to the contrary, including but not limited to Section 1.3(g) of the Lease, Landlord may enter parking agreements with an affiliate of Landlord that owns property adjacent to the east of the Project commonly known as 1951 Harbor Bay Parkway, Alameda, California (the “BTS Site”) to permit a parking allocation for the buildings at the Project (other than the building located at 1750 North Loop Road) and the BTS Site of three (3) spaces per 1,000 square feet of building area (the “Targeted Parking Allocation”). Notwithstanding the foregoing and anything to the contrary contained herein, the parking allocation for the building located at 1750 North Loop Road shall be two (2)

spaces per 1,000 square feet of building area. Section 21.3 of the Lease is hereby amended so that Tenant may install exterior signs on the 1601 Building and, effective as of the first "Start Date" for the 1701 Space, the 1701 Building in accordance with the terms of Section 21.3 of the Lease. Such signage shall be substantially similar to the signage at the 1801 Building and the 1851 Building."

3. Landlord Obligations Regarding Parking. Landlord and Tenant acknowledge that (i) because a prior landlord of the Project allocated parking spaces at the Project in excess of the Targeted Parking Allocation to certain existing tenants of the Project (the "Excess Parking Tenants"), the parking allocations for Tenant set forth in Section 10 of the Fourth Amendment (as amended by Section 2 of this Amendment) are not in accordance with the Targeted Parking Allocation and (ii) the number of parking spaces that have been allocated to Excess Parking Tenants in excess of the Targeted Parking Allocation is approximately 103 parking spaces. Landlord agrees that (a) in connection with a lease extension for a lease with an Excess Parking Tenant pursuant to an Excess Parking Tenant's right to extend under such lease, Landlord shall request that such Excess Parking Tenant amend any such lease so that such Excess Parking Tenant is allocated parking at the Project and BTS Site in accordance with the Targeted Parking Allocation, (b) in connection with any other lease extension for a lease with an Excess Parking Tenant or an expansion or contraction of the premises leased to an Excess Parking Tenant, Landlord shall amend any such leases so that such Excess Parking Tenant is allocated parking at the Project and BTS Site in accordance with the Targeted Parking Allocation, and (c) in connection with any other amendments to leases with Excess Parking Tenants, Landlord shall use commercially reasonable efforts to amend any such leases so that such Excess Parking Tenant is allocated parking at the Project and BTS Site in accordance with the Targeted Parking Allocation. Additionally, Landlord shall ensure that new leases for space at the Project reflect a parking allocation in accordance with the Targeted Parking Allocation. In each instance where Landlord reduces the parking allocated to an Excess Parking Tenant resulting in the Excess Parking Tenant's parking allocation being in accordance with the Targeted Parking Allocation, or a lease with an Excess Parking Tenant terminates, such excess parking spaces shall be automatically added to Tenant's parking rights under the Lease, and Landlord and Tenant shall amend the Lease to reflect an equivalent increase in Tenant's allocated parking at the Project, until Tenant's allocated parking at the Project is in accordance with the Targeted Parking Allocation.

4. 1601 Building Parking Plan. In connection with any agreement between Landlord and Tenant to demolish and reconstruct the 1601 Building, Landlord agrees to reasonably cooperate with Tenant to devise a parking plan for the 1601 Building, acceptable to Landlord in its reasonable discretion and the City of Alameda, that eliminates the need for the additional parking stackers at the BTS Site that are currently required to satisfy the City-approved parking plan at the BTS Site (the approved parking plan requires an estimated 12 parking stackers).

5. Brokers. Landlord and Tenant represent and warrant that no broker or agent negotiated or was instrumental in negotiating or consummating this Amendment. Neither party knows of any real estate broker or agent who is or might be entitled to a commission or compensation in connection with this Amendment. Tenant will indemnify and hold Landlord harmless from all damages paid or incurred by Landlord resulting from any claims asserted against Landlord by brokers or agents claiming through Tenant. Landlord will indemnify and hold Tenant harmless from all damages paid or incurred by Tenant resulting from any claims asserted against Tenant by brokers or agents claiming through Landlord.

6. Whole Agreement. This Amendment sets forth the entire agreement between the parties with respect to the matters set forth herein. There have been no additional oral or written representations or agreements with respect thereto. Except as amended herein, or in a future writing signed by both parties, there shall be no other changes or modifications to the Lease between the parties and the Lease and the terms and provision contained therein shall remain in full force and effect. The terms of this Amendment will control over any conflicts between it and the terms of the Lease.

7. Successors and Assigns. This Amendment shall be binding upon the parties hereto, their heirs, successors and assigns.

8. Ratification. Except as amended by this Amendment, the Lease has not been amended, and the parties ratify and confirm the Lease, as amended by this Amendment, as being in full force and effect.

9. Counterparts; Execution by Telecopy. This Amendment may be executed in counterparts, each of which will constitute an original, but all of which, when taken together, will constitute but one agreement. Executed copies hereof may be delivered by telecopier or other electronic means, and upon receipt will be deemed originals and binding upon the parties hereto, regardless of whether originals are delivered thereafter.

[Signatures appear on next page]

IN WITNESS WHEREOF, the parties hereto have executed this Amendment as of the Execution Date.

LANDLORD:

ALAMEDA WATERFRONT EDP, LLC,
a Delaware limited liability company

By: Alameda Waterfront & BTS EDP, LLC,
a Delaware limited liability company,
its sole member

By: Waterfront – EXEL BTS Manager, LLC,
a Delaware limited liability company,
its managing member

By: /s/ Joseph Ernst
Name: Joseph Ernst
Title: Manager

TENANT:

EXELIXIS, INC.,
a Delaware corporation

By: /s/ Christopher J. Senner
Name: Christopher J. Senner
Title: EVP & CFO

By: /s/ Michael M. Morrissey
Name: Michael M. Morrissey
Title: President and CEO

Exhibit 10.39

FIRST AMENDMENT TO LEASE AGREEMENT

THIS FIRST AMENDMENT TO LEASE AGREEMENT (this "**Amendment**") is made and entered into on January 16, 2020 (the "**Execution Date**") by and between ALAMEDA BTS EDP, LLC, a California limited liability company ("**Landlord**"), and EXELIXIS, INC., a Delaware corporation ("**Tenant**").

RECITALS

A. Ernst Development Partners, Inc., a California corporation ("**EDP**"), and Tenant entered into that certain Lease Agreement (Commercial Single-Tenant Net Lease) dated October 25, 2019 (the "**Lease**"), with respect to premises known as 1951 Harbor Bay Parkway, Alameda, California, as more particularly described in the Lease. EDP assigned the Lease to Landlord pursuant to that certain Assignment and Assumption of Lease Agreement dated as of October 31, 2019.

B. The City of Alameda approved a parking plan for the Project that requires construction of approximately 12 parking stackers (the "**Parking Stackers**") at the Project to satisfy the required three (3) parking spaces per one thousand (1,000) rentable square feet of building area (the exact number of Parking Stackers will depend on the final design of the Building and the actual number of surface parking space constructed).

C. Tenant has requested that Landlord defer construction of the Parking Stackers to provide Tenant time to obtain the City of Alameda's approval of a Waterfront Parking Plan (as defined below). Landlord and Tenant agree to defer construction of the Parking Stackers, and amend the Lease in certain other respects, on the terms and conditions of this Amendment.

AMENDMENT

NOW THEREFORE, in consideration of good and valuable consideration and the mutual agreements herein contained, and other good and valuable consideration, the receipt and sufficiency of which is hereby acknowledged, the parties do hereby agree as follows:

1. Defined Terms. All capitalized terms used but not defined in this Amendment will have the meanings set forth for such terms in the Lease. All terms that are defined in this Amendment and used in any provisions that are added to the Lease pursuant to this Amendment will have the meanings in the Lease set forth for such terms in this Amendment.

2. Parking.

(a) Landlord and Tenant agree that, although the Parking Stackers are part of Landlord's Work, without constituting a Tenant Delay, Landlord shall defer construction of the Parking Stackers pending the City of Alameda's approval of the to-be-devised Waterfront Parking Plan (as defined below), provided that, if (i) Waterfront Landlord or Tenant has not completed construction of parking spaces at the Adjacent Project in accordance with a Waterfront Parking Plan on or before January 1, 2024, (ii) the City of Alameda requires the installation of the Parking Stackers at the Project on or before January 1, 2024 to comply with applicable Laws or permit the occupancy of the Premises, as reasonably determined by Landlord, or (iii) Tenant ceases to diligently pursue a Waterfront Parking Plan (and construction of parking spaces related to such plan) for more than six (6) months and such failure continues for thirty (30) days after written notice thereof from Landlord at any time prior to January 1, 2024, as reasonably determined by Landlord (each of the events under clauses (i), (ii), and (iii), a "**Parking Stacker Trigger Event"**), then Landlord shall, as soon as reasonably practical thereafter (but in no event longer than twelve (12) months after the Parking Stacker Trigger Event), cause the construction of the Parking Stackers at the Project in accordance with the City-approved parking plan for the Project, with the plans and specifications approved by Tenant (or deemed approved by Tenant) as provided below, and with this Section 2. Notwithstanding the foregoing, if Waterfront Landlord or Tenant has commenced construction of parking spaces at the Adjacent Project in accordance with a Waterfront Parking Plan on or before January 1, 2024, then all references to January 1, 2024 in the preceding sentence

are hereby revised to January 1, 2026. Landlord's selection of a contractor to construct the Parking Stackers shall be based on at least two (2) competitive bids (which shall include timelines for the performance of the work and be shared with Tenant), and shall be subject to Tenant's approval, which shall not be unreasonably withheld, conditioned, or delayed. If Landlord does not receive Tenant's response within five (5) business days of Landlord's request for approval of a contractor, Landlord's selection of the contractor shall be deemed approved. Prior to commencing construction of the Parking Stackers, Landlord shall submit to Tenant for its approval, which approval shall not be unreasonably withheld, conditioned or delayed: (x) plans and specifications for the Parking Stackers and (y) a cost estimate for the construction of the Parking Stackers. If Tenant has not delivered an objection to such plans and specifications or cost estimate within five (5) business days after receipt of Landlord's plans and specifications or cost estimate, as applicable, Tenant shall be deemed to have approved such plans and specifications or such cost estimate. Additionally, if such cost estimate estimates that the Parking Stacker Costs (as defined below) will be less than the amount of the Parking Stacker Allowance, then Tenant shall be deemed to have approved such cost estimate. If Tenant timely disapproves of such plans and specifications or cost estimate, then Tenant shall specify a reasonable basis for such disapproval and Landlord and Tenant shall use good faith efforts to agree on revisions to such plans and specifications or cost estimate within five (5) business days after Landlord's receipt of Tenant's disapproval. Upon approval (or deemed approval) of such cost estimate by Tenant, Landlord shall enter into a guaranteed maximum price contract or lump sum contract with the approved general contractor (in the amount of such contractor's bid approved by Tenant as described above) and any other lump sum contracts with other contractors for the construction of the Parking Stackers. Promptly after Landlord enters contracts for the construction of the Parking Stackers, Landlord shall deliver to Tenant a budget showing the portion of the Parking Stacker Costs that will be paid from the Parking Stacker Allowance (as defined below) and that portion that will be paid by Tenant. Notwithstanding the foregoing, if the cost estimate delivered to Tenant pursuant to clause (y) immediately above estimates that the Parking Stacker Costs will exceed the Parking Stacker Allowance, then Tenant shall be permitted to value engineer the Parking Stackers to reduce costs; provided, however, (A) any cost associated with such value engineering by Tenant will be the responsibility of Tenant, subject to Landlord's obligations with respect to the Parking Stacker Allowance pursuant to this Section, (B) any delays associated with the Tenant's efforts to value engineer the Parking Stackers will constitute an Excusable Delay to the extent such value engineering (or delays associated therewith) causes actual delays in the completion of the Parking Stackers, and (C) Tenant's efforts to value engineer the Parking Stackers, including any delay caused thereby, shall not cause Landlord to violate Laws. After commencement of construction of the Parking Stackers, Landlord shall use commercially reasonable efforts to cause its contractors to diligently pursue completion of construction of the Parking Stackers in a good and workmanlike manner, in accordance with all laws and the plans and specifications approved by Landlord and Tenant pursuant to this Section, free of defects and using new materials and equipment of good quality and shall use commercially reasonable efforts to minimize interference with Tenant's use of and access to the Premises and other parking spaces at the Project during the construction period. All Parking Stackers that may be installed or placed in or about the Project shall be and become the property of Landlord. Provided that the warranties described in this sentence are available on commercially reasonable terms, Landlord shall obtain from the contractor for the Parking Stackers and each manufacturer of equipment installed as part of the Parking Stackers a standard construction or manufacturer's warranty or guaranty, as applicable, in favor of Landlord and Tenant warranting that the Parking Stackers, in the case of the contractor, or the equipment provided, in the case of the manufacturers, shall be free from any defects of workmanship and materials for a period of not less than one (1) year from the date of substantial completion of the Parking Stackers. Substantial Completion and final completion of the Improvements shall be deemed to have occurred notwithstanding that the Parking Stackers have not been completed unless completion of the Parking Stackers is required by the City of Alameda for the legal occupancy of the Premises.

(b) In lieu of performing the work at its sole cost as provided in Section 1.2 of Exhibit B to the Lease, Landlord shall pay towards the costs of construction of the Parking Stackers, including all pre-construction costs, permit fees, project management, costs of constructing the Parking Stackers, and the Parking Construction Fee (collectively, the "**Parking Stacker Costs**"), up to $300,000 (the "**Parking Stacker Allowance**"). In consideration for Landlord's managing the construction of the Parking Stackers, Tenant shall pay to Landlord a management fee equal to five percent (5%) of hard and soft costs for the Parking Stackers (the "**Parking Construction Fee**"), which fee shall be paid from the Parking Stacker Allowance on a monthly basis in lieu of the management fee set forth in Exhibit D to the Lease. Tenant shall be solely responsible for

the Parking Stacker Costs in excess of the Parking Stacker Allowance. Once Landlord has applied the full amount of the Parking Stacker Allowance toward the Parking Stacker Costs, then within thirty (30) days after Tenant's receipt of a monthly invoice from Landlord for the portion of the Parking Stacker Costs in excess of the Parking Stacker Allowance that are due that month, Tenant shall pay to Landlord such portion of the Parking Stacker Costs, subject to the foregoing.

(c) Notwithstanding anything in the Lease to the contrary, including without limitation Section 3(a)(iii) of the Lease, upon a Parking Stacker Trigger Event (or, if earlier, Base Rent Commencement, provided that Tenant has not completed construction of the parking spaces at the Adjacent Project in accordance with the Waterfront Parking Plan), Total Development Costs shall include the full amount of the Parking Stacker Allowance (and no other Parking Stacker Costs shall be included in Total Development Costs) and Landlord shall re-calculate Initial Base Rent in accordance with Exhibit D-1 of the Lease. Any change to Initial Base Rent pursuant to this subsection shall be documented by notice from Landlord to Tenant, and any adjustments to Base Rent pursuant to this subsection shall be reflected in the Base Rent schedule in the Verification Memorandum. If Landlord increases Initial Base Rent pursuant to this subsection and the Parking Stacker Allowance exceeds the Parking Stacker Costs, then within thirty (30) days following construction of the Parking Stackers, Landlord shall pay to Tenant such excess Parking Stacker Allowance. Additionally, if a Parking Stacker Trigger Event has not occurred prior to Base Rent Commencement and if Tenant has not completed construction of the parking spaces at the Adjacent Project in accordance with the Waterfront Parking Plan prior to Base Rent Commencement, then within thirty (30) days after Base Rent Commencement, Landlord shall deposit an amount equal to the Parking Stacker Allowance in an escrow account with Commonwealth Land Title Insurance Company, as escrow agent, or another escrow agent to be agreed upon by Landlord and Tenant, and such amount shall be held by such escrow agent pursuant to an escrow agreement to be agreed on by Landlord, Tenant and the escrow agent in their reasonable discretion; provided that the escrow agreement shall (i) permit Landlord to draw on the escrow funds to construct the Parking Stackers if a Landlord is obligated to construct the Parking Stackers in accordance with Section 2(a) and (ii) permit the disbursement of the escrowed funds to Tenant if Tenant completes construction of the parking spaces at the Adjacent Project in accordance with the Waterfront Parking Plan prior to a Parking Stacker Trigger Event.

(d) Tenant shall promptly notify Landlord of completion of construction of parking spaces at the Adjacent Project in accordance with the Waterfront Parking Plan and shall deliver to Landlord documentation reasonably requested by Landlord to evidence such completion.

(e) "**Waterfront Parking Plan**" shall mean a to-be-devised parking plan with respect to Tenant's premises located at the Adjacent Project, that (i) is approved by the City of Alameda in connection with the further development of the Adjacent Project, (ii) eliminates the need for Parking Stackers at the Project, and (iii) maintains a parking ratio of three parking spaces per 1,000 rentable square feet of building area at the Project and the Adjacent Project, other than the building at 1750 North Loop Road, as to which the ratio will only be two parking spaces for 1,000 square foot of such building. For the avoidance of doubt, no Waterfront Parking Plan has been devised or approved by Alameda Waterfront EDP, LLC (such entity or its successor, as landlord, the "**Waterfront Landlord**"), as the landlord under the lease between Waterfront Landlord and Tenant with respect to premises at the Adjacent Project (the "**Waterfront Lease**"), and any approval by Waterfront Landlord shall be governed by the terms of the Waterfront Lease; provided, however, Landlord shall cooperate reasonably with Tenant in its efforts to devise and obtain the approval of the City of Alameda of the Waterfront Parking Plan and eliminate the need for the Parking Stackers.

3. Closing. Landlord and Tenant acknowledge that the Closing occurred December 20, 2019 and that, in connection with the Closing, Peet's recorded a certificate of compliance (a copy of which is attached hereto as **Exhibit A**), which consolidated the land acquired by Landlord pursuant to the Land Purchase Agreement into legal parcel, in the Official Records. Accordingly, Landlord has satisfied its obligations under the eleventh sentence of Section 26(u) of the Lease, neither Landlord nor Tenant shall have a right to terminate the Lease pursuant to the ninth sentence of Section 26(u) of the Lease, and Tenant shall have no right to terminate the Lease pursuant to Section 2.7(e) of the Work Letter.

4. Brokers. Landlord and Tenant each represent and warrant that it has had no dealings with any real estate broker or agent in connection with this Amendment. Neither party knows of any real estate broker or agent

who is or might be entitled to a commission or compensation in connection with this Amendment. Tenant will indemnify and hold Landlord harmless from all damages paid or incurred by Landlord resulting from any claims asserted against Landlord by brokers or agents claiming through Tenant. Landlord will indemnify and hold Tenant harmless from all damages paid or incurred by Tenant resulting from any claims asserted against Tenant by brokers or agents claiming through Landlord.

5. Whole Agreement. This Amendment sets forth the entire agreement between the parties with respect to the matters set forth herein. There have been no additional oral or written representations or agreements with respect thereto. Except as amended herein, or in a future writing signed by both parties, there shall be no other changes or modifications to the Lease between the parties and the Lease and the terms and provision contained therein shall remain in full force and effect. The terms of this Amendment will control over any conflicts between it and the terms of the Lease.

6. Successors and Assigns. This Amendment shall be binding upon the parties hereto, their heirs, successors and assigns.

7. Ratification. Except as amended by this Amendment, the Lease has not been amended, and the parties ratify and confirm the Lease, as amended by this Amendment, as being in full force and effect.

8. Counterparts; Execution by Telecopy. This Amendment may be executed in counterparts, each of which will constitute an original, but all of which, when taken together, will constitute but one agreement. Executed copies hereof may be delivered by telecopier or other electronic means, and upon receipt will be deemed originals and binding upon the parties hereto, regardless of whether originals are delivered thereafter.

[Signatures appear on next page]

IN WITNESS WHEREOF, the parties hereto have executed this Amendment as of the Execution Date.

LANDLORD:

ALAMEDA BTS EDP, LLC,
a Delaware limited liability company

By: Alameda Waterfront & BTS EDP, LLC,
a Delaware limited liability company,
its sole member

By: Waterfront – EXEL BTS Manager, LLC,
a Delaware limited liability company,
its managing member

By: /s/ Joseph Ernst
Name: Joseph Ernst
Title: Manager

TENANT:

EXELIXIS, INC.,
a Delaware corporation

By: /s/ Christopher J. Senner
Name: Christopher J. Senner
Title: EVP & CFO

By: /s/ Michael M. Morrissey
Name: Michael M. Morrissey
Title: President and CEO

Exhibit A

Copy of Certificate of Compliance

[See Appendix A of the Attached Deed]

Exhibit 10.57

AMENDMENT No. 3

This Amendment No. 3 (this ***"Amendment No. 3"***) is entered into as of November 22, 2019 (the **"*Amendment No. 3 Date*"**), and is made and entered into by and between Exelixis, Inc., a Delaware corporation, located at 1851 Harbor Bay Parkway, Alameda, CA 94502 (***"Exelixis"***) and Bristol-Myers Squibb Company, a Delaware corporation, headquartered at 345 Park Avenue, New York, New York 10154 (**"*BMS*"**)

RECITALS

WHEREAS, Exelixis and BMS entered into that certain Clinical Trial Collaboration Agreement dated February 24, 2017, which was supplemented and amended by the Ono Territory Supplement Agreement having an effective date of July 6, 2018 and entered into by Exelixis, BMS and Ono Pharmaceutical Co. Ltd. (the ***"Ono Territory Supplemental Agreement"***) and amended by Amendment No. 1 to the Clinical Trial Collaboration Agreement having an effective date of March 8, 2019 (***"Amendment No. 1"***) and by Amendment No. 2 to the Clinical Trial Collaboration Agreement having an effective date of August 15, 2019 (***"Amendment No. 2"***) (such agreement, as amended by the Ono Territory Supplemental Agreement, Amendment No. 1, and Amendment No. 2, the **"*Agreement"***);

WHEREAS, beginning on February 1, 2019, Exelixis and BMS began joint discussions regarding potential filings with Regulatory Authorities relating to the Combined Therapy Clinical Trials; and

WHEREAS, Exelixis and BMS want to amend the Agreement to ensure that all such exchanges are covered by the Agreement.

NOW, THEREFORE, in consideration of the foregoing premises and the mutual promises and covenants contained herein, Exelixis and BMS agree as follows:

1. The terms in this Amendment No. 3 with initial letters capitalized, whether used in the singular or the plural, shall have the meaning set forth herein, or if not defined herein, as set forth in the Agreement.

2. The terms of this Amendment No. 3 are effective as of February 1, 2019, including without limitation the addition of the new paragraph below to the end of Section 9.1 of the Agreement, and apply to all discussions or other exchanges under the Agreement occurring on or after February 1, 2019, including those discussions or other exchanges relating to seeking approval of the use of the Exelixis Compound in combination with the BMS Compound(s) or vice versa for a Combined Therapy and to the preliminary meeting comments received by BMS from the FDA and provided to Exelixis after February 1, 2019.

3. Section 9.1 of the Agreement is hereby amended by adding the following as a new paragraph at the end of Section 9.1:

> "The Parties agree that Confidential Information includes information and materials a Party discloses to the other Party relating to seeking approval of the use of the Exelixis Compound in combination with the BMS Compound(s) or vice versa for a Combined Therapy, including the type of submission a Party intends to file with a Regulatory Authority, potential and actual questions submitted to a Regulatory Authority seeking guidance on administrative aspects, the technical format, and the proposed content of such submission, answers of a Regulatory Authority to such questions, and guidance provided by a Regulatory Authority with respect to such submission, such as preliminary meeting comments from the FDA. The Parties also agree that such Confidential Information may only be used for discussing the seeking of such approval and that the fact that the Parties are having discussions about the seeking of such approval is Confidential Information of each Party."

4. Except as expressly set forth herein, all provisions of the Agreement shall remain unchanged and in full force and effect.

5. This Amendment No. 3 shall be governed and construed in accordance with the internal laws of the State of New York, USA, excluding any choice of law rules that may direct the application of the laws.

6. This Amendment No. 3 may be executed in two (2) or more counterparts, each of which shall be deemed an original, but all of which together shall constitute one (1) and the same instrument. This Amendment No. 3 may be executed by facsimile or electronic (e.g., .pdf) signatures and such signatures shall be deemed to bind each party hereto as if they were original signatures.

[Signature page follows]

IN WITNESS WHEREOF, Exelixis and BMS, intending to be legally bound hereby, have caused this Amendment No. 3 to be executed by their duly authorized representatives as of the Amendment No. 3 Date.

Exelixis, Inc.

By: /s/ Gisela M. Schwab, M.D.
Name: Gisela M. Schwab, M.D.
Title: President, Product Development and Medical Affairs and CMO

Date: 12/3/2019

Bristol-Myers Squibb Company

By: /s/ Nancy P. Forrest
Name: Nancy P. Forrest
Title: Vice President, Development and Commercial Alliances

Date: 12/3/2019

[*] = CERTAIN CONFIDENTIAL INFORMATION CONTAINED IN THIS DOCUMENT, MARKED BY BRACKETS, HAS BEEN OMITTED BECAUSE IT IS BOTH (I) NOT MATERIAL AND (II) WOULD BE COMPETITIVELY HARMFUL IF PUBLICLY DISCLOSED.

EXHIBIT 10.62

JOINT CLINICAL RESEARCH AGREEMENT

This **JOINT CLINICAL RESEARCH AGREEMENT** (the "**Agreement**") is made and entered into effective as December 18, 2019 (the "**Effective Date**") by and between **Exelixis, Inc.**, a Delaware corporation having an address at 1851 Harbor Bay Parkway, Alameda, CA 94502 ("**Exelixis**") and **F. Hoffmann-La Roche Ltd**, a Swiss corporation having an address at Grenzacherstrasse 124, CH 4070 Basel, Switzerland ("**Roche**"). Exelixis and Roche may be referred to herein individually as a "**Party**," or collectively as the "**Parties**".

RECITALS

WHEREAS, Exelixis has developed a tyrosine kinase inhibitor known as Cabozantinib;

WHEREAS, Roche has developed an anti-PD-L1 monoclonal antibody known as Atezolizumab;

WHEREAS, the Parties desire to collaborate with each other to sponsor one or more clinical trials of a combination therapy using Cabozantinib and Atezolizumab;

WHEREAS, certain rights related to Cabozantinib have been licensed by Exelixis to Ipsen Pharma SAS ("**Ipsen**") and Takeda Pharmaceutical Company Ltd. ("**Takeda**");

NOW THEREFORE, in consideration of the foregoing premises and the mutual promises and covenants contained herein, the Parties, intending to be legally bound, hereby agree as follows:

ARTICLE 1
DEFINITIONS

For all purposes of this Agreement, the capitalized terms defined in this Article 1 and throughout this Agreement have the meanings herein specified.

1.1 "**Additional Study Protocol Summary**" has the meaning set forth in Section 2.9.

1.2 "**Affiliates**" means, with respect to a particular Party, an entity that, directly or indirectly, through one or more intermediaries, controls, is controlled by, or is under common control with such Party. As used in this section, the term "control" means (a) to possess, directly or indirectly, the power to direct the management or policies of an entity, whether through ownership of voting securities, by contract relating to voting rights or corporate governance; or (b) direct or indirect beneficial ownership of more than fifty percent (50%) (or such lesser percentage which is the maximum allowed to be owned by a foreign corporation in a particular jurisdiction) of the voting share capital or other equity interest in such entity. Notwithstanding the foregoing, unless expressly specified otherwise, for the purposes of this Agreement, [*].

1.3 "**Aggregate Safety Information**" means, with respect to a Party's Compound(s), the (a) safety and toxicity information for such Compound(s) that is Combined Therapy Study Data, plus (b) safety and toxicity information from other relevant clinical trials of such Compound(s), whether alone or in combination with another pharmaceutical agent, in each case including information related to serious adverse events, adverse drug reactions, adverse events, discontinuations due to adverse events and Grade 3 and Grade 4 laboratory abnormalities. Aggregate Safety Information shall be provided by a Party to the other in the same format as is contained in the Investigators' Brochures prepared by such Party for its Compound(s) in each country where a Combined Therapy Trial will be conducted.

1.4 "**Applicable Law**" means all applicable laws, rules, and regulations (whether federal, state, or local) that may be in effect from time to time and applicable to conduct under this Agreement, including current Good Clinical Practices (GCP), Good Laboratory Practices (GLP), and Good Manufacturing Practices (GMP).

1.5 "**Bioanalysis Plan**" means the bioanalysis plan for any Samples as may be contemplated by a Protocol or another subsequent written agreement between the Parties.

1.6 "**Business Day**" means a day other than Saturday, Sunday, or any day on which commercial banks located in San Francisco, CA (USA), Welwyn (UK), Mississauga (Canada), Shanghai (China), Tokyo (Japan), or Basel (Switzerland) are authorized or obligated by Applicable Law to close.

1.7 "**Clinical Hold**" means that (a) with respect to a clinical investigation in the U.S., the FDA has issued an order to a Party pursuant to 21 CFR §312.42 to delay a proposed clinical investigation or to suspend an ongoing clinical investigation of the Combined Therapy or such Party's Single Agent Compound(s), and (b) with respect to a clinical investigation outside the U.S., a Regulatory Authority has issued an order equivalent to the order specified in subsection (a).

1.8 "**Combined Therapy**" means a therapeutic treatment that consists of a combination of the Exelixis Compound and the Roche Compound, wherein each Compound of the combination treatment is used as an individual formulation, with or without another agent.

1.9 "**Combined Therapy IND**" has the meaning set forth in Section 2.3.

1.10 "**Combined Therapy Invention(s)**" means all Inventions that are not Exelixis Study Inventions or Roche Study Inventions. For the avoidance of doubt, Combination Therapy Inventions include any Invention comprising or claiming, whether generically or specifically, (a) the Roche Compound and/or any other molecule(s) that is/are designed to selectively bind to PD-1 or PD-L1 and (b) the Exelixis Compound and/or any other molecule(s) that is/are designed to selectively inhibit the activity of MET, VEGF receptors, AXL, and RET.

1.11 "**Combined Therapy Patents**" means any and all Patents that Cover a Combined Therapy Invention or Combined Therapy Study Data, excluding Roche Independent Patents and Exelixis Independent Patents.

1.12 "**Combined Therapy Study Data**" has the meaning set forth in Section 9.2.

1.13 "**Combined Therapy Trial**" has the meaning set forth in Section 2.1.

1.14 "**Combined Therapy Trial Regulatory Documentation**" means any and all Regulatory Documentation to be submitted for the conduct of a Combined Therapy Trial, but excluding (a) any Exelixis Regulatory Documentation and (b) any Roche Regulatory Documentation.

1.15 "**Commercially Reasonable Efforts**" means the level of effort and resources normally devoted by each Party to conduct a clinical trial for a biopharmaceutical product or compound that is owned by it or to which it has rights, which is of similar market potential, profit potential, or strategic value, and is at a similar stage in its development or product life based on conditions then prevailing.

1.16 "**Compound**" means the Exelixis Compound or the Roche Compound, as the context dictates.

1.17 "**Conducting Party**" has the meaning set forth in Section 2.2.

1.18 "**Conducting Party Compound(s)**" means (a) in the case of Roche as the Conducting Party, the Roche Compound and (b), in the case of Exelixis as the Conducting Party, the Exelixis Compound.

1.19 "**Confidential Information**" means all non-public information or data that is generated by or on behalf of a Party or its Affiliates or which one Party or any of its Affiliates has supplied or otherwise made available to the other Party or its Affiliates, whether made available orally, in writing, or in electronic form, including information comprising or relating to concepts, discoveries, inventions, data, designs, or formulae in relation to this Agreement; provided that all Exelixis Study Inventions, Exelixis Technology and Exelixis Regulatory Documentation shall be Confidential Information of Exelixis, all Roche Study Inventions, Roche Technology, and Roche Regulatory Documentation shall be Confidential Information of Roche, and all joint owned Inventions shall be deemed both Parties' Confidential Information. Confidential Information shall include: (a) the terms and conditions of this Agreement, and (b) Confidential Information disclosed by either Party pursuant to the Confidentiality Agreement.

1.20 **"Confidentiality Agreement"** means that certain confidentiality agreement between the Parties, dated [*].

[*] = Certain confidential information contained in this document, marked by brackets, has been omitted because it is both (I) not material and (II) would be competitively harmful if publicly disclosed.

1.21 "**Control**" or "**Controlled**" means, with respect to any particular information, Patent, or other intellectual property rights, the legal authority or right (whether by ownership, license, or otherwise but without taking into account any rights granted by one Party to the other Party pursuant to this Agreement) of a Party to grant access, a license, or a sublicense of or under such information, Patent, or other intellectual property rights to the other Party, or to otherwise disclose proprietary or trade secret information to such other Party, in each case without breaching the terms of any agreement with a Third Party, or misappropriating the proprietary or trade secret information of a Third Party.

1.22 "**Cover**" means, with respect to a particular subject matter at issue and a relevant Patent, that, in the absence of ownership of or a license under such Patent, the manufacture, use, sale, offer for sale, or importation of such subject matter would infringe one or more claims of such Patent, or, as to a pending claim included in such Patent, the manufacture, use, sale, offer for sale, or importation of such subject matter would infringe such Patent if such pending claim were to issue in an issued patent.

1.23 "**CRO**" means any Third Party contract research organization engaged in connection with the conduct of a Combined Therapy Trial, including laboratories and Third Parties used to maintain the safety database from a Combined Therapy Trial, but, for clarity, excluding clinical trial sites and any Third Parties who are individuals.

1.24 "**Executive Officers**" means [*] of Exelixis, or his/her designee (such designee [*]), and [*] of Roche.

1.25 "**Exelixis Compound**" means Exelixis' tyrosine kinase inhibitor known as Cabozantinib.

1.26 "**Exelixis Indemnitees**" has the meaning set forth in Section 12.1 of this Agreement.

1.27 "**Exelixis Independent Patents**" means any and all Patents Controlled by Exelixis (or its Affiliates) as of the Effective Date or during the Term that Cover the use (whether alone or in combination with other agents), manufacture, formulation, or composition of matter of the Exelixis Compound, but excluding Exelixis Study Patents and Exelixis' interest in Combined Therapy Patents.

1.28 "**Exelixis Regulatory Documentation**" means any and all Regulatory Documentation related to the Exelixis Compound that exists as of the Effective Date or during the Term, but excluding all Combined Therapy Trial Regulatory Documentation.

1.29 "**Exelixis Study Data**" has the meaning set forth in Section 9.2 of this Agreement.

1.30 "**Exelixis Study Invention**" means any and all Inventions that relate to (a) the composition of matter of the Exelixis Compound (and not any Roche Compound), (b) a method of manufacture or formulation of the Exelixis Compound (and not any Roche Compound) as a Single Agent, or (c) a method of use of the Exelixis Compound as a monotherapy or as used in combination with agents, antibodies, or compounds, in each case that are not the Roche Compound.

1.31 "**Exelixis Study Patents**" means any and all Patents that Cover an Exelixis Study Invention (and not a Roche Study Invention or Combined Therapy Invention) or any Exelixis Study Data, but excluding Exelixis Independent Patents and Exelixis Technology. For the avoidance of doubt, any Patent that Covers both (a) an Exelixis Study Invention and (b) any other type of Invention shall be a Combined Therapy Patent.

1.32 "**Exelixis Technology**" means all Technology that is (a) Controlled by Exelixis (or its Affiliates) as of the Effective Date or during the Term and (b) related to the Exelixis Compound or the Combined Therapy and necessary for the conduct of the Combined Therapy Trials, but excluding all Inventions, Study Data, and Combined Therapy Trial Regulatory Documentation.

1.33 "**Exelixis Territory**" means the U.S.

1.34 "**FDA**" means the United States Food and Drug Administration, or any successor agency having the same or similar authority.

1.35 "**Field**" means the treatment of patients with indication(s) to be studied in a Combined Therapy Trial as set forth in the Protocol(s).

[*] = Certain confidential information contained in this document, marked by brackets, has been omitted because it is both (I) not material and (II) would be competitively harmful if publicly disclosed.

1.36 "Full Time Equivalent" or **"FTE"** shall mean the equivalent of full-time work of an employee or appropriately qualified person otherwise engaged by a Party ("Personnel") over a twelve-month period (excluding normal vacations, sick days and holidays). The portion of an FTE year devoted by Personnel for activities under the Agreement shall be determined by dividing the number of full days dedicated by such Personnel to the activities under this Agreement during any twelve-month period by the number of working days during such twelve-month period, such number of working days to accurately reflect actual working days for Personnel who were not employed or engaged by a Party for the entirety of such twelve-month period.

1.37 "**FTE Rate**" means the yearly rate [*]. The Parties may re-negotiate the FTE Rate in good faith, if either Party finds that the FTE Rate no longer represents a reasonable estimate of FTE cost.

1.38 "**GCP**" means the current good clinical practice as set out in (a) ICH Harmonized Guidance on current Good Clinical Practice (CPMP/ICH/135/95), (b) U.S. 21 C.F.R. Parts 50, 54, 56, 58, 210, 211 and 312, as amended from time to time, and (c) the equivalent law or regulation in any other applicable jurisdiction in the Territory.

1.39 "**GLP**" means the current good laboratory practice standards promulgated or endorsed by the FDA, as defined in U.S. 21 C.F.R. Part 58 (or such other comparable regulatory standards in jurisdictions outside the U.S.), as amended from time to time.

1.40 "**GMP**" means the current minimum standards for methods to be used in, and the facilities or controls to be used for, the manufacture, processing, packing, or holding of a drug as specified by applicable laws of the relevant countries at the time of manufacturing conducted in accordance with this Agreement, defined under (a) 21 C.F.R. Parts 210 and 211, (b) Directive 2003/94/EC, (c) Volume 4, Rules Governing Medicinal Products in the European Union Part I and II, and (d) equivalent law or regulations in any other applicable jurisdiction in the Territory, in each case (a) – (d), as amended from time to time.

1.41 "**IND**" means an application filed with a Regulatory Authority for authorization to commence clinical studies, including (a) an Investigational New Drug Application as defined in the United States Food, Drug and Cosmetic Act, (b) any equivalent of a United States IND in other countries or regulatory jurisdictions, (e.g., a Clinical Trial Application ("**CTA**")), and (c) all supplements, amendments, variations, extensions, and renewals thereof that may be filed with respect to the foregoing.

1.42 "**Independent Combined Therapy Trial**" has the meaning set forth in Section 2.9.

1.43 "**Independent Trial Costs**" has the meaning set forth in Section 8.2.

1.44 "**Initial Trials**" has the meaning set forth in Section 2.1.

1.45 "**Initiation**" means dosing of the first patient in a Combined Therapy Trial.

1.46 "**Invention**" means all inventions, whether or not patentable, discovered, made, conceived, or reduced to practice in the course of performance of activities under this Agreement, together with all intellectual property rights therein, but excluding all Study Data.

1.47 "**Ipsen**" has the meaning set forth in the recitals of this Agreement.

1.48 "**Ipsen-Exelixis Agreements**" means that certain Collaboration and License Agreement between Exelixis and Ipsen dated as February 29, 2016, as amended from time to time, and agreements between Exelixis and Ipsen and their Affiliates relating thereto that may be in effect from time to time.

1.49 "**Ipsen Territory**" means all the countries of the world other than those in the Exelixis Territory and the Takeda Territory (i.e., all countries other than the United States and Japan).

1.50 "**Manufacture**" or "**Manufacturing**" means manufacturing, processing, formulating, packaging, labeling, holding (including storage), and quality control testing of a Single Agent Compound or the Combined Therapy, in each case so as to be suitable under Applicable Law for use in the Combined Therapy Trials.

1.51 "**Material Safety Issue**" means a Party's good faith belief that there is an unacceptable risk for harm in humans based upon: (a) pre-clinical safety data, including data from animal toxicology studies; or (b) the observation of serious adverse effects in humans after the Exelixis Compound or the Roche Compound, either as

[*] = Certain confidential information contained in this document, marked by brackets, has been omitted because it is both (I) not material and (II) would be competitively harmful if publicly disclosed.

a Single Agent or in combination with another pharmaceutical agent (including as the Combined Therapy), has been administered to or taken by humans, such as during the Combined Therapy Trial.

1.52 "Non-Conducting Party" means, for any particular Combined Therapy Trial, the Party who is not the Conducting Party.

1.53 "**Non-Conducting Party Compound(s)**" means (a) in the case of Roche as the Non-Conducting Party, the Roche Compound and (b) in the case of Exelixis as the Non-Conducting Party, the Exelixis Compound.

1.54 "Operational Matters" has the meaning set forth in Section 3.6(c).

1.55 "**Patents**" means (a) all patents, certificates of invention, applications for certificates of invention, priority patent filings, and patent applications, and (b) any renewals, divisions, continuations (in whole or in part), or requests for continued examination of any of such patents, certificates of invention and patent applications, and any and all patents or certificates of invention issuing thereon, and any and all reissues, reexaminations, extensions, supplementary protection certificates, divisions, renewals, substitutions, confirmations, registrations, revalidations, revisions, and additions of or to any of the foregoing.

1.56 "**Person**" means an individual, sole proprietorship, partnership, limited partnership, limited liability partnership, corporation, limited liability company, business trust, joint stock company, trust, unincorporated association, joint venture or other similar entity or organization, including a government or political subdivision, department or agency of a government.

1.57 "**Proposing Party**" has the meaning set forth in Section 2.9.

1.58 "**Protocol**" has the meaning set forth in Section 2.1.

1.59 "**Quarter**" means each respective period of three (3) consecutive months ending on March 31, June 30, September 30, and December 31.

1.60 "**Regulatory Authority**" means any applicable supra-national, federal, national, regional, state, provincial, or local governmental or regulatory authority, agency, department, bureau, commission, council, or other entities (e.g., the FDA, EMA, and PMDA) regulating or otherwise exercising authority with respect to activities contemplated in this Agreement.

1.61 "**Regulatory Documentation**" means, with respect to a product containing the Roche Compound as a monotherapy or the Exelixis Compound as a monotherapy, all submissions to Regulatory Authorities in connection with the development of such product, including all INDs, BLAs, and NDAs, drug master files, correspondence with regulatory agencies, safety update reports, adverse event files, complaint files, inspection reports, and manufacturing records, in each case together with all applicable supporting documents (including documents with respect to clinical data).

1.62 "**Responding Party**" has the meaning set forth in Section 2.9.

1.63 "**Right of Reference**" means the "right of reference or use" as defined in 21 C.F.R. § 314.3(b) and any equivalent regulation outside the U.S., in each case as amended from time to time, to Regulatory Documentation (including the data contained or referenced therein) pertaining to a Party's Compound (and, in the case of the Non-Conducting Party, an existing IND or the Combined Therapy IND) that is filed with a Regulatory Authority solely to the extent necessary for the conduct of a Combined Therapy Trial in such country, or as otherwise expressly permitted under this Agreement or required to enable a Party to exercise its rights or perform its obligations under this Agreement.

1.64 "**Roche Compound**" means Roche's anti-PD-L1 monoclonal antibody known as Atezolizumab.

1.65 "**Roche Indemnitees**" has the meaning set forth in Section 12.2 of this Agreement.

1.66 "**Roche Independent Patents**" means any and all Patents Controlled by Roche (or its Affiliates) as of the Effective Date or during the Term that Cover the use (whether alone or in combination with other agents), manufacture, formulation, or composition of matter of the Roche Compound, but excluding Roche Study Patents and Roche's interest in Combined Therapy Patents.

1.67 "**Roche Regulatory Documentation**" means any and all Regulatory Documentation related to the Roche Compound that exists as of the Effective Date or during the Term, but excluding all Combined Therapy Trial Regulatory Documentation.

1.68 "**Roche Study Data**" has the meaning set forth in Section 9.2 of this Agreement.

1.69 "**Roche Study Invention**" means any and all Inventions that relate to (a) the composition of matter of the Roche Compound (and not the Exelixis Compound), (b) a method of manufacture or formulation of the Roche Compound (and not the Exelixis Compound) as a Single Agent, or (c) a method of use of the Roche Compound as a monotherapy or as used in combination with agents, antibodies, or compounds, in each case that are not the Exelixis Compound.

1.70 "**Roche Study Patents**" means any and all Patents that Cover a Roche Study Invention (and not an Exelixis Study Invention or Combined Therapy Invention) or any Roche Study Data, but excluding Roche Independent Patents and Roche Technology. For the avoidance of doubt, any Patent that Covers both (a) a Roche Study Invention and (b) any other type of Invention shall be a Combined Therapy Patent.

1.71 "**Roche Technology**" means all Technology that is (a) Controlled by Roche (or its Affiliates) as of the Effective Date or during the Term and (b) related to the Roche Compound or the Combined Therapy and necessary for the conduct of the Combined Therapy Trials, but excluding all Inventions, Study Data, and Combined Therapy Trial Regulatory Documentation.

1.72 **"Roche Territory"** means worldwide.

1.73 "**Safety Database**" means the database documenting safety reports for the Combined Therapy, including pregnancy reports.

1.74 "**Samples**" means biological specimens collected from Combined Therapy Trial study subjects (including [*]).

1.75 "**Shared Costs**" means the costs incurred by a Party [*] directly attributable or reasonably allocable to the conduct of the Combined Therapy Trial, including [*].

1.76 "**Single Agent Compound**" means, (a) with respect to Exelixis, the Exelixis Compound, and (b) with respect to Roche, the Roche Compound, in each case as a monotherapy.

1.77 "**Statistical Analysis Plan**" means a document that prespecifies statistical analyses, focusing on statistical methods for the primary and key secondary endpoints (efficacy and safety) to be prepared by the Conducting Party for each Combined Therapy Trial. In consultation with the Non-Conducting Party, this document shall be finalized before the first formal efficacy analysis.

1.78 "**Takeda**" has the meaning set forth in the recitals of this Agreement.

1.79 "**Takeda-Exelixis Agreements**" means that certain Collaboration and License Agreement between Exelixis and Takeda dated as January 30, 2017, as amended from time to time, and agreements between Exelixis and Takeda and their Affiliates relating thereto that may be in effect from time to time.

1.80 "**Takeda Territory**" means Japan.

1.81 "**Technology**" means information, inventions, discoveries, trade secrets, knowledge, technology, methods, processes, practices, formulae, instructions, skills, techniques, procedures, experiences, ideas, technical assistance, designs, drawings, assembly procedures, computer programs, specifications, data and results not generally known to the public (including biological, chemical, pharmacological, toxicological, pharmaceutical, physical and analytical, pre-clinical, clinical, safety, manufacturing and quality control data and know-how, including study designs and protocols), in all cases, whether or not patentable, in written, electronic or any other form now known or hereafter developed, materials, data and results, including Regulatory Documentation.

1.82 "**Third Party**" means any Person or entity other than Exelixis and Roche and their respective Affiliates.

[*] = Certain confidential information contained in this document, marked by brackets, has been omitted because it is both (I) not material and (II) would be competitively harmful if publicly disclosed.

1.83 "**Third Party License Payments**" means any and all payments due by a Party to a Third Party under a license agreement or other written agreement between such Party and Third Party, pursuant to which agreement such Party is granted rights under intellectual property owned or controlled by such Third Party that are necessary for (a) making, using, or importing such Party's Compound for the conduct of a Combined Therapy Trial, or (b) the conduct of a Combined Therapy Trial.

1.84 "**United States**" or "**U.S.**" means the United States of America, and its territories, districts, and possessions.

ARTICLE 2
COLLABORATION SCOPE

2.1 Combined Therapy Trials. The Parties shall, pursuant to this Agreement, conduct (i) the registrational clinical trials set forth in Exhibit A (the "**Initial Trials**") and (ii) each other registrational clinical trial designed to evaluate a Combined Therapy as the Parties agree in writing (each Initial Trial and additional trial, a "**Combined Therapy Trial**"). Prior to commencing any Combined Therapy Trial, the Conducting Party, in consultation with the Non-Conducting Party, shall prepare a protocol for such Combined Therapy Trial ("**Protocol**") for review and approval by a JPT. Any amendment to a Protocol shall be subject to review and approval by a JPT. The Conducting Party shall, and shall ensure that, the Combined Therapy Trial is conducted in accordance with its Protocol.

2.2 The Conducting Party. The Party primarily responsible for the conduct of a Combined Therapy Trial (such Party with respect to such Combined Therapy Trial, the "**Conducting Party**") shall be agreed by the Parties (via the JSC) on a trial-by-trial basis. The Conducting Party for each Initial Trial is identified in Exhibit A. Subject to the oversight of the JSC, as between the Parties, the Conducting Party shall have decision making authority with respect to all non-material operational issues in the conduct of the Combined Therapy Trial and shall be the regulatory lead and the sponsor of record with respect to such Combined Therapy Trial. Such Conducting Party operational and decision-making authority is further described in at least Sections 3.6 and 3.7 of this Agreement.

2.3 Combined Therapy IND. Unless otherwise required by a Regulatory Authority, for each Combined Therapy Trial, the Conducting Party shall determine whether a combination IND (a "**Combined Therapy IND**") is necessary.

2.4 Right of Reference. Each Party (regardless of whether such Party is the Conducting Party or the Non-Conducting Party) shall have a Right of Reference to all Combined Therapy INDs (including Combined Therapy INDs for Independent Combined Therapy Trials) or such other IND upon which a Conducting Party is relying on for the conduct of a Combined Therapy Trial. Each Party hereby grants to the other Party a Right of Reference to any of such Party's effective INDs for its Compound to the extent necessary for the conduct of a Combined Therapy Trial. Neither Party shall grant any Third Party any Right of Reference with respect to any portion of the Combined Therapy IND relating to the other Party's Compound for use either as a monotherapy or in combination with any other molecules without the prior written consent of such other Party, such consent not to be unreasonably withheld, conditioned, or delayed.

2.5 Investigator Brochure. Each Party shall be responsible for (a) drafting and updating as necessary the investigator's brochure for its Compound, and (b) filing all necessary Regulatory Documentation for its Compound with each applicable Regulatory Authority.

2.6 Information Exchange.

(a) Each Party shall provide the other Party the following information with respect to its Compound promptly after the Effective Date:

(i) the most current investigator's brochure;

(ii) safety signals and safety issues impacting the Initial Trials;

(iii) toxicology and efficacy signals relevant to the Initial Trials; and

(iv) any information specified to be provided in the Pharmacovigilance Agreement.

[*] = Certain confidential information contained in this document, marked by brackets, has been omitted because it is both (I) not material and (II) would be competitively harmful if publicly disclosed.

(b) The Conducting Party shall provide the Non-Conducting Party the following relating to the Combined Therapy within [*] after the completion of each Initial Trial:

(i) safety analyses for each Combined Therapy Trial in accordance with the applicable Protocol and/or Statistical Analysis Plan;

(ii) safety signals and safety issues relevant to the Combined Therapy Trials;

(iii) toxicology and efficacy signals;

(iv) any other information and data relevant to the Combined Therapy Trials, including any information specified to be provided in the Pharmacovigilance Agreement.

(c) The Conducting Party shall provide the Non-Conducting Party, within [*] after the completion of each Combined Therapy Trial a copy of all of the Study Data generated for such Combined Therapy Trial.

(d) The Conducting Party shall provide the Non-Conducting Party a copy of all of the Clinical Study Reports (CSRs) generated for such Combined Therapy Trial, and as applicable, safety analyses for Non-Conducting Party Compound as a monotherapy in accordance with the applicable Protocol and/or Statistical Analysis Plan, within [*] of publication. For clarity, the Non-Conducting Party may use the safety information provided pursuant to this section for any purpose.

(e) Except as provided in Section 2.6(c), each Party shall use the data and information exchanged pursuant to this Section 2.6 solely: (i) to evaluate the safety and efficacy of the Combined Therapy in Combined Therapy Trials, (ii) to meet any regulatory requirements pertaining to its Compound and to the conduct of the Combined Therapy Trials, and (iii) as permitted elsewhere in this Agreement. All such information and disclosures: (A) pertaining to the Combined Therapy shall be the Confidential Information of both Parties, (B) pertaining to the Exelixis Compound as a monotherapy (or used with agents other than the Roche Compound) shall be the Confidential Information of Exelixis, and (C) pertaining to the Roche Compound as a monotherapy (or used with agents other than the Exelixis Compound) shall be the Confidential Information of Roche.

2.7 Conditional Studies. If additional studies, including toxicity studies, are required or recommended by a Regulatory Authority as a prerequisite for conducting any Combined Therapy Trial, the Parties shall negotiate in good faith to agree upon a protocol for such studies, each of which shall be a Combined Therapy Trial under this Agreement. If the Parties are unable to agree upon a protocol for any such additional study, or if the conduct of such study would cause a delay unacceptable to a Party, then the matter shall be referred to the JPT for resolution. If the JPT is unable to reach a decision and the JSC is also unable to reach a resolution after such matter is escalated to them, then this Agreement shall automatically terminate solely as it relates to such individual Combined Therapy Trial.

2.8 Post-Marketing Commitments. In the case where both Parties have sought a labeled indication based on the Combined Therapy, if post-marketing commitments are required by a Regulatory Authority (e.g.: US post-marketing commitments and post marketing requirements, EU post approval commitments etc), the Parties shall negotiate in good faith.

2.9 Additional Studies. If a Party is interested in conducting an additional Combined Therapy study (in addition to the Initial Trials) (the "**Proposing Party**"), then the Proposing Party shall provide the other Party (the "**Responding Party**") with a written summary for such proposed Combined Therapy study (the "**Additional Study Protocol Summary**") prior to initiating the protocol development for such study. Within [*] after receipt of the Additional Study Protocol Summary, the JSC shall meet to review and discuss the Additional Study Protocol Summary. If the JSC agrees to jointly conduct a study under this Agreement based on such Additional Study Protocol Summary, then such study shall be deemed a Combined Therapy Trial, the Parties will amend this Agreement to add such Combined Therapy Trial to Exhibit A, and the Parties shall commence Protocol development for such study in accordance with this Agreement. If the JSC does not agree to jointly conduct such study under this Agreement, the Proposing Party may conduct up to [*] such studies per year independently (each an "**Independent Combined Therapy Trial**"), provided that [*] such Proposing Party shall conduct such Independent Combined Therapy Trial: (a) in accordance with all Applicable Laws; (b) under the oversight of the JSC; and (c) in a manner that would not have a material adverse effect on the Combined Therapy or on the Responding Party's Compound. For clarity, decisions relating to whether a proposed study will have a material adverse effect on the Responding

Party's Compound shall be made in the sole reasonable judgment of the Responding Party. Unless otherwise required by a Regulatory Authority, each Independent Combined Therapy Trial shall be conducted under either an existing IND or a Combined Therapy IND. For clarity, the Proposing Party for an Independent Combined Therapy Trial shall be the Conducting Party with respect thereto, and shall have all operational responsibility therefor, but shall not be obliged to provide the Responding Party with any Study Data, other than safety data (and any other data required under the Pharmacovigilance Agreement), or any other information described in Sections 6.2(g), (h), (i), (j), (l), (o), (s), and (u) from such Independent Combined Therapy Trial unless the Responding Party reimburses the Proposing Party as set forth in Section 8.2. For further clarity, the Responding Party shall only have the right to use data generated by the Proposing Party in an Independent Combined Therapy Trial to the extent reasonably necessary for the Responding Party to comply with its regulatory reporting and compliance obligations, including safety reporting obligations, and shall have the right to use such data to support its own development, but shall not have the right to use such data for regulatory approval, publications, or commercialization activities except pursuant to Section 8.2. [*]

2.10 Safety Data Exchange. The Parties shall comply with Applicable Law for safety reporting requirements. Prior to First Patient In occurring in the first Combined Therapy Trial using the Combination, the Parties shall execute a separate pharmacovigilance agreement that defines the Parties' responsibilities and obligations with respect to the procedures and timeframes for compliance with Applicable Law pertaining to safety reporting for the Compounds and the Combination used in a Study (the "**Pharmacovigilance Agreement**").

2.11 Amendments. Any amendment to this Agreement, a Protocol, Bioanalysis Plan, Statistical Analysis Plan, Pharmacovigilance Agreement, or Quality Agreement shall require the written mutual agreement of the Parties (with neither Party having final say). Amendments to this Agreement, the Pharmacogivilance Agreement, and Quality Agreement shall be executed in the form of a written amendment in accordance with Section 14.1. Amendments to a Protocol, Bioanalysis Plan or Statistical Analysis Plan may be made in writing by approval of a JPT (without a formal amendment to this Agreement pursuant to Section 14.1).

ARTICLE 3
GOVERNANCE

3.1 Joint Steering Committee. Promptly after the Effective Date, the Parties shall form a Joint Steering Committee (the "**JSC**"), composed of an equal number of [*] members of each Party, to oversee the collaboration of the Parties under this Agreement and the conduct of the Combined Therapy Trials. The JSC shall act as a joint consultative body and in particular shall:

(a) establish one or more Joint Project Team(s) (as defined below) and other subcommittees and working groups as the JSC decides is necessary;

(b) oversee the activities of, and provide guidance to the JPTs and mediate any unresolvable Disputes arising at the JPT;

(c) review the regulatory strategy for each Combined Therapy Trial;

(d) review the status, progress, and results of each Combined Therapy Trial led by JPTs;

(e) review and approve study summaries as well as the initial budget for each protocol;

(f) discuss any additional Combined Therapy Trials that either Party may be interested in conducting under this Agreement; and

(g) discuss and provide guidance on commercial issues (e.g. post-approval issues).

(h) discuss any post-marketing commitments as contemplated in Section 2.8; and

(i) establish a mechanism for the Non-Conducting Party to be informed and updated on a timely periodic basis regarding relevant Operational Matters.

3.2 JSC Membership and Meetings.

(a) JSC Members. Each JSC representative shall have appropriate knowledge and expertise and sufficient seniority within the applicable Party to make decisions arising within the scope of the JSC's

[*] = Certain confidential information contained in this document, marked by brackets, has been omitted because it is both (I) not material and (II) would be competitively harmful if publicly disclosed.

responsibilities. Each Party may replace its representatives on the JSC on written notice to the other Party. Each Party shall appoint one of their respective representatives on the JSC to serve as a co-chair of the committee. The co-chairpersons shall prepare and circulate agendas to JSC members at least [*] before each JSC meeting and shall direct the preparation of reasonably detailed minutes for each JSC meeting (such preparation to alternate between the Parties), which shall be approved by the co-chairpersons and circulated to the other JSC members within [*] after each such meeting. The initial members of each of the JSC shall be determined by the Parties promptly following the Effective Date.

(b) Meetings. The JSC shall hold meetings at such times as it elects to do so, but in no event less frequently than [*] during the Term. The first JSC meeting shall be held within [*] after the Effective Date. JSC meetings may be held in person, or by audio or video teleconference. In-person meetings shall be held at locations alternately selected by the Parties. Each Party shall be responsible for all of its own expenses of participating in any JSC meeting. No action taken at any meeting of the JSC shall be effective unless at least one (1) representative of each Party is participating. In addition, upon written notice to the other Party, either Party may request that a special *ad hoc* meeting of the JSC be convened for the purpose of resolving Disputes or for the purpose of reviewing or making decisions pertaining to material subject-matter, the review or resolution of which cannot be reasonably postponed until the following scheduled JSC meeting. Such *ad hoc* meeting shall be convened at such time as may be mutually agreed by the Parties, but no later than [*] following the notification date of request that such meeting be held.

(c) Non-Member Attendance. Each Party may from time to time invite a reasonable number of participants, in addition to its representatives, to attend JSC meetings in a non-voting capacity; provided that if either Party intends to have any Third Party (including any consultant) attend such a meeting, such Party shall provide reasonable prior written notice to the other Party and obtain the other Party's approval for such Third Party to attend such meeting, which approval shall not be unreasonably withheld or delayed. Such Party shall ensure that such Third Party is bound by written confidentiality and non-use obligations consistent with the terms of this Agreement.

3.3 Joint Project Team. The JSC shall appoint one or more joint project teams (each a "**JPT**") for each Combined Therapy Trial, composed of any number of appropriate cross-functional members from each Party, with one (1) such member serving as the chair from each Party. The JPT(s) shall manage the conduct of the Combined Therapy Trial and in particular shall:

(a) oversee and monitor the status and progress of the Combined Therapy Trial and the activities of the Parties with respect to such Combined Therapy Trial;

(b) discuss any conditional studies required to be conducted prior to a Combined Therapy Trial (pursuant to Section 2.7);

(c) provide a forum for the Parties to discuss, monitor, and coordinate activities and communications for the Combined Therapy Trial, including recruitment status, results analysis (interim and final), and other information relevant to the conduct of the Combined Therapy Trial;

(d) review and approve each plan for medical monitoring, exchange information from site audits, and review the results of all such medical monitoring and site audits and agree on any actions in response to same;

(e) review and approve the Protocol, Statistical Analysis Plan, Bioanalysis Plan, and any amendments to any of the foregoing (including associated budget amendments after initial approval by the JSC);

(f) review, and approve the final clinical trial report (and/or final statistical analysis in accordance with the Statistical Analysis Plan) from the Combined Therapy Trial;

(g) review, and approve communication strategies with Regulatory Authorities regarding the Combined Therapy Trial;

(h) review, and approve all material Combined Therapy Trial Regulatory Documentation, or portions thereof, that relate to the Combined Therapy;

(i) review and approve each Combined Therapy IND to be submitted to a Regulatory Authority, and any amendments thereto;

(j) review, and approve any analysis of any Combined Therapy Study Data (other than any monotherapy data) proposed by a Party that is not included in the Statistical Analysis Plan;

(k) review, and approve use of any Samples in accordance with Section 9.5 that are not described in the applicable Protocol and ICF for a Combined Therapy Trial so long as the JSC/JPT remains in force and effect (and if not in force and effect, by mutual written agreement of the Parties);

(l) review and approve the template ICF form, the template case report form, and template clinical trial site agreement (or minimum language to be included therein) to be used in the Combined Therapy Trial; the Conducting Party may authorize changes to such template or minimum language without review and approval of the JPT, provided that changes to information pertaining to the Non-Conducting Party's Compound must be approved by the JPT;

(m) approve the countries in which the Combined Therapy Trial will be conducted, which shall be limited to those countries in which both the Roche Compound and the Exelixis Compound are then being commercialized or, if not then being commercialized by a Party, for which such Party plans to commercialize;

(n) review each Party's drug supply forecasts for the Combined Therapy Trial;

(o) approve any immunogenicity analysis for the Combined Therapy Trial, including the protocol and the entity to do the analysis, to the extent not already included in the Protocol;

(p) endorse the selection of clinical trial sites, Recruitment Plans and Study Timelines and endorse material communications with trial sites or IRBs relating to patient safety or early termination/cessation of the Combined Therapy Trial;

(q) select and approve any Third Party committees, reviewers, or other contractors; and

(r) coordinate the transfer of materials and information between the Parties, including Study Data, Final Study Report, Tangible Materials (if any), Samples, and Sample Data;

(s) review quarterly budget reports; and

(t) perform other activities requested by the JSC.

3.4 JPT Membership and Meetings.

(a) JPT Members. Each JPT representative shall have appropriate knowledge and expertise and sufficient seniority within the applicable Party to make decisions arising within the scope of the JPT's responsibilities. Each Party may replace its representatives on the JPT on written notice to the other Party. Each Party shall appoint one of their respective representatives on the JPT to serve as a co-chair of the group; provided that where more than one Combined Therapy Trial is overseen by one JPT, additional co-chairs may serve with respect to those additional trials. The co-chairpersons shall prepare and circulate agendas to JPT members at least [*] before each JPT meeting and shall direct the preparation of reasonably detailed minutes for each JPT meeting, which shall be approved by the co-chairpersons and circulated to the other JPT members within [*] after each such meeting. The initial members of each of the JPT shall be determined by the Parties promptly following the Effective Date.

(b) Meetings. The JPT shall hold meetings at such times as it elects to do so, or as requested by a Party's chair, but in no event less frequently than [*] during the conduct of the applicable Combined Therapy Trial. JPT meetings may be held in person, or by audio or video teleconference. In-person meetings shall be held at locations alternately selected by the Parties. Each Party shall be responsible for all of its own expenses of participating in any JSC meeting. No action taken at any meeting of the JPT shall be effective unless at least one (1) representative of each Party is participating. In addition, upon written notice to the other Party, either Party may request that a special *ad hoc* meeting of the JPT be convened for the purpose of resolving Disputes or for the purpose of reviewing or making decisions pertaining to material subject-matter, the review or resolution of which cannot be reasonably postponed until the following scheduled JPT meeting. Such *ad hoc* meeting shall be convened at such time as may be mutually agreed by the Parties, but no later than [*] following the notification date of request that such meeting be held.

(c) Non-Member Attendance. Each Party may from time to time invite a reasonable number of participants, in addition to its representatives, to attend JPT meetings in a non-voting capacity; provided that if either Party intends to have any Third Party (including any consultant) attend such a meeting, such Party shall provide reasonable prior written notice to the other Party and obtain the other Party's approval for such Third Party to attend such meeting, which approval shall not be unreasonably withheld or delayed. Such Party shall ensure that such Third Party is bound by written confidentiality and non-use obligations consistent with the terms of this Agreement.

(d) Decision Making. Except for decisions expressly reserved to the JSC, the JPT(s) shall be responsible for the coordination and execution of all joint operations (e.g., clinical drug supply, response to regulatory agency questions, data exchange, pharmacovigilance, etc.).

3.5 Data Monitoring and Coordination.

(a) iDMC. The Conducting Party for a Combined Therapy Trial shall establish an independent data monitoring committee ("**iDMC**") to monitor the safety of the Combined Therapy and the conduct of such Combined Therapy Trial and to review efficacy data at interim points during the conduct of the study (with such time points to be agreed by the Parties in advance of the Initiation of such study). The members of the iDMC shall have appropriate levels of experience in the relevant disease area, statistical knowledge, and other relevant expertise, and shall be approved by a JPT.

(b) iDCC and DRB. The Conducting Party shall establish (i) an independent Data Coordinating Center ("**iDCC**") to prepare then-current accurate and unblinded analyses for the iDMC to review and (ii) a Data Review Board ("**DRB**"), that updates and in good faith, considers input from the JPT, to review all Study Data from a Combined Therapy Trial to advise on key determinations, including whether to accept a recommendation from the iDMC to stop a Combined Therapy Trial.

3.6 Conducting Party Operational Authority. The Conducting Party for a Combined Therapy Trial shall, subject to the oversight and determinations of the JSC and JPT and the terms of the applicable Protocol and this Agreement, the Quality Agreement, the Pharmacovigilance Agreement, and the Supply Agreement:

(a) manage and be primarily responsible for the conduct of such Combined Therapy Trial;

(b) be the sponsor and regulatory lead for such Combined Therapy Trial;

(c) as between the Parties, be the lead with respect to (i) the identification, selection, and management of clinical trial sites (including the negotiation and execution of clinical trial site agreements and related budgets, timelines, and contingency planning), (ii) the conduct of clinical study start-up activities, communications with, and obtaining approval from institutional review boards and/or ethics committees, as applicable, and draft the template informed consent form ("**ICF**") or other relevant documents for such Combined Therapy Trial, (iii) subject recruitment and retention activities, (iv) ongoing trial site monitoring and quality assurance audits, (v) management of safety reporting by CROs and clinical trial sites, (vi) ongoing medical monitoring, (vii) management, monitoring, and audits of CROs, (viii) inquiries from clinical study subjects, (ix) packaging, labeling, and distributing the Combined Therapy for use in such Combined Therapy Trial, and (x) management of health authority inspections at clinical trial sites ((i)-(x), collectively, the "**Operational Matters**"). The Conducting Party shall use Commercially Reasonable Efforts to perform all Operational Matters;

(d) in the event that the Conducting Party receives a telephonic communication from a Regulatory Authority requesting an immediate response regarding the Combined Therapy that the Conducting Party reasonably determines must be immediately given to protect patient safety or to prevent undue and significant disruption in the conduct of a Combined Therapy Trial, the Conducting Party shall provide such response as it reasonably deems advisable (and that is consistent with the terms of this Agreement); provided, that it immediately notifies the Non-Conducting Party via the JPT or JSC for approval; and provided further that in no event shall the Conducting Party make any response relating to the Non-Conducting Party Compound as a monotherapy without the Non-Conducting Party's prior written consent; and

(e) shall establish an External Study Steering Committee ("ESSC") to provide scientific and medical advice and guidance of the Combined Therapy and the conduct of such Combined Therapy Trial during the conduct of the study. The members of the ESSC shall have appropriate levels of experience in the relevant

disease area, scientific, medical, and clinical trial management experience, as well as shall function as investigative sites to evaluate and provide guidance on the design and conduct of the study.

3.7 Decision Making.

(a) All decisions of the JSC and JPT shall be made by unanimous vote, with each Party's representatives collectively having one (1) vote. In the case of the JPTs, such one (1) vote shall rest with the designated chair for each Party. If after reasonable discussion and good faith consideration of each Party's view on a particular matter before a committee, the representatives of the Parties cannot reach an agreement as to such matter within [*] after such matter was brought to such committee for resolution, then, if such disagreement arose within the JPT, it shall be referred to the JSC for resolution. If the JSC cannot resolve such matter within [*], or if the disagreement first arose within the JSC, then either Party at any time may refer such issue to the Executive Officers for resolution.

(b) If the Executive Officers are unable to reach a resolution within [*] of such referral, then:

(i) if such dispute is with respect to an amendment to a Protocol or protocol synopsis (including any immunogenicity analysis), Bioanalysis Plan, Statistical Analysis Plan, or Combined Therapy Trial budget, the status quo shall persist unless and until the Parties agree; and

(ii) the Conducting Party shall have final decision making authority with respect to the day-to-day management and operations (inclusive of trivial changes to the Protocol, Protocol synopsis, Sample Analysis Plan, and/or Statistical Analysis Plan) of the Combined Therapy Trial for which it is the Conducting Party; provided that the Conducting Party shall not have the right to make changes to day-to-day management and operations of the Combined Therapy Trial that will or are reasonably likely to have a material adverse effect on the Combined Therapy Trial or either Party's rights under this Agreement; and provided further that if or to the extent that any such change results in an increase to the then-current budget, the terms of Section 8.4(b) shall govern the Parties' rights and obligations in respect of any such increased costs.

(c) All other disputes under this Agreement which do not fall under Sections 3.7 (a) or (b) shall be resolved in accordance with Section 14.3.

3.8 Limitations on Authority. The JSC and JPT shall have only such powers as are expressly assigned to such committee in this Agreement, and such powers shall be subject to the terms and conditions of this Agreement. Without limiting the generality of the foregoing, neither the JSC nor the JPT will have the power to amend or interpret this Agreement, and no JSC or JPT decision may be in contravention of any term or condition of this Agreement.

3.9 Alliance Managers. Promptly after the Effective Date, each Party shall appoint an individual who shall be an employee of such Party having appropriate qualification and experience to act as the alliance manager for such Party (the "**Alliance Manager**"). Each Alliance Manager shall be responsible for coordinating and managing processes and interfacing between the Parties on a day-to-day basis throughout the Term. If not already a member of the JSC, each Alliance Manager shall be permitted to attend JSC meetings as appropriate as non-voting participants. The Alliance Managers shall be the primary contact for the Parties regarding the activities contemplated by this Agreement and shall facilitate communication between the Parties with respect to all such activities hereunder. Each Party may replace its Alliance Manager with an alternative representative at any time with prior written notice to the other Party. Any Alliance Manager may designate a substitute to temporarily perform the functions of that Alliance Manager. Each Party shall bear its own costs of its Alliance Manager.

ARTICLE 4
LICENSE GRANTS

4.1 Grant by Roche. Subject to the terms of this Agreement, Roche hereby grants, and shall cause its Affiliates to grant, to Exelixis a non-exclusive, worldwide, non-transferable, royalty-free license, with the right to sublicense in accordance with Section 4.3, under the Roche Independent Patents, Roche Technology, and Roche Regulatory Documentation to use the Roche Compound solely as necessary to perform Exelixis' obligations under this Agreement. To the extent that a CRO or other Third Party assigns or licenses to Roche any right, title, or interest in any intellectual property rights to be owned by or licensed to Exelixis pursuant to the terms of this Agreement,

[*] = Certain confidential information contained in this document, marked by brackets, has been omitted because it is both (I) not material and (II) would be competitively harmful if publicly disclosed.

Roche shall, where and to the extent expressly provided in this Agreement, assign or license same to Exelixis as provided in this Agreement and confirm such assignment or license in writing upon Exelixis' request.

4.2 Grant by Exelixis. Subject to the terms of this Agreement, Exelixis hereby grants, and shall cause its Affiliates to grant, to Roche a non-exclusive, worldwide, non-transferable, royalty-free license, with the right to sublicense in accordance with Section 4.3, under the Exelixis Independent Patents, Exelixis Technology, and Exelixis Regulatory Documentation to use the Exelixis Compound, solely as necessary to perform its obligations under this Agreement, but excluding the Takeda Territory. To the extent that a CRO or other Third Party assigns or licenses to Exelixis any right, title, or interest in any intellectual property rights to be owned by or licensed to Roche pursuant to the terms of this Agreement, Exelixis will, where and to the extent expressly provided in this Agreement, assign or license same to Roche as provided in this Agreement and confirm such assignment or license in writing upon Roche's request.

4.3 Sublicensing.

(a) Each Party shall have the right to grant sublicenses under the licenses granted to it under Section 4.1 or Section 4.2, as applicable, to Affiliates and Third Parties to perform its obligations with respect to the conduct of the Combined Therapy Trials, except that, (i) neither Roche nor any of its sublicensees shall have the right to grant Chugai (or any of Chugai's Affiliates) any sublicense under the licenses granted to Roche in Section 4.2 without Exelixis' prior written consent, and (ii) neither Exelixis nor any of its sublicensees shall have the right to grant Ipsen, Takeda, or any of their respective Affiliates any sublicense under the licenses granted to Exelixis in Section 4.1 without Roche's prior written consent.

(b) Before allowing any subcontractor to begin performing any activity for a Combined Therapy Trial, the subcontracting Party shall enter into a written agreement with such subcontractor that obligates such subcontractor (and its personnel involved in the performance of such activity) to be bound by the terms and conditions of this Agreement applicable to the activity to be performed by such subcontractor in the same manner as such terms and conditions apply to such Party. The subcontracting Party shall be responsible for the direction and coordination of the services of each subcontractor, and shall ensure the subcontractor's compliance with the terms and conditions of this Agreement. No contractual relationship shall be created between the non-subcontracting Party and the subcontracting Party's subcontractors, other than the non-subcontracting Party's position as a third-party beneficiary of the services of such subcontractors and to the written agreements between the subcontracting Party and its subcontractors. Each Party shall provide written notice to the other of any sublicense granted by it. The sublicensing Party shall remain liable for the actions of its sublicensees.

4.4 No Implied Licenses. Except as specifically set forth in this Agreement, neither Party shall acquire any license or other intellectual property right, by implication or otherwise, in any intellectual property of the other Party, including Confidential Information disclosed to it under this Agreement or under any Patents Controlled by the other Party or its Affiliates.

ARTICLE 5
MANUFACTURE AND SUPPLY

5.1 Exelixis Compound.

(a) Manufacture, Supply, and Packaging. Exelixis shall Manufacture or have Manufactured the Exelixis Compound in drug product and/or drug substance form (as necessary) in reasonable quantities and at the points in time as agreed by the JSC for each Combined Therapy Trial and each Independent Combined Therapy Trial. If Exelixis is the Non-Conducting Party for a Combined Therapy Trial (or the Responding Party for an Independent Combined Therapy Trial), it shall supply such Exelixis Compound to Roche or its designee for use in such Combined Therapy Trial, and Roche shall package and label the Exelixis Compound for use in such Combined Therapy Trial.

(b) Cost. The cost of Manufacture and supply (including shipping, taxes and duty, if applicable) of Exelixis Compound for the Combined Therapy Trials shall be borne solely by Exelixis. Exelixis shall deliver the Exelixis Compound to Roche or its designee DAP (Roche site or its designated consignee site) Incoterms® 2010. Exelixis shall be responsible for the payment of any Third Party License Payments that may be due as a result of the manufacture, supply, and use of the Exelixis Compound for use in the Combined Therapy Trials. Reasonable out-of-pocket costs incurred by Roche in packaging and labeling the Exelixis Compound for use in the Combined Therapy Trials shall be included in the Shared Costs under the Agreement.

[*] = Certain confidential information contained in this document, marked by brackets, has been omitted because it is both (I) not material and (II) would be competitively harmful if publicly disclosed.

(c) Quality. The Exelixis Compound shall be manufactured in accordance with Applicable Law (including GMP) and shall be of equivalent quality to the Exelixis Compound used by Exelixis for its other clinical trials of the Exelixis Compound. Exelixis shall deliver certificates of analysis, and any other documents specified in the Quality Agreement for the Exelixis Compound provided under this Agreement. Exelixis shall inform Roche as to the GMP Manufacturing and testing site of bulk drug substance for the Exelixis Compound, as well as the Exelixis Compound drug product GMP Manufacturing and testing site, prior to the start of the Combined Therapy Trials and provide [*] written notice if there is any change to any such site.

(d) Use of Exelixis Compound by Roche. Roche shall use the quantities of Exelixis Compound supplied to it under this Agreement solely as necessary for, and in accordance with, this Agreement and the applicable Protocols, and for no other purpose. Except as may be required under this Agreement, a Bioanalysis Plan, or a Protocol, Roche shall not perform, and shall not permit any Third Party to perform, any analytical testing of the Exelixis Compound supplied to it under this Agreement.

5.2 Roche Compound.

(a) Manufacture, Supply, and Packaging. Roche shall Manufacture or have Manufactured the Roche Compound in drug product and/or drug substance form (as necessary) in reasonable quantities and at the points in time as agreed by the JSC for each Combined Therapy Trial and each Independent Combined Therapy Trial. If Roche is the Non-Conducting Party for a Combined Therapy Trial (or the Responding Party for an Independent Combined Therapy Trial), it shall supply such Roche Compound to Exelixis or its designee for use in such Combined Therapy Trial, and Exelixis shall package and label the Roche Compound for use in such Combined Therapy Trial.

(b) Cost. The cost of Manufacture and supply (including shipping, taxes and duty, if applicable) of Roche Compound for the Combined Therapy Trials shall be borne solely by Roche. Roche shall deliver the Roche Compound to Exelixis or its designee DAP (Exelixis site or its designated consignee site) Incoterms® 2010. Roche shall be responsible for the payment of any Third Party License Payments that may be due as a result of the manufacture, supply, and use of the Roche Compound for use in the Combined Therapy Trials. Reasonable out-of-pocket costs incurred by Exelixis in packaging and labeling the Roche Compound for use in the Combined Therapy Trials shall be included in the Shared Costs under the Agreement.

(c) Quality. The Roche Compound shall be manufactured in accordance with Applicable Law (including GMP) and shall be of equivalent quality to the Roche Compound used by Roche for its other clinical trials of the Roche Compound. Roche shall deliver to Exelixis certificates of analysis, and any other documents specified in the Quality Agreement for the Roche Compound provided under this Agreement. Roche shall inform Exelixis as to the GMP Manufacturing and testing site of bulk drug substance for the Roche Compound, as well as the Roche Compound drug product GMP Manufacturing and testing site, prior to the start of the Combined Therapy Trials and provide [*] written notice if there is any change to any such site.

(d) Use of Roche Compound by Exelixis. Exelixis shall use the quantities of Roche Compound supplied to it under this Agreement solely as necessary for, and in accordance with, this Agreement and the applicable Protocols, and for no other purpose. Except as may be required under this Agreement, a Bioanalysis Plan, or a Protocol, Exelixis shall not perform, and shall not permit any Third Party to perform, any analytical testing of the Roche Compound supplied to it under this Agreement.

5.3 Quality Agreement. Within [*] after the Effective Date, and in no event later than the date on which the first shipment of bulk Exelixis Compound or bulk Roche Compound is supplied for use in the Combined Therapy Trials, the Parties shall enter into a quality agreement with respect to such supply (the "**Quality Agreement**"). The Quality Agreement shall detail the documentation required to enable regulatory submissions (CTAs), final Qualified Persons release, and import licenses for the Combined Therapy Trials. The Quality Agreement shall also indicate whether any required transfer of analytical methods will be necessary to support identity testing of a Party's Compound.

5.4 Supply Agreement. Within [*] after the Effective Date (for the Initial Trials) or within [*] of finalizing a protocol for a Combined Therapy Trial, and in no event later than the date on which the first shipment of bulk Exelixis Compound or bulk Roche Compound is supplied for use in a Combined Therapy Trial, the Parties shall enter into a supply agreement with respect to such supply (a "**Supply Agreement**"), substantially in the form attached as Exhibit C. Each Supply Agreement shall set forth terms for forecasting, ordering, product acceptance

[*] = Certain confidential information contained in this document, marked by brackets, has been omitted because it is both (I) not material and (II) would be competitively harmful if publicly disclosed.

and rejection, and other customary provisions for the supply of the Compounds for use in the Combined Therapy Trials.

5.5 Customs Valuation. The Conducting Party will provide the Non-Conducting Party in writing with a list of all countries participating in a Combined Therapy Trial prior to Initiation of such Combined Therapy Trial. During the conduct of such Combined Therapy Trial, the Conducting Party will send in writing any changes to the list of participating countries to the Non-Conducting Party promptly after they become aware, and in any event, no later than [*] prior to the end of each [*]. If no changes are sent to the Non-Conducting Party by the Conducting Party for a particular [*], the prior [*] participating country list will be used as the basis for customs valuation for that [*]. The Non-Conducting Party will provide the Conducting Party with its Compound country-specific customs valuations prior to Initiation of the applicable Combined Therapy Trial and at the end of each [*] during the conduct of such Combined Therapy Trial. The Conducting Party will use the Non-Conducting Party values for the import/export process and shall not make any change to such valuations without the Non-Conducting Party's prior written consent.

ARTICLE 6
RESPONSIBILITIES

6.1 Specific Responsibilities of the Parties. Subject to the terms of this Agreement, each Party shall use Commercially Reasonable Efforts to (a) supply the quantities of its Compound as needed to conduct a Combined Therapy Trial on a timely basis; (b) conduct and complete each Combined Therapy Trial and any Statistical Analysis Plans and Bioanalysis Plans relating thereto on a timely basis in accordance with the Protocol, Bioanalysis Plans, Statistical Analysis Plans, and Third Party agreements relating thereto; (c) timely provide Rights of Reference where required by this Agreement; and (d) in the case of the Conducting Party, provide sufficient resources and personnel to conduct the Combined Therapy Trial for which it is the Conducting Party, and to adequately fund the Combined Therapy Trial, on a timely basis in accordance with the applicable Protocol and the terms of this Agreement.

6.2 Conducting Party's Responsibilities. Subject to JPT direction and JSC oversight, and without limiting the other terms of this Agreement, a Party shall be responsible for the following activities in connection with each Combined Therapy Trial for which it is the Conducting Party:

(a) packaging and labeling the Combined Therapy for use in the Combined Therapy Trials;

(b) providing the JPT with immediate notice of any Manufacturing and/or supply issues with respect to its Compound that may adversely impact the conduct or timelines of a Combined Therapy Trial;

(c) providing notice of any Regulatory Authority inspections, or any other events potentially impacting regulatory status of the Combined Therapy Trial and/or the Non-Conducting Party's Compound promptly after the Conducting Party becomes aware of such;

(d) with the Non-Conducting Party's cooperation, compiling, amending, and filing all necessary Combined Therapy Trial Regulatory Documentation with the applicable Regulatory Authorities;

(e) acting as the sponsor of record as provided in 21 CFR 312.50 (and applicable comparable ex-US laws), unless otherwise delegated in accordance with 21 CFR 312.52 (and applicable comparable ex-US laws), and making all required submissions to Regulatory Authorities related thereto on a timely basis;

(f) with the Non-Conducting Party's cooperation, and subject to the provisions of Section 9.6, listing each Combined Therapy Trial required to be listed on a public database, including clinicaltrials.gov or other public registry in any country in which such Combined Therapy Trial is being conducted in accordance with Applicable Law and in accordance with each Party's internal policies on clinical trial registration;

(g) providing the Non-Conducting Party with reasonable advance notice of scheduled meetings or other material non-written communications with a Regulatory Authority and the opportunity to participate in each such meeting (to the extent permitted by Applicable Law and such Regulatory Authority) or other non-written communication, and providing such opportunity to participate in such meetings (to the extent permitted by Applicable Law and such Regulatory Authority) to those licensees of the Non-Conducting Party (for their respective territories), and, unless otherwise agreed by the JSC, approving all submissions and written

correspondence with a Regulatory Authority that relates to the conduct of the Combined Therapy Trial or the Non-Conducting Party Compound; except that (i) in no event shall the Conducting Party or any Affiliate of the Conducting Party communicate with any Regulatory Authority solely with respect to the Non-Conducting Party Compound without the prior written consent of the Non-Conducting Party; (ii) the Non-Conducting Party shall step out of any portions of any such Regulatory Authority meetings or other non-written communications that relate solely to the Conducting Party Compound; and (iii) the Conducting Party shall step out of any portions of such Regulatory Authority meetings or other non-written communications that relate solely to the Non-Conducting Party Compound;

(h) unless otherwise agreed by the JPT, providing to the Non-Conducting Party a written summary of meetings or other non-written communications with a Regulatory Authority within [*] after such meeting or communication, and copies of any official correspondence to or from a Regulatory Authority within [*] after a Party's receipt or provision of such correspondence, and copies of all Combined Therapy Trial Regulatory Documentation within [*] after submission to Regulatory Authorities;

(i) drafting and providing to the Non-Conducting Party (through the JPT) for its review and approval each Protocol and investigator's brochure for a Combined Therapy Trial, and the related template informed consent form, template clinical site agreement, Bioanalysis Plan, and Statistical Analysis Plan, and any amendments to each of the foregoing;

(j) coordinating with the Non-Conducting Party and providing to the JPT at least [*] in advance of submission drafts of (A) submissions to the Combined Therapy IND, (B) Combined Therapy Trial Regulatory Documentation, and (C) all other written correspondence with a Regulatory Authority relating to the Combined Therapy Trials;

(k) managing the operations of the Combined Therapy Trials in accordance with the applicable Protocol, including overseeing compliance by any CRO engaged by the Conducting Party for the Combined Therapy Trial;

(l) providing to the Non-Conducting Party (via the JPT) a list of all proposed clinical trial sites and principal investigator(s) and recruitment plan for each Combined Therapy Trial;

(m) ensuring that all CRO agreements and clinical trial site agreements (i) are consistent with the relevant terms of this Agreement, including confidentiality and intellectual property provisions consistent with those set forth in this Agreement, and (ii) permit the Parties to audit trial sites for quality assurance and to inspect and copy all data, documentation and work products relating to the Combined Therapy Trial;

(n) coordinating all iDMC, iDCC, and DRB activities;

(o) providing the Non-Conducting Party with minutes from all external drug safety monitoring boards for the Combined Therapy Trials;

(p) providing the Non-Conducting Party with updates on the status and details of the Combined Therapy Trials through the JPT and otherwise at the Non-Conducting Party's reasonable request;

(q) pursuant to Section 2.10 and the Pharmacovigilance Agreement, owning and being responsible for the maintenance of the Safety Database and safety reporting for the Combined Therapy, and providing the Non-Conducting Party the opportunity to participate in and comment on such pharmacovigilance activities;

(r) providing the Non-Conducting Party with the most current Investigator's Brochure for the Conducting Party's Compound;

(s) analyzing the Study Data in a timely fashion and providing the Non-Conducting Party with access to the Study Data from the applicable Combined Therapy Trial as follows:

(i) pursuant to a timetable determined by the JPT: (A) sharing with the Non-Conducting Party for review and comment drafts of interim and final clinical trial reports and statistical analysis conducted in accordance with the Statistical Analysis Plan from each Combined Therapy Trial and (B) providing the Non-Conducting Party the raw Study Data in electronic or other mutually agreed format;

[*] = Certain confidential information contained in this document, marked by brackets, has been omitted because it is both (I) not material and (II) would be competitively harmful if publicly disclosed.

(ii) data set specifications (i.e., that define the structure, variables, and derivations for raw, SDTM, and ADAM data sets) upon finalization and amendment of such specifications during and throughout the conduct of the Combined Therapy Trial;

(iii) within [*] after either unblinding of a study, or following extracts for planned or unplanned analyses, a copy of the database (including, to the extent available, raw data (all study sources), Study Data Tabulation Model (SDTM) data sets, and the Analysis Data Model analysis data sets (e.g., ADAM) with associated specifications) in a form and by a method to be approved by the JPT at all analysis time points as specified in the Study Analysis Plan (SAP);

(iv) concurrent with the delivery to the Non-Conducting Party of each version of the final clinical trial report (e.g. interim, final, amendments), the Conducting Party shall also provide the SDTM data sets and the ADaM data sets used to generate such report or summary (to the extent not already provided), and other appropriate documentation including a Study Data Reviewers Guide, an Analysis Data Reviewers Guide that is provided to Health Authorities, a blank CRF, and an SDTM-annotated CRF; provided that (A) all data and information for cohorts that are not part of the Combined Therapy Trial will be redacted from the foregoing; and (B) prior to finalization of such reports, the Conducting Party shall provide a redacted draft of the Study Data Tabulation Model (SDTM) and the Analysis Data Model (ADaM) data sets used to generate the report or summary (unless the Protocol for such Combined Therapy Trial provides otherwise or the JSC agrees otherwise);

(v) within [*] after either unblinding of a study, or following extracts for formal planned or unplanned analyses, access to safety databases that will be used for an interim review by an external consultant (or drug safety monitoring board, if required) to be agreed upon by the Parties;

(vi) within [*] after database lock access to case report forms or patient profiles for all patients in each Combined Therapy Trial. Access to the aforementioned documents following extracts for formal planned or unplanned analyses will be subject to JPT discussion and approval.

(vii) within [*] after the creation of a locked database for the Combined Therapy Trial, copies of the Form 1572s, financial disclosures, and other relevant documents required to meet regulatory requirements related to the Combined Therapy Trials (including any data or documents that may be required to provide Aggregate Safety Information to a Regulatory Authority with respect to the Non-Conducting Party Compound). Access to the aforementioned documents following extracts for formal planned or unplanned analyses will be subject to JPT discussion and approval; and

(viii) promptly providing the Non-Conducting Party with any programs or SAS codes to be used for the Statistical Analysis Plan for the Combined Therapy Trial;

(t) obtaining supplies of co-medications required for use in a Combined Therapy Trial pursuant to the applicable Protocol, and promptly providing the Non-Conducting Party a copy of the information provided to the manufacturer of such co-medication;

(u) providing the Non-Conducting Party with information on the pharmacokinetics, efficacy, and safety of the Conducting Party Compound in combination with the Non-Conducting Party Compound; provided however that such requests regarding the Non-Conducting party Compound alone shall be brought to JPT for discussion and approval to ensure proper input from the Non-Conducting Party on these analyses.

(v) collecting Samples;

(w) providing the Non-Conducting Party, as provided in the Quality Agreement and based on the Non-Conducting Party sampling instructions, with samples of the Non-Conducting Party Compound (bulk and post packaging material) for analytical testing performed by the Non-Conducting Party; and

(x) such other responsibilities as may be agreed to by the Parties or determined by the JPT or JSC.

Where the Conducting Party is to provide the Non-Conducting Party with the opportunity to review or comment on any document, the Conducting Party shall ensure the Non-Conducting Party has at least [*] from the date on which the Conducting Party provides the applicable document to the Non-Conducting Party to provide any comments.

[*] = Certain confidential information contained in this document, marked by brackets, has been omitted because it is both (I) not material and (II) would be competitively harmful if publicly disclosed.

6.3 Responsibilities of the Non-Conducting Party. Subject to JPT direction and JSC oversight, and without limiting the other terms of this Agreement, a Party shall be responsible for the following activities in connection with each Combined Therapy Trial for which it is the Non-Conducting Party:

(a) providing the JPT or JSC with immediate notice of any Manufacturing and/or supply issues with respect to its Compound that may adversely impact the conduct or timelines of a Combined Therapy Trial;

(b) where and to the extent provided in the Quality Agreement, providing for the release by a Qualified Person (as such term is defined in the Quality Agreement), or providing the necessary documentation in support of such quality release, of the Non-Conducting Party Compound;

(c) performing analytical and biological testing of samples taken by the Conducting Party as necessary for the purpose of identification of the Non-Conducting Party Compound after receipt and packaging by the Conducting Party, and providing the results to the Conducting Party to permit a timely release of the Non-Conducting Party Compound for shipment to clinical trial sites;

(d) promptly reviewing each Protocol (including any immunogenicity analysis plan) and investigator's brochure for the Combined Therapy, and the corresponding template informed consent form, Bioanalysis Plan, Statistical Analysis Plan, and any amendments to each of the foregoing;

(e) to the extent necessary for the conduct of such Combined Therapy Trial, providing a Right of Reference to the relevant Regulatory Documentation for the Non-Conducting Party Compound;

(f) assisting with the compilation, amendment, and filing of all necessary Combined Therapy Trial Regulatory Documentation with the applicable Regulatory Authorities, and providing the Conducting Party with copies of the Non-Conducting Party Regulatory Documentation necessary to obtain and maintain the Combined Therapy IND and prepare and file any other Combined Therapy Trial Regulatory Documentation in accordance with this Agreement, or otherwise comply with Applicable Law;

(g) analyzing clinical pharmacokinetic Samples, or ADA, as required with the Non-Conducting Party Compound assay and providing copies of such data and data analysis to the Conducting Party or transferring the Non-Conducting Party Compound assays to the Conducting Party to perform the analysis;

(h) providing comment and input on the management of each Combined Therapy Trial;

(i) reviewing and, if applicable, suggesting alternatives to the Conducting Party's proposed list of principal investigators for each Combined Therapy Trial;

(j) providing and making available information and/or persons with knowledge on the Non-Conducting Party Compound as necessary to support the Combined Therapy Trial;

(k) providing the JPT with prompt notice of any interactions with Regulatory Authorities relating to the Non-Conducting Party Compound that might reasonably be expected to materially impact such Combined Therapy Trial; and

(l) such other responsibilities as may be agreed to by the Parties or determined by the JPT.

6.4 Other Clinical Trials. For clarity, except for the Combined Therapy Trials, each clinical trial of a Party's Compound, alone or in combination with other pharmaceutical agents, shall not be subject to this Agreement (subject to each Party's obligation to share relevant safety information as provided in this Agreement, the Quality Agreement, and the Pharmacovigilance Agreement). Nothing in this Agreement shall preclude a Party from conducting a clinical trial of its Compound outside this Agreement so long as it does not use or rely on the Confidential Information of the other Party in doing so.

6.5 Additional Combined Therapy Trials. If the Parties agree in writing to conduct any additional Combined Therapy Trial beyond the Initial Trials, the Pharmacovigilance Agreement and the Quality Agreement shall be amended to provide for such additional Combined Therapy Trial(s).

ARTICLE 7
INTELLECTUAL PROPERTY

7.1 Inventions. All ownership and rights in and to Inventions shall be allocated as follows:

(a) Exelixis Ownership. All Exelixis Study Inventions shall be owned solely by Exelixis, and Exelixis will have the full right to exploit such Exelixis Study Inventions without the consent of, or any obligation to account to, Roche. Roche shall assign and hereby does assign (and shall cause its Affiliates and contractors to assign) all right, title, and interest in and to all Exelixis Study Inventions to Exelixis. Roche shall execute such further documents and provide such other assistance as may be reasonably requested by Exelixis to perfect Exelixis' rights in such Exelixis Study Inventions, at Exelixis' expense. Exelixis shall have the sole right, but not the obligation, to prepare, file, prosecute, and maintain all Exelixis Study Patents at its own expense.

(b) Roche Ownership. All Roche Study Inventions shall be owned solely by Roche, and Roche will have the full right to exploit such Roche Study Inventions without the consent of, or any obligation to account to, Exelixis. Exelixis shall assign and hereby does assign (and shall cause its Affiliates and contractors to assign) all right, title, and interest in and to all Roche Study Inventions to Roche. Exelixis shall execute such further documents and provide such other assistance as may be reasonably requested by Roche to perfect Roche's rights in such Roche Study Inventions, at Roche's expense. Roche shall have the sole right, but not the obligation, to prepare, file, prosecute, and maintain all Roche Study Patents at its own expense.

(c) Combined Therapy Inventions.

(i) Ownership. All Combined Therapy Inventions shall be jointly and equally owned by the Parties. Each Party shall be entitled to practice and exploit the Combined Therapy Inventions and Combined Therapy Patents without the duty of accounting or seeking consent from the other Party (except as expressly set forth in Section 7.1(d) and Section 7.3(d) with regard to the filing, prosecution, maintenance, and enforcement of Combined Therapy Patents).

(ii) Prosecution and Maintenance. "Prosecution and Maintenance" with regard to a given Patent, means the preparation, filing, prosecution and maintenance of such Patent, as well as any ex parte and inter partes proceedings, including reexaminations, reissues, applications for patent term extensions, interferences, derivation proceedings, post grant review proceedings, oppositions, litigations, arbitrations and other similar proceedings with respect to such Patent. The Parties shall agree as to which of Roche or Exelixis shall be responsible for Prosecution and Maintenance of the Combined Therapy Patents, and such Party shall use outside counsel acceptable to the other Party. Each Party shall cooperate with and assist the other Party in the Prosecution and Maintenance of any Combined Therapy Patent, including consulting with the other Party after receiving any substantial action, communication or development in the Prosecution and Maintenance of such Patent and making its relevant scientists and scientific records reasonably available. In addition, each Party shall sign and deliver, or use commercially reasonable efforts to have signed and delivered, at no charge to the other Party, all documents necessary in connection with such Prosecution and Maintenance. With respect to any Combined Therapy Patent, the outside counsel (if any) shall be instructed to (a) keep the Parties informed regarding the Prosecution and Maintenance thereof; (b) promptly furnish to each Party a copy of such Patent and copies of documents relevant to such Prosecution and Maintenance, including copies of correspondence with any patent office, foreign associates and outside counsel; and (c) act on the Parties' instructions relating to such Prosecution and Maintenance, provided that if there is a conflict in the instructions given by the Parties, outside counsel shall inform the Parties and allow for their resolution of this conflict. Notwithstanding the foregoing, the Prosecuting Party shall not take any position in a submission to a Patent office that interprets the scope of a Patent or Patent application of the Non-Prosecuting Party without the prior written consent of such Non-Prosecuting Party. The Non-Prosecuting Party shall reimburse the Prosecuting Party for [*] costs incurred by the Prosecuting Party in the prosecution and maintenance of the Combined Therapy Patents.

(iii) Abandonment. If a Party elects to not file or maintain a Combined Therapy Patent in a given country (or elects to not reimburse the other Party for [*] costs of prosecution and maintenance of such Combined Therapy Patent in such country), the other Party shall have the right to file or maintain such Patent in such country in its own name and at its own expense. In such event, the Party who decides not to file and maintain (or not to reimburse the other Party) a joint Patent for a given country shall promptly assign its rights to the joint invention in said country to the Party who wishes to file or maintain said Patent.

(iv) Dispute. If the Parties cannot agree with respect to the decision to file or maintain a Combined Therapy Patent within [*] after the initiation of the Parties' good faith efforts to resolve any disagreement, then either Party shall have the right to file or maintain a patent application for the Combined

[*] = Certain confidential information contained in this document, marked by brackets, has been omitted because it is both (I) not material and (II) would be competitively harmful if publicly disclosed.

Therapy Patent in the names of both Parties, provided that: (A) any resulting Patent shall be deemed to be a Combined Therapy Patent jointly owned by the Parties and subject to this Section 7.1(c).

(d) Separation of Patent Rights. To more efficiently enable the prosecution and maintenance of the Roche Study Patents, Exelixis Study Patents, and Combined Therapy Patents, the Parties shall use commercially reasonable efforts to separate Roche Study Patents, Exelixis Study Patents, Combined Therapy Patents, Roche Independent Patents, and Exelixis Independent Patents into separate patent filings to the extent possible and without adversely impacting such prosecution and maintenance.

7.2 Disclosure and Assignment of Inventions. Each Party shall disclose promptly to the other Party in writing and on a confidential basis all Inventions, prior to any public disclosure or filing of Patent applications and allowing sufficient time for comment by the other Party. In addition, each Party shall assign, and hereby does assign, and shall cause its Affiliates and contractors to so assign, to the other Party, without additional compensation, such right, title, and interest in and to any Inventions as is necessary to effect the sole ownership provided for in Sections 7.1(a) and 7.1(b) and the joint ownership provided for in Section 7.1(c), as applicable.

7.3 Infringement of Patent Rights by Third Parties.

(a) Notice. Each Party shall promptly notify the other Party in writing of any alleged or threatened (in writing) infringement, or misappropriation by a Third Party, of any Combined Therapy Patent of which it becomes aware (an "**Infringement**").

(b) Infringement of Exelixis Study Patents. Exelixis shall have the exclusive right to prosecute any and all Infringement of any Exelixis Study Patents as it may determine in its discretion, at its own expense. Roche shall reasonably cooperate with Exelixis in any such action (to the extent Roche has relevant information arising out of this Agreement), at Exelixis' request and expense.

(c) Infringement of Roche Study Patents. Roche shall have the exclusive right to prosecute any and all Infringement of any Roche Study Patents as it may determine in its discretion, at its own expense. Exelixis shall reasonably cooperate with Roche in any such action (to the extent Exelixis has relevant information arising out of this Agreement), at Roche's request and expense.

(d) Infringement of Combined Therapy Patents. With respect to Infringement of any Combined Therapy Patents, the Parties shall mutually agree whether to bring an enforcement action and, if so, which Party shall bring such action. The non-prosecuting Party shall reasonably cooperate in any such action, including, if required, by joining such action. If the Parties mutually agree to bring an enforcement action, each Party shall be responsible for [*] costs incurred in connection with such action. Any damages recovered from a Third Party in an Infringement action shall be first allocated to reimburse the Parties for their costs and expenses in making such recovery (which amounts shall be allocated *pro rata* if insufficient to cover the totality of such expenses), and any remaining amounts shall be [*], unless the Parties agree in writing to a different allocation. In connection with any proceeding under this Section 7.3(d), neither Party shall enter into any settlement without the prior written consent of the other Party.

7.4 Infringement of Third Party Rights.

(a) Notice. If the performance of a Combined Therapy Trial becomes the subject of a claim of infringement of a patent, copyright, or other proprietary right by a Third Party, the Party first having notice of the claim shall promptly notify the other Party and, without regard to which Party is charged with said infringement and the venue of such claim, the Parties shall promptly confer to discuss the claim and the appropriate course of action and may, if appropriate, agree on and enter into a "common interest agreement" wherein the Parties agree to their shared, mutual interest in the outcome of such potential dispute.

(b) Defense. If an infringement claim described in Section 7.4(a) is brought against one or both Parties, the Parties shall defend such claim jointly, unless they agree otherwise in writing. If the Parties jointly defend the claim, the Parties shall [*]. If only one Party is charged with infringement, such Party will have the first right, but not the obligation, to defend such claim. If the charged Party does not commence actions to defend such claim within [*] after being so charged, then the other Party shall have the right, but not the obligation, to defend such claim. The non-defending Party shall reasonably cooperate with the Party conducting the defense of the claim and shall have the right to participate with separate counsel at its own expense, and the defending Party shall consider in good faith the non-defending Party's comments and suggestions on strategy for defending such

action. The Party defending the claim shall [*]. No Party shall enter into any settlement concerning activities under this Agreement or the Combined Therapy that affects the other Party's rights under this Agreement or imposes any obligations on the other Party, including any admissions of wrongdoing on behalf of the other Party, without such other Party's prior written consent, such consent not to be unreasonably withheld or delayed. Notwithstanding the foregoing, if a claim relates solely to one Party's Compound, such Party shall have the sole right, but not the obligation, to defend and settle the disposition of such claim, at its sole expense, so long as the other Party's rights under this Agreement are not materially adversely impacted.

7.5 Combined Therapy Trial Regulatory Documentation. The Parties shall jointly and equally own all right, title, and interest in and to the Combined Therapy Trial Regulatory Documentation. For clarity, Roche shall retain sole and exclusive ownership of the Roche Regulatory Documentation that is submitted with or referenced in the Combined Therapy Trial Regulatory Documentation, and Exelixis shall retain sole and exclusive ownership of the Exelixis Regulatory Documentation that is submitted with or referenced in the Combined Therapy Trial Regulatory Documentation.

7.6 Joint Research Agreement. The Parties acknowledge and agree that this Agreement is a "Joint Research Agreement" as defined in 35 USC § 100 (h).

ARTICLE 8
FINANCIAL TERMS

8.1 Combined Therapy Trial Expenses. Roche shall be responsible for fifty percent (50%), and Exelixis shall be responsible for fifty percent (50%), of the Shared Costs for each Combined Therapy Trial. Shared Costs shall be incurred consistent with the JSC-approved budget for such Combined Therapy Trial. The Parties must approve, under the JSC, a final budget prior to [*] for a given Combined Therapy Trial. A JPT will review the budget on a [*] basis, and re-calibration of study forecast will be conducted by the Conducting Party if the applicable JPT determines it is necessary. Each Party shall calculate Shared Costs in accordance with US GAAP (Generally Accepted Accounting Principles) or International Financial Reporting Standards. For clarity, expenses incurred as described in Article 5 (regarding manufacturing and supply) and Article 7 (regarding intellectual property) shall not be considered "Shared Costs", and shall be borne or shared by the Parties as provided in such Articles. In addition, each Party shall bear its own Third Party License Payments as set forth in Section 5.1(b). For the avoidance of doubt, nothing in this Agreement shall establish an employment relationship between one Party and the employees of the other Party regardless of the reimbursement to such other Party for work performed by its employees under this Agreement.

8.2 Independent Combined Therapy Trial Costs. The Party conducting an Independent Combined Therapy Trial shall be solely responsible for the costs incurred in the performance of such Independent Combined Therapy Trial, subject to Section 5.1(a) and 5.2(a), as applicable ("**Independent Trial Costs**"). [*] If the Responding Party desires to submit any portion of the data resulting from an Independent Combined Therapy Trial to support a regulatory approval, or use the data for its own development, regulatory or commercial purposes, then the Responding Party shall notify the Proposing Party in writing at any time following the completion of such Independent Combined Therapy Trial. Within [*] after its receipt of such notice, the Proposing Party shall submit to the Responding Party a [*] invoice setting forth [*], and the Responding Party shall pay the amount invoiced [*]. Once payment is made, data transfer to the Responding Party shall occur as provided in this Agreement for a Combined Therapy Trial.

8.3 Background Data Costs. If either Party wishes to include any data from the other Party's clinical trials of the Combined Therapy conducted prior to or outside of this Agreement ("**Background Combined Therapy Trials**") in an application for regulatory approval or marketing approval of the Combined Therapy, or wishes to use such data for their own development, regulatory or commercial activities, then the conducting Party shall deliver a copy of the database and data generated in such Background Combined Therapy Trial, on a cohort-by-cohort basis, at a cost equal to [*] the costs incurred in connection with the relevant cohort within such Background Combined Therapy Trial, to the requesting Party. Prior to the delivery of such data, the conducting Party shall submit a reasonably detailed invoice [*] for [*] such costs and the requesting Party shall pay the amount invoiced within [*] after its receipt of such invoice; provided however that the requesting Party shall have a right to request supporting documentation for such invoice and any dispute over the accuracy of such invoice shall be resolved by the applicable JPT. The conducting Party shall provide the requested data to the requesting Party within [*] of receipt of such payment. The method for calculating such costs on a cohort-by-cohort basis shall be [*]. For

clarity, the foregoing payment shall not apply to safety data required by a Regulatory Authority, and each Party shall provide all such safety data to such Regulatory Authority at no additional cost to the other Party.

8.4 Shared Costs Invoicing; Payment.

(a) Reporting and Invoicing. Within [*] after the end of each Quarter, each Party shall provide to the other Party a reasonably detailed report setting forth the Shared Costs incurred by such Party during such Quarter (a "**Quarterly Report**"). The Parties shall cooperate to promptly resolve any questions or Disputes related to such reports within [*] following the end of each Quarter. Using the Quarterly Reports, the Parties' respective finance teams shall determine the amount, if any, owed by one Party to the other Party for such Quarter within [*] the end of each Quarter. The Party owing the other Party shall make a "**True-Up Payment**" to such other Party within [*] after end of each Quarter. Disputes that cannot be resolved by the Parties' respective finance teams shall be escalated to the JSC for resolution.

(b) Budget Overruns. Any amounts incurred by a Party that exceed [*] amounts approved by the JSC in the applicable budget (i.e., more than [*] over the budgeted amount) shall require approval of the JSC to be deemed a Shared Cost. To the extent that such overruns can be [*] by the Conducting Party, the JSC shall approve such increases to the applicable budget. If the JSC so agrees, the Parties shall bear the cost of any such budget overrun equally; except that if the reason for the overrun [*], then the amount of any overrun that [*] shall be [*].

8.5 Audit. Each Party shall keep, and shall require its Affiliates to keep, complete and accurate records pertaining to the performance of its activities under this Agreement. Each Party shall keep such books and records for [*] following the calendar year to which they pertain, or such longer period of time as may be required by Applicable Laws. Upon reasonable prior notice and during regular business hours at such place or places where such records are customarily kept, a Party's records may be inspected on the other Party's behalf by an independent certified public accountant (the "**Auditor**") selected by the auditing Party and reasonably acceptable to the audited Party for the sole purpose of verifying the accuracy of the Quarterly Reports furnished by the audited Party pursuant to this Agreement or of any payments made, or required to be made, to a Party pursuant to this Agreement. Before beginning its audit, the Auditor shall execute an undertaking acceptable to each Party by which the Auditor agrees to keep confidential all information reviewed during the audit. Such audits shall be limited to results in and further limited to the [*] prior to audit notification. Such audits shall not be performed more frequently than [*] each calendar year and once with respect to records covering any specific period of time. Such auditor shall not disclose a Party's Confidential Information to the other Party, and shall only verify the accuracy or inaccuracy of the Quarterly reports furnished by a Party or the amount of payments to or by a Party under this Agreement, and, in the case of any inaccuracy, the amount of such inaccuracy. In the event that the final result of the inspection reveals an undisputed underpayment or overpayment, the underpaid or overpaid amount shall be settled within [*] after the Auditor's report. The auditing Party shall bear the full cost of such audit unless such audit reveals an underpayment of more than [*] by the audited Party, in which case the audited Party shall reimburse the auditing Party for the reasonable costs of such audit.

ARTICLE 9
RECORDS AND STUDY DATA

9.1 Records. Each Party shall maintain complete and accurate records of all work conducted with respect to the Combined Therapy Trials and of all results, information, data, data analyses, reports, records, methods, processes, practices, formulae, instructions, skills, techniques, procedures, experiences and developments made by or provided to either Party, or by the Parties together, in the course of such Party's efforts with respect to the Combined Therapy Trials (including the Statistical Analysis Plan and Bioanalysis Plan to be conducted pursuant to this Agreement) (all of the foregoing, the "Study Data"). Such records shall fully and properly reflect all work done and results achieved in the performance of the Combined Therapy Trials in sufficient detail and in good scientific manner appropriate for patent and regulatory purposes.

9.2 Ownership of Study Data. Roche shall own the Study Data that relates exclusively to the Roche Compound ("**Roche Study Data**"), Exelixis shall own the Study Data that relates exclusively to the Exelixis Compound ("**Exelixis Study Data**"), and the Parties shall jointly and equally own all other Study Data ("**Combined Therapy Study Data**"). Each Party shall assign, and hereby does assign, and shall cause its Affiliates to so assign, to the other Party, without additional compensation, such right, title, and interest in and to all Study Data as is necessary to fully effect the foregoing, and agrees to execute all instruments as may be reasonably necessary to effect same.

[*] = Certain confidential information contained in this document, marked by brackets, has been omitted because it is both (I) not material and (II) would be competitively harmful if publicly disclosed.

9.3 Use of Study Data.

(a) Use of a Party's Own Study Data. Roche may use and analyze the Roche Study Data for any purpose without obligation or accounting to Exelixis. Exelixis may use and analyze the Exelixis Study Data for any purpose without obligation or accounting to Roche.

(b) Use of Combined Therapy Study Data by Roche. Roche and its Affiliates and (sub)licensees of the Roche Compound shall have the right to use and analyze the Combined Therapy Study Data for any and all purposes without the consent of, or any obligation to account to, Exelixis, including (i) in connection with their independent development, commercialization or other exploitation of the Roche Compound (alone or in combination with the Exelixis Compound and/or other pharmaceutical agents) and for inclusion in the safety database for the Roche Compound, and (ii) to conduct studies with Samples pursuant to Section 9.5. Subject to Section 9.5, the results of all such uses or analyses shall be owned by Roche, including any intellectual property rights therein, unless the Parties otherwise agree in writing.

(c) Use in Regulatory Filings by Roche. In addition, Roche and its Affiliates and (sub)licensees of the Roche Compound shall have the right to use the Combined Therapy Study Data during and following the term of this Agreement to (i) submit regulatory filings and seek approvals for the Roche Compound as part of the Combined Therapy and (ii) following the applicable approval of the Combined Therapy, to promote indications based on, and to disseminate, the Combined Therapy Study Data for the benefit of the Roche Compound as part of the Combined Therapy, where permitted by and in accordance with Applicable Law. If Roche submits Combined Therapy Study Data to a Regulatory Authority in a filing for approval for the use of the Roche Compound in combination with the Exelixis Compound, then Roche shall be granted a Right of Reference to the relevant Regulatory Documentation Controlled by Exelixis for the Exelixis Compound and the Combined Therapy solely to the extent required for the purpose of such approval (which right shall survive any expiration or termination of this Agreement). In such case, Exelixis shall reasonably cooperate with Roche and make written authorizations and other filings with the applicable Regulatory Authority reasonably required to effect such Right of Reference. Such grant to Roche of a Right of Reference shall not include a Right of Reference for use in the Takeda Territory, without Exelixis' prior written consent; provided, however, that Exelixis shall use all reasonable efforts to obtain rights for Roche in Japan, subject to their agreement with Takeda in Japan.

(d) Use of Combined Therapy Study Data by Exelixis. Exelixis and its Affiliates and (sub)licensees of the Exelixis Compound shall have the right to use and analyze the Combined Therapy Study Data for any and all purposes without the consent of, or any obligation to account to, Roche, including (i) in connection with their independent development, commercialization or other exploitation of the Exelixis Compound (alone or in combination with the Roche Compound and/or other pharmaceutical agents) and for inclusion in the safety database for the Exelixis Compound, and (ii) to conduct studies with Samples pursuant to Section 9.5. Subject to Section 9.5, the results of all such uses or analyses shall be owned by Exelixis, including any intellectual property rights therein, unless the Parties otherwise agree in writing.

(e) Use in Regulatory Filings by Exelixis. In addition, Exelixis and its Affiliates and (sub)licensees of the Exelixis Compound shall have the right to use the Combined Therapy Study Data during and following the term of this Agreement to (i) submit regulatory filings and seek approvals for the Exelixis Compound as part of the Combined Therapy and (ii) following the applicable approval of the Combined Therapy, to promote indications based on, and to disseminate, the Combined Therapy Study Data for the benefit of the Exelixis Compound as part of the Combined Therapy, where permitted by and in accordance with Applicable Law. If Exelixis submits Combined Therapy Study Data to a Regulatory Authority in a filing for approval for the use of the Exelixis Compound in combination with the Roche Compound, then Exelixis shall be granted a Right of Reference to the relevant Regulatory Documentation Controlled by Roche for the Roche Compound and the Combined Therapy solely to the extent required for the purpose of such approval (which right shall survive any expiration or termination of this Agreement). In such case, Roche shall reasonably cooperate with Exelixis and make written authorizations and other filings with the applicable Regulatory Authority reasonably required to effect such Right of Reference. Such grant to Exelixis of a Right of Reference shall not include a Right of Reference for use in Japan, without Roche's prior written consent; provided, however, that Roche shall use all reasonable efforts to obtain rights for Exelixis in Japan, subject to any agreement Roche may have with a local Affiliate.

(f) Biomarker Development. Each Party may use and disclose to a Third Party the Combined Therapy Study Data and its Compound's Study Data, under obligations of confidentiality consistent with this Agreement, to develop and commercialize a biomarker or diagnostic test for use with its Compound and/or the Combined Therapy, and, unless otherwise mutually agreed by the Parties in writing, will own any intellectual

property arising out of the work funded or conducted by it with or through such Third Party. The Parties will discuss in good faith any opportunities to jointly participate in the development of any such biomarker or diagnostic test for use with the Combined Therapy.

(g) [*]

(h) No Other Uses. Except as expressly set forth in this Agreement, neither Party may use Study Data for any other purpose without the consent of the other Party during and after the Term of this Agreement.

9.4 Access to Study Data. Subject to the Pharmacovigilance Agreement, each Party shall have access to all Study Data (including, but not limited to, de-identified patient records) as soon as reasonably practicable after Study Data is available to or generated by the Party responsible for generating or collecting such Study Data.

9.5 Samples. Samples collected in the course of activities conducted under this Agreement shall be jointly and equally owned by the Parties (to the extent not owned by the patient and/or the clinical trial site). Any such Samples shall be collected in accordance with the applicable Protocol and ICFs. Except as set forth in a Bioanalysis Plan, no Party shall be permitted to use such Samples for any purpose without the approval of the JPT. All data and intellectual property arising out of such Sample use shall be owned by the Party conducting such study; provided that to the extent that any such data or intellectual property relates to the Combined Therapy (or biomarkers solely for use with the Combined Therapy), such data and intellectual property shall be considered Combined Therapy Study Data or Combined Therapy Inventions, and Combined Therapy Patents, as applicable. The Parties shall agree on which Party shall store the Samples for PK and ADA analysis for future use; provided that [*]. If neither Party has any further use for the Samples, then the remaining Samples shall be destroyed pursuant to the respective Party's standard operating procedures for sample destruction, subject to the terms of and permission(s) granted in the ICFs signed by the subjects contributing such Samples in the Combined Therapy Trials.

9.6 Existing Trials. If a Combined Therapy Trial is added to a pre-existing clinical trial of one of the Parties, none of the cohorts of such pre-existing clinical trial shall be deemed part of the Combined Therapy Trial and none of the results, information, data, data analyses, reports, records, methods, processes, practices, formulae, instructions, skills, techniques, procedures, experiences, and developments from such cohorts will be Study Data unless the Protocol expressly provides otherwise. Where a cohort of a Combined Therapy Trial is a monotherapy cohort with just the Exelixis Compound or with just the Roche Compound, then the Study Data from such cohort will be Exelixis Study Data in the case where such cohort is a monotherapy cohort with just the Exelixis Compound and Roche Study Data in the case where such cohort is a monotherapy cohort with just the Roche Compound.

ARTICLE 10
CONFIDENTIALITY

10.1 Confidential Information. Except to the extent expressly authorized by this Agreement or otherwise agreed in writing by the Parties, the Parties agree that, during the Term and for [*] thereafter, the receiving Party shall keep confidential and shall not publish or otherwise disclose, and shall not use for any purpose other than as expressly provided for in this Agreement, any Confidential Information of the other Party, and both Parties shall keep confidential and, subject to the remainder of this Article 10, shall not publish or otherwise disclose the terms of this Agreement. Each Party may use the other Party's Confidential Information only to the extent required to accomplish the purposes of this Agreement, including exercising its rights or performing its obligations under this Agreement. Each Party will use at least the same standard of care as it uses to protect proprietary or confidential information of its own (but no less than reasonable care) to ensure that its employees, agents, consultants, contractors, and other representatives do not disclose or make any unauthorized use of the other Party's Confidential Information. Each Party will promptly notify the other upon discovery of any loss or unauthorized use or disclosure of the other Party's Confidential Information. For clarity, Combined Therapy Study Data shall be treated as Confidential Information of both Parties and shall not be disclosed to Third Parties unless it falls within the exceptions set forth in Section 10.2 below or is reasonably necessary to be disclosed in order for a Party to exercise its rights under Section 9.3.

10.2 Exceptions. The obligations of confidentiality and restriction on use under Section 10.1 will not apply to any information that the receiving Party can prove by competent written evidence:

[*] = Certain confidential information contained in this document, marked by brackets, has been omitted because it is both (I) not material and (II) would be competitively harmful if publicly disclosed.

(a) is now, or hereafter becomes, through no act or failure to act on the part of the receiving Party, generally known or available to the public;

(b) is known by the receiving Party at the time of receiving such information, other than by previous disclosure of the disclosing Party, or its Affiliates, employees, agents, consultants, or contractors;

(c) is hereafter furnished to the receiving Party without restriction by a Third Party who has no obligation of confidentiality or limitations on use with respect thereto, as a matter of right; or

(d) is independently discovered or developed by the receiving Party without the use of the disclosing Party's Confidential Information.

10.3 Authorized Disclosure. Notwithstanding any other provision of this Agreement, each Party may disclose Confidential Information belonging to the other Party to the extent such disclosure is reasonably necessary in the following instances:

(a) prosecuting or defending litigation as permitted by this Agreement;

(b) complying with Applicable Law (including regulations promulgated by any securities exchange);

(c) disclosure, in connection with the performance of this Agreement, to Affiliates, permitted sublicensees, contractors, manufacturers, ethics committees and IRBs, academic institutions, consultants, agents, investigators, and employees engaged in connection with the performance of a Combined Therapy Trial, each of whom prior to disclosure must be bound by similar terms of confidentiality and non-use at least equivalent in scope to those set forth in this Article 10;

(d) disclosure of the Combined Therapy Study Data, Combined Therapy Inventions, and Combined Therapy Patents to Regulatory Authorities in connection with the development of the Combined Therapy, the Exelixis Compound, or the Roche Compound; and

(e) disclosure of relevant safety information contained within the Combined Therapy Study Data to investigators, IRBs, and/or ethics committees and Regulatory Authorities that are involved in other clinical trials of the Exelixis Compound with respect to Exelixis, and the Roche Compound with respect to Roche, and (in the event of a Material Safety Issue) to Third Parties that are collaborating with Exelixis or Roche, respectively in the conduct of such other clinical trials of the Exelixis Compound or the Roche Compound, in each case solely to the extent necessary for the conduct of such clinical trials and/or to comply with Applicable Law and regulatory requirements.

Notwithstanding the foregoing, in the event that a Party is required to make a disclosure of the other Party's Confidential Information pursuant to Section 10.3(a) or (b), it will, except where impracticable, give reasonable advance notice to the other Party of such disclosure and use efforts to secure confidential treatment of such Confidential Information at least as diligent as such Party would use to protect its own confidential information of a similar nature, but in no event less than reasonable efforts. In any event, the Parties agree to take all reasonable action to avoid disclosure of Confidential Information. Any information disclosed pursuant to any of Sections 10.3(a)-(e) shall remain Confidential Information and subject to the restrictions set forth in this Agreement.

10.4 Disclosure to Ipsen and Takeda. Notwithstanding any other provision of this Agreement, Roche hereby expressly authorizes Exelixis to disclose to Ipsen and Takeda (a) this Agreement, the Protocols, Combined Therapy Inventions, and Combined Therapy Patents, and (b) any other Roche Confidential Information necessary for Exelixis to fulfill its obligations to Ipsen and Takeda under the Ipsen-Exelixis Agreements and the Takeda-Exelixis Agreements; provided that Ipsen and Takeda are each under confidentiality obligations at least as restrictive as set forth herein. Exelixis shall be free to disclose the Exelixis Study Data and the Combined Therapy Study Data to Ipsen and Takeda as Exelixis may determine as provided in Section 10.3(c) or 10.3(d) and otherwise to fulfill its obligations under each of the Ipsen-Exelixis Agreements and the Takeda-Exelixis Agreements.

10.5 Press Releases and Publications.

(a) The Parties shall jointly agree to the content and timing of all external communications with respect to this Agreement, including an initial press release by Exelixis, the content of which shall be as

attached hereto as Exhibit B, subsequent press releases, media Q&As, and the content and wording of any listing of a Combined Therapy Trial on a public database or public registry (such as clinicaltrials.gov).

(b) Exelixis and Roche agree to collaborate to publicly disclose, publish, or present (with the Conducting Party to lead) (i) top-line results from each Combined Therapy Trial, limited if possible to avoid jeopardizing the future publication of the Study Data at a scientific conference or in a scientific journal, solely for the purpose of disclosing, as soon as reasonably practicable, the safety or efficacy results and conclusions that are material to any Party under applicable securities laws, and (ii) the conclusions and outcomes (the "**Results**") of each Combined Therapy Trial at a scientific conference as soon as reasonably practicable following the completion of such Combined Therapy Trial, subject to the following terms and conditions. The Party proposing to disclose, publish, or present the Results shall deliver to the other Party a copy of the proposed disclosure, publication, or presentation: (a) for abstracts, slide presentations or posters, at least [*] prior to submission (in the case of abstracts) or first public presentation (in the case of slide presentations and posters); and (b) at least [*] in advance of first submission and each subsequent submission in the case of manuscripts; or (c) within such other timeframe as the Parties may agree. The reviewing Party shall determine whether any of its Confidential Information that may be contained in such disclosure, publication, or presentation should be modified or deleted, whether to file a patent application on any Exelixis Study Invention (solely with respect to Exelixis) or Roche Study Invention (solely with respect to Roche) or Combined Therapy Invention disclosed therein. The disclosure, publication, or presentation shall be delayed for an additional [*] if a reviewing Party reasonably requests such extension to allow time for the preparation and filing of relevant patent applications. If a reviewing Party reasonably requests modifications to the disclosure, publication, or presentation to prevent the disclosure of such Party's Confidential Information, the publishing Party shall remove such information prior to submission of the disclosure, publication, or presentation. In the event of a disagreement as to content, timing, and/or venue or forum for any disclosure, publication, or presentation of the Results, such dispute (a "**Publication Dispute**") shall be referred to the Executive Officers (or their respective designees) for resolution; provided that, in the absence of agreement after such good faith discussions, and upon expiration of an additional [*], (A) academic collaborators engaged by the Conducting Party in connection with the performance of the Combined Therapy Trials may publish Combined Therapy Study Data obtained by such academic collaborator solely to the extent that such ability to publish such Combined Therapy Study Data is set forth in an agreement between the Conducting Party and such academic collaborator relating to the conduct of Combined Therapy Trials and (B) the publishing Party may proceed with the disclosure, publication, or presentation provided that such disclosure, publication, or presentation is consistent with its internal publication guidelines and customary industry practices for the publication of similar data and does not contain any Confidential Information of the non-publishing Party. Authorship of any publication shall be determined based on the accepted standards used in peer-reviewed academic journals at the time of the proposed disclosure, publication, or presentation.

(c) Notwithstanding the foregoing, nothing herein shall prevent or restrict Chugai, Ipsen, or Takeda from making any disclosures of published Study Data disclosed to it by Roche pursuant to Section 10.4 or Exelixis pursuant to Section 10.5 of the existence of this Agreement, in each case in order for Chugai, Ipsen, or Takeda to comply with requirements of Applicable Law, the rules or regulations of any securities exchange or listing entity on which its stock may be traded, or pursuant to an order of a court or governmental entity to publicly disclose the existence of the Agreement and the Study Data.

10.6 Compliance with Sunshine Laws.

(a) For purposes of compliance with reporting obligations under Sunshine Laws, as between the Parties, the Conducting Party will report payments or other transfers of value ("**POTV**") made by the Conducting Party or the CRO related to the conduct of the Combined Therapy Trials and any applicable associated contractor engagements as required under the Sunshine Laws for each Combined Therapy Trial. Interpretation of the Sunshine Laws for purposes of reporting any POTV by a Party shall be in such Party's sole discretion so long as the interpretation complies with Applicable Law.

(b) The Conducting Party (i) will provide (to the extent in the possession of the Conducting Party), or will utilize Commercially Reasonable Efforts to obligate and ensure that each CRO and other applicable Third Party contractors for a Combined Therapy Trial provides, the Non-Conducting Party with any information requested by the Non-Conducting Party as the Non-Conducting Party may reasonably determine for the Non-Conducting Party to comply with its reporting obligations under Sunshine Laws (with such amounts paid to, or at the direction of, each recipient to be reported to the Non-Conducting Party within a reasonable time period specified by the Non-Conducting Party) and (ii) will reasonably cooperate with, and will use Commercially

[*] = Certain confidential information contained in this document, marked by brackets, has been omitted because it is both (I) not material and (II) would be competitively harmful if publicly disclosed.

Reasonable Efforts to obligate and ensure that each CRO and other applicable Third Party contractors for a Combined Therapy Trial reasonably cooperates with, the Non-Conducting Party in connection with its compliance with such Sunshine Laws. The form in which the Conducting Party provides any such information shall be mutually agreed, but in any case sufficient to enable the Non-Conducting Party to comply with its reporting obligations and the Non-Conducting Party may disclose any information that it reasonably believes is necessary to comply with Sunshine Laws. Without limiting the foregoing, the Non-Conducting Party shall have the right to allocate payments or other transfers of value in connection with this Agreement in any required reporting under Sunshine Laws in accordance with its normal business practices. These obligations shall survive the expiration and termination of the agreement to the extent necessary for the Non-Conducting Party to comply with Sunshine Laws.

(c) For purposes of this Section 10.6, "**Sunshine Laws**" means Applicable Laws requiring collection, reporting and disclosure of POTVs to certain healthcare providers, entities and individuals. These Applicable Laws may include, without limitation, relevant provisions of the Patient Protection and Affordable Health Care Act of 2010 and implementing regulations thereunder. "**Recipients**" means healthcare providers, teaching hospitals and/or any other persons for whom transfers of value or payments must be reported under Sunshine Laws.

10.7 Destruction of Confidential Information. Upon expiration or termination of the Agreement, the receiving Party shall, upon request by the other Party, immediately destroy all of the other Party's Confidential Information relating solely to its Compound(s) as monotherapy (but not to the Combined Therapy or the Combined Therapy Study Data) in its possession; provided, however, that the receiving Party shall be entitled to retain one (1) copy of Confidential Information solely for record-keeping purposes and shall not be required to destroy any off-site computer files created during routine and automatic system back up which are subsequently stored securely by the receiving Party.

ARTICLE 11
REPRESENTATIONS AND WARRANTIES

11.1 Authority and Binding Agreement. Exelixis and Roche each represents and warrants to the other that, as of the Effective Date, (a) it has the corporate power and authority and the legal right to enter into this Agreement and perform its obligations hereunder; (b) it has taken all necessary corporate action on its part required to authorize the execution and delivery of the Agreement and the performance of its obligations hereunder; and (c) the Agreement has been duly executed and delivered on behalf of each Party and constitutes a legal, valid, and binding obligation of such Party that is enforceable against it in accordance with its terms.

11.2 No Conflicts. Exelixis and Roche each represents and warrants that, to the best of its knowledge, as of the Effective Date it has not entered, and shall not enter, into any agreement with any Third Party that is in conflict with the rights granted to any other Party under this Agreement, and has not taken any action that would in any way prevent it from granting the rights granted to any other Party under this Agreement, or that would otherwise materially conflict with or adversely affect the rights granted to any other Party under this Agreement.

11.3 Litigation. Exelixis and Roche each represents and warrants that, to the best of its knowledge, as of the Effective Date it is not aware of any pending or threatened litigation (and has not received any communication) that alleges that its activities related to this Agreement have violated, or that by conducting the activities as contemplated in this Agreement it would violate, any of the intellectual property rights of any other Person (after giving effect to the license grants in this Agreement).

11.4 No Adverse Proceedings. Exelixis and Roche each represents and warrants that, to the best of its knowledge, as of the Effective Date there is no pending or threatened, in writing, claim, suit, action, or governmental proceeding against such Party that would, if adversely determined, materially impair the ability of such Party to perform its obligations under this Agreement.

11.5 Consents. Exelixis and Roche each represents and warrants that, to the best of its knowledge, as of the Effective Date all necessary consents, approvals, and authorizations of all regulatory and governmental authorities and other Persons (a) required to be obtained by such Party in connection with the execution and delivery of this Agreement have been obtained and (b) required to be obtained by such Party in connection with the performance of its obligations under this Agreement have been obtained or will be obtained prior to such performance.

[*] = Certain confidential information contained in this document, marked by brackets, has been omitted because it is both (I) not material and (II) would be competitively harmful if publicly disclosed.

11.6 No Debarment. Each Party represents, warrants, and covenants to the other Party that it is not debarred or disqualified under the U.S. Federal Food, Drug and Cosmetic Act, as may be amended, or comparable laws in any country or jurisdiction other than the U.S., and it does not, and will not during the Term, employ or use the services of any person who is debarred or disqualified, in connection with activities relating to any Product. In the event that either Party becomes aware of the debarment or disqualification or threatened debarment or disqualification of any person providing services to such Party, including the Party itself or its Affiliates or Sublicensees, that directly or indirectly relate to activities contemplated by this Agreement, such Party shall immediately notify the other Party in writing and such Party shall cease employing, contracting with, or retaining any such person to perform any such services.

11.7 Compliance with Applicable Law. Exelixis and Roche each represents and warrants that it shall comply, and shall cause its and its Affiliates' employees and contractors to comply, with all Applicable Laws of the country or other jurisdiction, or any court or agency thereof, applicable to the performance of its activities hereunder or any obligation or transaction hereunder.

11.8 Affiliates. Exelixis and Roche each represents and warrants that, to the extent the intellectual property, Regulatory Documentation, or Technology licensed by it hereunder are Controlled by its Affiliates or a Third Party, it has the right to use, and has the right to grant (sub)licenses to the other Party to use, such intellectual property, Regulatory Documentation, or Technology in accordance with the terms of this Agreement.

11.9 Ethical Business Practices. Exelixis and Roche each represents and warrants that neither it nor its Affiliates will make any payment, either directly or indirectly, of money or other assets, including the compensation such Party derives from this Agreement (collectively a "Payment"), to government or political party officials, officials of International Public Organizations, candidates for public office, or representatives of other businesses or persons acting on behalf of any of the foregoing (collectively "Officials") where such Payment would constitute violation of any law, including the Foreign Corrupt Practices Act of 1977, 15 U.S.C. §§ 78dd-1, et seq. In addition, regardless of legality, neither it nor its Affiliates will make any Payment either directly or indirectly to Officials if such Payment is for the purpose of improperly influencing decisions or actions with respect to the subject matter of this Agreement. All activities will be conducted in compliance with the U.S. False Claims Act and the U.S. Anti-Kickback Statute.

11.10 Single Agent Compound Safety Issues. Each Party represents and warrants that, to the best of its knowledge, as of the Effective Date it is not aware of any material safety or toxicity issue with respect to its Single Agent Compound that is not reflected in the investigator's brochure(s) for its Single Agent Compound existing as of the Effective Date.

11.11 Accounting. Each Party represents and warrants that all transactions under the Agreement shall be properly and accurately recorded in all material respects on its books and records and that each document upon which entries in such books and records are based is complete and accurate in all material respects.

11.12 Compliance with Ipsen-Exelixis Agreements and Takeda-Exelixis Agreements. Exelixis will use Commercially Reasonable Efforts to comply with its obligations under the Ipsen-Exelixis Agreements and the Takeda-Exelixis Agreements (and not to voluntarily terminate same) to the extent necessary for each Combined Therapy Trial to be completed in accordance with the terms of this Agreement and for Roche to receive the rights and benefits provided to it under this Agreement.

11.13 DISCLAIMER OF WARRANTY. EXCEPT FOR THE EXPRESS WARRANTIES SET FORTH IN THIS AGREEMENT, EACH PARTY EXPRESSLY DISCLAIMS ANY AND ALL WARRANTIES OF ANY KIND, WHETHER EXPRESS, IMPLIED, OR STATUTORY, INCLUDING WARRANTIES OF DESIGN, MERCHANTABILITY, FITNESS FOR A PARTICULAR PURPOSE, NONINFRINGEMENT OF THE INTELLECTUAL PROPERTY RIGHTS OF THIRD PARTIES, OR ARISING FROM A COURSE OF DEALING, USAGE, OR TRADE PRACTICES, IN ALL CASES WITH RESPECT THERETO.

ARTICLE 12
INDEMNIFICATION

12.1 Roche Indemnification. Roche hereby agrees to defend, indemnify, and hold harmless Exelixis, its Affiliates, and their respective directors, officers, employees, and agents (each, an "**Exelixis Indemnitee**") from and against any and all liabilities, expenses, and losses, including reasonable legal expenses and attorneys' fees (collectively, "**Losses**"), to which any Exelixis Indemnitee may become subject as a result of any claim, demand, action, or other proceeding (each, a "**Claim**") by any Third Party to the extent such Losses arise out of:

(a) the negligence or intentional misconduct of Roche, any Roche Indemnitee, or any (sub)licensee of Roche conducting activities on behalf of Roche under this Agreement;

(b) any breach by Roche of any provision of this Agreement;

(c) any injury to a subject in a Combined Therapy Trial caused solely by the development, use, or manufacture of the Roche Compound;

(d) the use by Roche, its Affiliates, contractors, or (sub)licensees of any Combined Therapy Study Data, Roche Study Data, Roche Study Inventions, Roche Study Patents, Combined Therapy Inventions, and Combined Therapy Patents outside the scope of this Agreement (other than with respect to Third Party Claims that are covered under Section 7.4); but excluding, in each case ((a) through (e)), any such Losses to the extent Exelixis is obligated to Indemnify the Roche Indemnitees pursuant to Section 12.2.

12.2 Exelixis Indemnification. Exelixis hereby agrees to defend, indemnify, and hold harmless Roche, its Affiliates, and their respective directors, officers, employees, and agents (each, a "**Roche Indemnitee**") from and against any and all Losses to which any Roche Indemnitee may become subject as a result of any Claim by any Third Party to the extent such Losses arise out of:

(a) the negligence or intentional misconduct of Exelixis, any Exelixis Indemnitee, or any (sub)licensee of Exelixis conducting activities on behalf of Exelixis under this Agreement;

(b) any breach by Exelixis of any provision of this Agreement;

(c) any injury to a subject in a Combined Therapy Trial caused solely by the development, use, or manufacture of the Exelixis Compound;

(d) the use by Exelixis, its Affiliates, contractors, or (sub)licensees of Combined Therapy Study Data, Exelixis Study Data, Exelixis Study Inventions, Exelixis Study Patents, Combined Therapy Inventions and Combined Therapy Patents outside the scope of this Agreement (other than with respect to Third Party Claims that are covered under Section 7.4), but excluding, in each case ((a) through (e)), any such Losses to the extent Roche is obligated to Indemnify the Exelixis Indemnitees pursuant to Section 12.1.

12.3 Indemnification Procedure. A Party that intends to claim indemnification under this Article 12 (the "**Indemnitee"**) shall promptly notify the indemnifying Party (the "**Indemnitor**") in writing of any Claim in respect of which the Indemnitee intends to claim such indemnification, and the Indemnitor shall have sole control of the defense or settlement of such Claim. The Indemnitee may participate at its expense in the Indemnitor's defense of and settlement negotiations for any Claim with counsel of the Indemnitee's own choice. The indemnity arrangement in this Article 12 shall not apply to amounts paid in settlement of any action with respect to a Claim if such settlement is effected without the consent of the Indemnitor, which consent shall not be unreasonably withheld or delayed. The failure to deliver written notice to the Indemnitor within a reasonable time after the commencement of any action with respect to a Claim shall only relieve the Indemnitor of its indemnification obligations under this Article 12 if and to the extent the Indemnitor is actually prejudiced thereby. The Indemnitee shall cooperate fully with the Indemnitor and its legal representatives in the investigation of any action with respect to a Claim covered by this indemnification.

12.4 Separate Defense of Claims. In the event that the Parties cannot agree as to the application of Sections 12.1 and/or 12.2 to any particular Loss, the Parties may conduct separate defenses of such Loss. Each Party further reserves the right to claim indemnity from the other in accordance with Sections 12.1 and/or 12.2 upon resolution of the underlying claim, notwithstanding the provisions of Section 12.3.

12.5 Insurance. Each Party shall maintain commercially reasonable levels of insurance or other adequate and commercially reasonable forms of protection or self-insurance in light of its obligations under this Agreement. Each Party shall provide the other Party with written notice at least [*] prior to the cancellation, non-renewal, or material change in such insurance or self-insurance which would materially adversely affect the rights of the other Party hereunder. The maintenance of any insurance shall not constitute any limit or restriction on damages available to a Party under this Agreement.

12.6 LIMITATION OF LIABILITY. EXCEPT FOR DAMAGES THAT (A) ARISE IN CONNECTION WITH A PARTY'S (I) WILLFUL MISCONDUCT OR FRAUD OR (II) BREACH OF ITS OBLIGATIONS UNDER ARTICLE 10, OR (B) ARE SUBJECT TO INDEMNIFICATION UNDER SECTION 12.1 OR 12.2, NEITHER PARTY SHALL BE LIABLE IN CONTRACT,

[*] = Certain confidential information contained in this document, marked by brackets, has been omitted because it is both (I) not material and (II) would be competitively harmful if publicly disclosed.

TORT, NEGLIGENCE, BREACH OF STATUTORY DUTY, OR OTHERWISE FOR ANY INDIRECT, INCIDENTAL, SPECIAL, EXEMPLARY, PUNITIVE, OR CONSEQUENTIAL DAMAGES OR FOR LOSS OF PROFITS SUFFERED BY THE OTHER PARTY (OR ITS AFFILIATES OR (SUB)LICENSEES), REGARDLESS OF ANY NOTICE OF THE POSSIBILITY OF SUCH DAMAGES.

ARTICLE 13
TERM AND TERMINATION

13.1 Term. This Agreement shall be effective as of the Effective Date and, unless earlier terminated as provided in this Agreement, shall continue in effect until completion by all centers or institutions participating in the Combined Therapy Trials for such Combined Therapy combination, the delivery of all Study Data, including all completed case report forms, all final analyses, and all final clinical study reports for the Combined Therapy Trials to both Parties, and the completion of any then agreed upon Statistical Analysis and Bioanalysis Plan (the "**Term**").

13.2 Termination for Material Breach. Each Party shall have the right to terminate this Agreement immediately in its entirety upon written notice to the other Party if such other Party materially breaches this Agreement and has not cured such breach to the reasonable satisfaction of the other Party within [*] after notice of such breach from the non-breaching Party. If cure of such breach (other than non-payment) cannot reasonably be effected within such [*] period, the breaching Party shall deliver to the non-breaching Party a plan reasonably calculated to cure such breach within a reasonable timeframe, but in any event within [*]. So long as the breaching Party is diligently carrying out such plan, the non-breaching Party shall not have the right to terminate this Agreement. If the breaching Party fails to diligently carry out such plan and cure such breach as provided above, then the non-breaching Party may terminate this Agreement upon written notice to the breaching Party.

13.3 Termination for Bankruptcy. Each Party shall have the right to terminate this Agreement immediately in its entirety upon written notice to the other Party if such other Party makes a general assignment for the benefit of creditors, files an insolvency petition in bankruptcy, petitions for or acquiesces in the appointment of any receiver, trustee, or similar officer to liquidate or conserve its business or any substantial part of its assets, commences under the laws of any jurisdiction any proceeding involving its insolvency, bankruptcy, reorganization, adjustment of debt, dissolution, liquidation, or any other similar proceeding for the release of financially distressed debtors or becomes a party to any proceeding or action of the type described above and such proceeding is not dismissed within [*] after the commencement thereof.

13.4 Termination due to Material Safety Issue; Clinical Hold.

(a) Roche or Exelixis shall each have the independent right to immediately suspend the treatment of subjects in the Combined Therapy Trial and terminate this Agreement upon written notice if it deems it necessary to protect the safety, health, or welfare of subjects enrolled in any Combined Therapy Trial due to the existence of a Material Safety Issue. In the event of a termination due to a Material Safety Issue, prior to the terminating Party providing written notice, each Party's safety committee shall, to the extent practicable, meet and discuss in good faith the safety concerns raised by the terminating Party and consider in good faith the input, questions and advice of the non-terminating Party, but should any dispute arise in such discussion, the dispute resolution processes set forth herein shall not apply to such dispute and the terminating Party shall have the right to issue such notice and such suspension shall take effect without the Parties first following the dispute resolution procedures set forth herein and the Agreement shall subsequently terminate once the Combined Therapy Trial has been wound down pursuant to Section 13.5.

(b) If a Clinical Hold with respect to either the Roche Compound(s) or the Exelixis Compound should arise at any time after the Effective Date, the Parties will meet and discuss the basis for the Clinical Hold, how long the Clinical Hold is expected to last, and how they might address the issue that caused the Clinical Hold. If, after [*] of discussions following the Clinical Hold, a Party reasonably concludes that the issue is not solvable or that unacceptable and material additional costs/delays have been and/or will continue to be incurred in the conduct of the Combined Therapy Trial, then such Party may immediately terminate this Agreement upon written notice to the other Party.

13.5 Effect of Termination. Upon expiration or termination of this Agreement:

(a) Licenses. The licenses granted to each Party under this Agreement shall terminate upon completion of any ongoing activities under this Agreement; and

(b) Wind Down. The Parties shall use reasonable efforts to wind down activities under this Agreement in a reasonable manner and avoid incurring any additional expenditures or non-cancellable obligations; provided that, in the case of termination, the Conducting Party may continue to dose subjects enrolled in any then ongoing Combined Therapy Trial through completion of the applicable Protocol if dosing is required by the applicable Regulatory Authority(ies) and/or Applicable Law(s). Any such wind-down activities will include the return to a Party, or destruction, of all of such Party's Compound provided to the other Party and not used in the Combined Therapy Trials. If applicable, upon termination of this Agreement, the Parties shall remain responsible pursuant to the terms of this Agreement for any expenses incurred that are associated with terminating any ongoing clinical trial work and/or result from such ongoing activities under this Agreement solely to the extent such activities are deemed necessary by the Conducting Party (after agreement by the JSC) based on reasonable medical judgment to protect the health of subjects participating in any Combined Therapy Trial.

13.6 Survival. The following Articles and Sections of this Agreement and all definitions relating thereto shall survive any expiration or termination of this Agreement for any reason: Section 2.4, Section 2.6(b), Section 2.10, Article 7, Sections 8.1, 8.2, 8.3, and 8.5, Article 9, Article 10, Article 11, Article 12, Sections 13.5 and 13.6, and Sections 14.1, 14.2, 14.3, 14.5, 14.6, 14.7, 14.9, 14.10, 14.11, 14.12, 14.14, and 14.15

ARTICLE 14
MISCELLANEOUS

14.1 Entire Agreement. The Parties acknowledge that this Agreement shall govern all activities of the Parties with respect to the Combined Therapy Trials from the Effective Date forward. This Agreement, including the Exhibits hereto and together with the Protocol, Quality Agreement, and Pharmacovigilance Agreement, sets forth the complete, final, and exclusive agreement between the Parties concerning the subject matter hereof and supersedes all prior agreements and understandings between the Parties with respect to such subject matter. There are no covenants, promises, agreements, warranties, representations, conditions, or understandings, either oral or written, between the Parties with respect to such subject matter other than as are set forth in this Agreement. All Exhibits attached hereto are incorporated herein as part of this Agreement. This Agreement may only be modified or supplemented in a writing expressly stated for such purpose and signed by the Parties to this Agreement.

14.2 Governing Law. This Agreement shall be governed and construed in accordance with the internal laws of the State of California, USA, excluding any choice of law rules that may direct the application of the laws of another jurisdiction.

14.3 Dispute Resolution.

(a) General. Except as provided in Sections 3.7 and 8.5, any dispute between the Parties in connection with or relating to this Agreement or any document or instrument delivered in connection herewith (a "**Dispute**") shall be resolved pursuant to this Section 14.3.

(b) Executive Officers. Any Dispute shall first be referred to the Executive Officers of the Parties, who shall confer in good faith on the resolution of the issue. Any final decision mutually agreed to by the Executive Officers shall be conclusive and binding on the Parties.

(c) Arbitration. If the Executive Officers are not able to agree on the resolution of a Dispute within [*] (or such other period of time as mutually agreed by the Executive Officers) after such Dispute was first referred to them, then, if a Party wishes to pursue further resolution of such Dispute, such Dispute shall be finally resolved by binding arbitration in accordance with this Section 14.3(c). Such Dispute shall be referred to and finally resolved by arbitration JAMS pursuant to its Streamlined Arbitration Rules then in effect ("**Rules**"), as then in effect, by a tribunal of three (3) arbitrators. The seat and legal place of the arbitration shall be San Francisco, California. Each Party shall nominate one arbitrator and the third arbitrator shall be nominated by the two Party-nominated arbitrators within [*] after the second arbitrator's appointment. If a Party does not nominate its arbitrator within [*] following the expiry of the allotted period, then such arbitrator shall be appointed by the ICC in accordance with its rules. Any arbitrator appointed by JAMS shall have at least ten (10) years' experience in the pharmaceutical industry. The arbitration shall be conducted, and all documents submitted to the arbitrators shall be, in English. Each Party shall bear its own legal costs for its counsel and other expenses, and the Parties shall equally share the costs of the arbitration; provided that the arbitral tribunal shall have the discretion to provide that the losing party is responsible for all or a portion of such arbitration and legal costs, in such case the arbitral award will so provide. The arbitrators shall have no power to award damages prohibited pursuant to Section 12.6. In no event shall the

[*] = Certain confidential information contained in this document, marked by brackets, has been omitted because it is both (I) not material and (II) would be competitively harmful if publicly disclosed.

arbitrators assign a value to any issue greater than the greatest value for such issue claimed by either Party or less than the smallest value for such issue for such item claimed by either Party. The award shall be final and binding upon the Parties and the Parties undertake to carry out any award without delay. Judgment on the award may be entered in any court of competent jurisdiction. Except to the extent necessary to confirm, enforce, or challenge an award of the arbitration, to protect or pursue a legal right, or as otherwise required by Applicable Law or regulation or securities exchange, neither Party nor any arbitrator may disclose the existence, content, or results of any arbitration hereunder without the prior written consent of both Parties. Notwithstanding anything to the contrary in the foregoing, in no event shall an arbitration be initiated after the date when commencement of a legal or equitable proceeding based on the dispute, controversy, or claim would be barred by the applicable statute of limitations. Any Disputes concerning the propriety of the commencement of the arbitration shall be finally settled by the arbitral tribunal.

(d) Subject Matter Exclusions. Notwithstanding the provisions of Section 14.3(c), any Dispute not resolved internally by the Parties pursuant to Section 14.3(c) that involves the validity, enforceability, or infringement of a Patent relevant to this Agreement (a) that is issued in the United States shall be subject to actions before the United States Patent and Trademark Office and/or submitted exclusively to the federal court located in the jurisdiction of the district where any of the defendants resides; and (b) that is issued in any other country shall be brought before an appropriate regulatory or administrative body or court in that country, and the Parties hereby consent to the jurisdiction and venue of such courts and bodies.

(e) Interim Relief. Notwithstanding anything herein to the contrary, nothing in this Section 14.3 shall preclude either Party from seeking interim or provisional relief, including a temporary restraining order, preliminary injunction, or other interim equitable relief concerning a Dispute in any court of competent jurisdiction before or after the initiation of an arbitration as set forth in Section 14.3(c), if necessary to protect the interests of such Party. This Section shall be specifically enforceable.

14.4 Force Majeure. The Parties shall be excused from the performance of their obligations under this Agreement (other than the payment of monies owed to the other Party) to the extent that such performance is prevented by force majeure and the non-performing Party promptly provides notice of the prevention to each other Party. Such excuse shall be continued so long as the condition constituting force majeure continues and the nonperforming Party takes reasonable efforts to remove the condition. For purposes of this Agreement, force majeure means acts of God, strikes or other concerted acts of workers, civil disturbances, fires, earthquakes, acts of terrorism, floods, explosions, riots, war, rebellion, sabotage or failure or default of public utilities or common carriers or similar conditions beyond the control of the Parties.

14.5 Notices. Any notice required or permitted to be given under this Agreement shall be in writing, shall specifically refer to this Agreement and shall be deemed to have been sufficiently given for all purposes if such notice is timely and is: (a) mailed by first class certified or registered mail, postage prepaid, return receipt requested, (b) sent by express delivery service, or (c) personally delivered. Unless otherwise specified in writing, the mailing addresses of the Parties shall be as described below.

For Exelixis:	Exelixis, Inc. 1851 Harbor Bay Parkway Alameda, CA 94502 Attn: EVP and General Counsel
With invoices to:	[*]
For Roche:	F. Hoffmann-La Roche Ltd Grenzacherstrasse 124 CH-4070 Basel, Switzerland Attention: Group Legal Department
With invoices to:	Genentech, Inc. 1 DNA Way South San Francisco, California 94080 Attention: Customer Finance

[*] = Certain confidential information contained in this document, marked by brackets, has been omitted because it is both (I) not material and (II) would be competitively harmful if publicly disclosed.

Any such communication shall be deemed to have been received when delivered. It is understood and agreed that this Section 14.5 is not intended to govern the day-to-day business communications necessary between the Parties in performing their duties, in due course, under the terms of this Agreement.

14.6 Waiver. The waiver by either Party of any right under this Agreement or of the failure to perform or of a breach by the other Party shall not be deemed a waiver of any other right hereunder or of any other breach or failure by such other Party whether of a similar nature or otherwise. Any waiver by a Party of a particular term or condition will be effective only if set forth in a written instrument duly executed by or on behalf of the Party waiving such term or condition.

14.7 No Strict Construction. This Agreement has been prepared jointly and shall not be strictly construed against either Party. No presumption as to construction of this Agreement shall apply against either Party with respect to any ambiguity in the wording of any provision(s) of this Agreement irrespective of which Party may be deemed to have authored the ambiguous provision(s).

14.8 Independent Contractor. The Parties' relationship, as established by this Agreement, is solely that of independent contractors. This Agreement does not create any partnership, joint venture, or similar business relationship between the Parties. Neither Party is a legal representative of the other Party, and neither Party can assume or create any obligation, representation, warranty, or guarantee, express or implied, on behalf of the other Party for any purpose whatsoever.

14.9 Assignment; Licensees.

(a) Assignment. Except as expressly provided hereunder, neither this Agreement nor any rights or obligations hereunder may be assigned or otherwise transferred by either Party without the prior written consent of the other Party (which consent shall not be unreasonably withheld, conditioned, or delayed); provided, however, that either Party may assign or otherwise transfer this Agreement and its rights and obligations hereunder without the other Party's consent:

(i) in connection with the transfer or sale of all or substantially all of the business or assets of such Party relating to this Agreement to a Third Party, whether by merger, consolidation, divesture, restructure, sale of stock, sale of assets, or otherwise; provided that in the event of any such transaction (whether this Agreement is actually assigned or is assumed by the acquiring Party by operation of law (e.g., in the context of a reverse triangular merger)), the intellectual property rights of the acquiring Party to such transaction (if other than one of the Parties to this Agreement) shall not be included in the technology for which rights have been granted under this Agreement, and notice is provided to the other Party; or

(ii) to an Affiliate, provided that if the entity to which this Agreement is assigned ceases to be an Affiliate of the assigning Party, the Agreement shall be automatically assigned back to the assigning Party or its successor.

The rights and obligations of the Parties under this Agreement shall be binding upon and inure to the benefit of the successors and permitted assigns of the Parties, and the name of a Party appearing herein will be deemed to include the name of such Party's successors and permitted assigns to the extent necessary to carry out the intent of this Section 14.9. Any assignment not in accordance with this Section 14.9 shall be null and void and of no legal effect.

(b) Licensees. If a Party grants a Third Party a license (other than a license solely to make a Product for a Party and other than any license rights granted Ipsen for the Ipsen Territory and Takeda for the Takeda Territory) to develop and commercialize its Single Agent Compound on a worldwide basis or in any geographic region and/or for all purposes or a limited field, such Party will obtain such Third Party licensee's agreement to abide by the relevant terms of this Agreement in the same manner as the licensor Party.

14.10 Headings. The captions to the several Sections and Articles hereof are not a part of this Agreement, but are included merely for convenience of reference only and shall not affect its meaning or interpretation.

[*] = Certain confidential information contained in this document, marked by brackets, has been omitted because it is both (I) not material and (II) would be competitively harmful if publicly disclosed.

14.11 Counterparts. This Agreement may be executed in two (2) or more counterparts, each of which shall be deemed an original, but all of which together shall constitute one (1) and the same instrument. This Agreement may be executed by facsimile or electronic (e.g., .pdf) signatures and such signatures shall be deemed to bind each Party hereto as if they were original signatures.

14.12 Severability. If, for any reason, any part of this Agreement is adjudicated invalid, unenforceable, or illegal by a court of competent jurisdiction, such adjudication shall not affect or impair, in whole or in part, the validity, enforceability, or legality of any remaining portions of this Agreement. The Parties will in such an instance use their best efforts to replace the invalid, unenforceable, or illegal provision(s) with valid, enforceable, and legal provision(s) that best implement the original intent of the Parties and purposes of this Agreement.

14.13 Further Assurance. Each Party shall duly execute and deliver, or cause to be duly executed and delivered, such further instruments and do and cause to be done such further acts and things, including the filing of such assignments, agreements, documents, and instruments, as may be necessary or as the other Party may reasonably request in order to perfect any license, assignment or other transfer or any properties or rights under, or pursuant, to this Agreement.

14.14 No Benefit to Third Parties. The representations, warranties, and agreements set forth in this Agreement are for the sole benefit of the Parties and their successors and permitted assigns, and they shall not be construed as conferring any rights on any other parties.

14.15 Interpretation. The headings of clauses contained in this Agreement preceding the text of the sections, subsections, and paragraphs hereof are inserted solely for convenience and ease of reference only and shall not constitute any part of this Agreement, or have any effect on its interpretation or construction. All references in this Agreement to the singular shall include the plural where applicable. Unless otherwise specified, references in this Agreement to any Article shall include all Sections, subsections, and paragraphs in such Article, references to any Section shall include all subsections and paragraphs in such Section, and references in this Agreement to any subsection shall include all paragraphs in such subsection. The word “including” and similar words means including without limitation. The word “or” means “and/or” unless the context dictates otherwise because the subjects of the conjunction are, or are intended to be, mutually exclusive. The words “herein”, “hereof”, and “hereunder” and other words of similar import refer to this Agreement as a whole and not to any particular Section or other subdivision. All references to days in this Agreement mean calendar days, unless otherwise specified. Ambiguities and uncertainties in this Agreement, if any, shall not be interpreted against either Party, irrespective of which Party may be deemed to have caused the ambiguity or uncertainty to exist. This Agreement has been prepared in the English language and the English language shall control its interpretation. In addition, all notices required or permitted to be given hereunder, and all written, electronic, oral, or other communications between the Parties regarding this Agreement shall be in the English language.

[Signature page follows]

[*] = Certain confidential information contained in this document, marked by brackets, has been omitted because it is both (I) not material and (II) would be competitively harmful if publicly disclosed.

IN WITNESS WHEREOF, the Parties hereto, intending to be legally bound hereby, have caused this Clinical Trial Collaboration Agreement to be executed by their duly authorized representatives as of the Effective Date.

Exelixis, Inc.

By: /s/ Michael M. Morrissey, Ph.D.

Name: Michael M. Morrissey, Ph.D.

Title: President and CEO

Date: 18 December 2019

F. Hoffmann-La Roche Ltd

By: /s/ Laurence Lehuu

Name: Laurence Lehuu

Title: Operation Program Leader

Date: 18 December 2019

By: /s/ Louis DuPasquier

Name: Louis DuPasquier

Title: Legal Counsel

[*] = Certain confidential information contained in this document, marked by brackets, has been omitted because it is both (I) not material and (II) would be competitively harmful if publicly disclosed.

2.

[Signature Page]

[*] = Certain confidential information contained in this document, marked by brackets, has been omitted because it is both (I) not material and (II) would be competitively harmful if publicly disclosed.

Exhibit A

[*]

Exhibit A-1

[*] = Certain confidential information contained in this document, marked by brackets, has been omitted because it is both (I) not material and (II) would be competitively harmful if publicly disclosed.

Exhibit B

Investors Contact:
Susan Hubbard
EVP, Public Affairs and
Investor Relations
Exelixis, Inc.
(650) 837-8194
shubbard@exelixis.com

Media Contact:
Lindsay Treadway
Senior Director, Public Affairs
and Advocacy Relations
Exelixis, Inc.
(650) 837-7522
ltreadway@exelixis.com

EXELIXIS ENTERS INTO A CLINICAL COLLABORATION FOR THREE PHASE 3 COMBINATION TRIALS FOR PATIENTS WITH ADVANCED SOLID TUMORS

– New pivotal trials will evaluate the combination of cabozantinib and atezolizumab in patients with advanced non-small cell lung cancer, castration-resistant prostate cancer and renal cell carcinoma –

– Collaboration based on data from phase 1b COSMIC-021 trial –

ALAMEDA, Calif. – December 19, 2019 – Exelixis, Inc. (NASDAQ: EXEL) today announced a collaboration agreement with Roche to evaluate cabozantinib (CABOMETYX®), Exelixis' small molecule inhibitor of receptor tyrosine kinases, in combination with atezolizumab (TECENTRIQ®), Roche's PD-L1 immune checkpoint inhibitor, in patients with locally advanced or metastatic solid tumors. The clinical program, which will be co-funded by the companies, is expected to include three phase 3 pivotal trials in advanced non-small cell lung cancer (NSCLC), castration-resistant prostate cancer (CRPC) and renal cell carcinoma (RCC).

"Encouraging phase 1 data suggests this combination of cabozantinib and atezolizumab may improve outcomes for patients with prostate, lung and kidney cancers, and we look forward to collaborating with Roche to learn more in these pivotal trials," said Michael M. Morrissey, Ph.D., President and Chief Executive Officer of Exelixis. "This clinical collaboration is an important further step in our committed efforts to maximize the value of the cabozantinib franchise through these cost-sharing clinical collaborations in additional high-impact indications, while building value with new compounds from internal and external sources in 2020 and beyond."

The clinical development collaboration builds on encouraging activity observed in the phase 1b COSMIC-021 trial. The trial is currently enrolling 24 expansion cohorts in 12 tumor types including RCC, NSCLC and CRPC.

TECENTRIQ® (atezolizumab) is a registered trademark of Genentech, a member of the Roche Group.

About CABOMETYX® (cabozantinib)

[*] = Certain confidential information contained in this document, marked by brackets, has been omitted because it is both (I) not material and (II) would be competitively harmful if publicly disclosed.

In the U.S., CABOMETYX tablets are approved for the treatment of patients with advanced RCC and for the treatment of patients with hepatocellular carcinoma who have been previously treated with sorafenib. CABOMETYX tablets have also received regulatory approvals in the European Union and additional countries and regions worldwide.

About Exelixis' Collaboration with Ipsen
On February 29, 2016, Exelixis and Ipsen jointly announced an exclusive licensing agreement for the commercialization and further development of cabozantinib indications outside of the United States, Canada and Japan. On December 21, 2016, this agreement was amended to include commercialization rights for Ipsen in Canada. Under the parties' collaboration agreement, if Ipsen opts to participate in funding these phase 3 trials, or future studies, Ipsen will have access to the respective study results to support potential future regulatory submissions in their territory.

About Exelixis' Collaboration with Takeda
On January 30, 2017, Exelixis and Takeda jointly announced an exclusive licensing agreement for the commercialization and further development of cabozantinib indications in Japan. Under the parties' collaboration agreement, if Takeda opts to participate in funding these phase 3 trials, or future studies, Takeda will have access to the respective study results to support potential future regulatory submissions in their territory.

Exelixis holds the exclusive rights to develop and commercialize cabozantinib in the United States.

About Exelixis
Founded in 1994, Exelixis, Inc. (NASDAQ: EXEL) is a commercially successful, oncology-focused biotechnology company that strives to accelerate the discovery, development and commercialization of new medicines for difficult-to-treat cancers. Following early work in model system genetics, we established a broad drug discovery and development platform that has served as the foundation for our continued efforts to bring new cancer therapies to patients in need. Our discovery efforts have resulted in four commercially available products, CABOMETYX® (cabozantinib), COMETRIQ® (cabozantinib), COTELLIC® (cobimetinib) and MINNEBRO® (esaxerenone), and we have entered into partnerships with leading pharmaceutical companies to bring these important medicines to patients worldwide. Supported by revenues from our marketed products and collaborations, we are committed to prudently reinvesting in our business to maximize the potential of our pipeline. We are supplementing our existing therapeutic assets with targeted business development activities and internal drug discovery — all to deliver the next generation of Exelixis medicines and help patients recover stronger and live longer. Exelixis is a member of the Standard & Poor's (S&P) MidCap 400 index, which measures the performance of profitable mid-sized companies. For more information about Exelixis, please visit www.exelixis.com, follow @ExelixisInc on Twitter or like Exelixis, Inc. on Facebook.

Exelixis Forward-Looking Statements
This press release contains forward-looking statements, including, without limitation, statements related to: Exelixis' expectation that the clinical program co-funded by Exelixis and Roche will include three phase 3 pivotal trials evaluating the combination of cabozantinib and atezolizumab in NSCLC, CRPC and RCC; the potential for the combination of cabozantinib and atezolizumab to improve outcomes for patients with prostate, lung and kidney cancers; Exelixis' belief that it can maximize the value of the cabozantinib franchise through these cost-sharing clinical collaborations in additional high-impact indications, while building value with new compounds from internal and external sources in 2020 and beyond; and Exelixis' plans to reinvest in its business to maximize the potential of the company's pipeline, including through targeted business development activities and internal drug discovery. Any statements that refer to expectations, projections or other characterizations of future events or circumstances are forward-looking statements and are based upon Exelixis' current plans, assumptions, beliefs, expectations, estimates and projections. Forward-looking statements involve risks and uncertainties. Actual results and the timing of events could differ materially from those anticipated in the forward-looking statements as a result of these risks and uncertainties, which

[*] = Certain confidential information contained in this document, marked by brackets, has been omitted because it is both (I) not material and (II) would be competitively harmful if publicly disclosed.

include, without limitation: risks and uncertainties related to regulatory review and approval processes and Exelixis' compliance with applicable legal and regulatory requirements; the potential failure of the combination of cabozantinib and atezolizumab to demonstrate safety and/or efficacy in COSMIC-021 or in future phase 3 pivotal trials; uncertainties inherent in the product development process; the costs of conducting clinical trials, including the ability or willingness of Exelixis' collaboration partners to invest in the resources necessary to complete the trials; Exelixis' dependence on third-party vendors for the development, manufacture and supply of cabozantinib; Exelixis' ability to protect its intellectual property rights; market competition, including the potential for competitors to obtain approval for generic versions of CABOMETYX; changes in economic and business conditions; and other factors affecting Exelixis and its development programs discussed under the caption "Risk Factors" in Exelixis' Quarterly Report on Form 10-Q filed with the Securities and Exchange Commission (SEC) on October 30, 2019, and in Exelixis' future filings with the SEC. All forward-looking statements in this press release are based on information available to Exelixis as of the date of this press release, and Exelixis undertakes no obligation to update or revise any forward-looking statements contained herein.

# # #

Exhibit B-3

[*] = Certain confidential information contained in this document, marked by brackets, has been omitted because it is both (I) not material and (II) would be competitively harmful if publicly disclosed.

Exhibit C

CLINICAL SUPPLY AGREEMENT SUPPLEMENT TEMPLATE
{insert consecutive numbers 1, 2, 3, etc}

This Clinical Supply Agreement Supplement (each, a "CSA Supplement") is entered into as of {DATE} (the "Effective Date"), by and between **Exelixis, Inc.** a Delaware corporation having an address at 1851 Harbor Bay Parkway, Alameda, CA 94502 ("**Exelixis**"), and **F. Hoffmann-La Roche Ltd**, a Swiss corporation having an address at Grenzacherstrasse 124, CH-4070 Basel, Switzerland ("**Roche**"). Exelixis and Roche may be referred to herein individually as a "**Party**," or collectively as the "**Parties**".

WHEREAS, Roche and Exelixis are parties to that Joint Clinical Research Agreement, effective as of December 18, 2019 (the "Agreement");

WHEREAS, pursuant to the terms of the Agreement, {Exelixis/Roche} desires to conduct a clinical trial entitled {INSERT STUDY TITLE} (the "Study"); and

WHEREAS, {Exelixis/Roche} agrees, consistent with the terms of the Agreement and this CSA Supplement, to provide the {Exelixis/Roche} COMPOUND for the Study.

NOW, THEREFORE, in consideration of the premises and of the following mutual promises, covenants and conditions and any sums to be paid, the Parties hereto agree as follows:

1. SUPPLY OF CLINICAL TRIAL MATERIAL.

(a) Shipment of the {Exelixis/Roche} Compound will require a lead time of approximately [*] after the provision of an IND number (for shipments to the US) and a lead time of approximately [*] for shipments to the EU/ROW and an import license (depending on import requirements) from the time of {Exelixis/Roche} request. {Exelixis/Roche} will provide {Exelixis/Roche} with a [*] demand forecast over the course of the trial. Individual supply orders must be placed by {Exelixis/Roche} with a lead time of [*] after receipt of a complete {Form} for Drug Supply by {Exelixis/Roche} and an Import License (depending on Import License). Individual order quantities may be adjusted as per mutual agreement between the supply teams, by up to [*] from the most recent demand forecast, provided this does not adversely affect conduct of the {Exelixis/Roche} Study and is available at {Exelixis/Roche}. If greater than [*] adjustment is required, both parties will discuss as applicable.

{Exelixis/Roche} will provide {Exelixis/Roche} with the following {Exelixis/Roche} Compound:

{compound name}

{describe packaging[*]}

{describe product[*]}

The total estimated demand of {units} and the estimated timeline for the Compound will be documented and communicated in the form set forth in ATTACHMENT 1. These estimated supply and delivery details will be updated [*] and would be documented in the [*] forecast {Exelixis/Roche} will provide to {Exelixis/Roche}:

(b) Shipment Delivery: "Sender" shall make delivery of Product to "Recipient" in accordance with Section 5.1b or 5.2b of the Agreement, as applicable. [*].

(c) Product Documents: {Exelixis/Roche} shall provide all relevant documents such as, but not limited to product value and appropriate supporting documents required by local regulatory authority for "Import License Application" during the conduct of the trial in accordance to terms set forth in section (a) and (b).

[*] = Certain confidential information contained in this document, marked by brackets, has been omitted because it is both (I) not material and (II) would be competitively harmful if publicly disclosed.

(d) Inspection and Acceptance of Product: In order to reject delivery of any portion of such delivered shipment in accordance to terms set forth in section (a), (b) and (c); "Recipient" must provide written notice to "Sender" of such rejection specifying [*] the reasons for such rejection within [*]. If no such notice of rejection is received within such [*], "Recipient" will be deemed to have accepted compound provided by "Sender". Following any notice of rejection given by "Recipient" in accordance with this Section, "Sender" shall have the right to inspect "Sender" Compound in question and "Recipient" shall cooperate with "Sender" inspection, including, upon "Sender" request, providing "Sender" with samples of the "Sender" Compound in question for testing. If "Sender" agrees with such notice of nonconformity, "Sender" shall replace such "Sender" Compound as soon as reasonably practicable after receipt of notification of such nonconformity.

Product is to be delivered to:

2. **TERM.** This CSA Supplement shall continue until the Study is completed and all information-sharing obligations under the Agreement are completed, or until terminated as provided in the Agreement.

3. **INCORPORATION BY REFERENCE.** The CSA Supplement is governed by the terms and conditions of the Agreement and forms an integral part of the Agreement. All defined terms within the Agreement shall have the same meaning when used in this CSA Supplement unless specifically defined in this CSA Supplement. If the event of a conflict between a term or terms in this CSA Supplement and a term or terms of the Agreement, the term(s) of the Agreement shall prevail.

4. **NOTICES.** In addition to the recipients of notice listed in the Agreement, notices applicable to this CSA Supplement directed to Roche shall be sent to the attention of {_____}. Notices applicable to this CSA Supplement directed to Exelixis shall be sent to the attention of {_____}.

IN WITNESS WHEREOF, the respective representatives of the parties have executed this CSA Supplement as of the day and year shown on the first page hereof.

F. HOFFMANN-LA ROCHE LTD

Signature	Signature
_____	_____
Name	Name

Exelixis, Inc.

Signature	Signature
_____	_____
Name	Name

ATTACHMENT 1:

<Study Number>,<Enter Study Protocol Description>

[*****]

[*] = Certain confidential information contained in this document, marked by brackets, has been omitted because it is both (I) not material and (II) would be competitively harmful if publicly disclosed.

[*] = CERTAIN CONFIDENTIAL INFORMATION CONTAINED IN THIS DOCUMENT, MARKED BY BRACKETS, HAS BEEN OMITTED BECAUSE IT IS BOTH (I) NOT MATERIAL AND (II) WOULD BE COMPETITIVELY HARMFUL IF PUBLICLY DISCLOSED.

EXHIBIT 10.63

SUPPLEMENT TO THE

JOINT CLINICAL RESEARCH AGREEMENT

This **SUPPLEMENT TO THE JOINT CLINICAL RESEARCH AGREEMENT** (the "***Supplement***") is made and entered into effective as of December 18, 2019 (the "***Effective Date***") by and among Exelixis, Inc. a Delaware corporation, located at 1851 Harbor Bay Parkway, Alameda, CA 94501, ("***Exelixis***"), F. Hoffmann-La Roche Ltd, a Swiss corporation having an address at Grenzacherstrasse 124, CH 4070 Basel, Switzerland ("***Roche***"), and Ipsen Pharma SAS, a French Corporation having an address at 65 Quai Georges Gorse, 92100 Boulogne-Billancourt, France ("***Ipsen***"). The terms in this Supplement with initial letters capitalized, whether used in the singular or the plural, shall have the meaning set forth herein, or if not defined herein, as set forth in the Agreement.

RECITALS

WHEREAS, Exelixis and Roche have entered into a certain Joint Clinical Research Agreement dated December 18, 2019 (the "***Agreement***") to collaborate with each other to sponsor one or more clinical trials of a combination therapy using Exelixis' tyrosine kinase inhibitor known as ***"Cabozantinib"***, certain rights to which are licensed by Exelixis to, and shared by Exelixis with Ipsen Pharma SAS (***"Ipsen")*** and Takeda Pharmaceutical Company Ltd. (***"Takeda"***), and Roche's human monoclonal antibody that binds PD-L1 known as ***"Atezolizumab"***.

WHEREAS, Exelixis and Ipsen entered into a Collaboration and License Agreement dated February 29, 2016 (such agreement, as amended from time to time, the ***"Ipsen-Exelixis Agreement"***), wherein Exelixis and Ipsen formed a collaboration for the continued development of and commercialization of Cabozantinib and wherein Exelixis granted to Ipsen certain exclusive rights to develop and commercialize Cabozantinib worldwide, with the exception of the United States and Japan (the "***Ipsen Territory***");

WHEREAS, Exelixis, under the Agreement, shall grant to Roche, *inter alia*, certain patent rights, access to Regulatory Documentation, and Right of Reference as contemplated therein;

WHEREAS, Roche further requires from Ipsen certain additional patent rights, access to Regulatory Documentation, and Right of Reference under Ipsen's control in the Ipsen Territory as contemplated in the Agreement;

WHEREAS, in consideration of Ipsen granting to Roche certain patent rights, access to Regulatory Documentation, and Right of Reference under Ipsen's control in the Ipsen Territory, Ipsen requires from Roche and Exelixis certain additional patent rights, access to Regulatory Documentation and Right of Reference under Roche's control, which shall be obtained from Roche for the sole purpose of submitting any portion of the Combined Therapy Study Data to support certain of Ipsen's regulatory filings and approval in the Ipsen Territory for a Combination Therapy under the Ipsen-Exelixis Agreement; and

WHEREAS, under the Agreement, Ipsen as Exelixis' collaboration partner and exclusive licensee in the Ipsen Territory will contribute to the fulfillment of the clinical trials contemplated in the Agreement, and will be provided data from Roche and Exelixis as well as Exelixis' interest in certain patent rights, Regulatory Documentation and Right of Reference under Exelixis' control arising from such clinical trials and the Agreement.

NOW, THEREFORE, in consideration of the foregoing premises and the mutual promises and covenants contained herein, Exelixis, Roche and Ipsen agree as follows:

1. COLLABORATION SCOPE; BACKGROUND

1.1 Scope of Collaboration between Exelixis and Roche. Exelixis and Roche intend, pursuant to the Agreement, to collaborate to conduct (i) the clinical trials identified in Exhibit A of the Agreement (referred to as the "***Initial Trials***") and (ii) such other clinical trials evaluating a Combined Therapy of the Roche Compound with the Exelixis Compound as Exelixis and Roche may agree to conduct pursuant to the terms of the Agreement (any such trial in (i) or (ii), a "***Combined Therapy Trial***").

1.2 Protocol review and conduct of Combined Therapy Trials.

(a) The final Protocol for each Combined Therapy Trial shall be subject to review and approval of the Exelixis-Roche JPT under the Agreement and review of the Exelixis-Ipsen Joint Steering Committee (as described in the Ipsen-Exelixis Agreements) before such Combined Therapy Trial can be initiated.

(b) Either Exelixis or Roche shall be primarily responsible for the conduct of each Combined Therapy Trial (either Exelixis or Roche, with respect to such Combined Therapy Trial, the "***Conducting Party***", and the other of Exelixis or Roche, with respect to the same Combined Therapy Clinical trial, the "***Non-Conducting Party***"). In each Combined Therapy Trial the Conducting Party will be the sponsor of record. Unless otherwise required by a Regulatory Authority, for each Combined Therapy Trial, the Conducting Party shall determine whether a combination IND (a "***Combined Therapy IND***") is necessary.

(c) Ipsen acknowledges and agrees to Article 6 of the Agreement, which sets forth the Responsibilities of the Conducting Party and the Non-Conducting Party in fulfillment of the Combined Therapy Trials.

1.3 Certain Definitions.

(a) The following terms when used in connection with Ipsen in this Supplement shall have the meaning set forth in the Agreement except that any reference in such terms to "a Party" or "Such Party" or "the applicable Party" shall be replaced with reference to "Ipsen" and any reference to "the other Party" shall be replaced with reference to "Roche" or "Exelixis" as the context requires: "***Affiliates***", "***Commercially Reasonable Efforts***", "***Control***" and "***Controlled***".

(b) When granted by Ipsen in this Supplement "***Right of Reference***" shall mean, with regard to Roche as the Conducting Party, allowing the applicable Regulatory Authority in a country to have access to relevant information (by cross-reference, incorporation by reference or otherwise) contained in Regulatory Documentation (and any data contained therein) filed with such Regulatory Authority with respect to Exelixis Compound (and, in the case of Roche as the Non-Conducting Party, the Right of Reference to the IND or the Combined Therapy IND), only to the extent necessary for the conduct of a Combined Therapy Trial in such country or as otherwise expressly permitted or required under the Agreement and/or this Supplement to enable Roche to exercise its rights or perform its obligations under the Agreement and/or this Supplement, and, except as to information contained in the IND or Combined Therapy IND relating to the Combined Therapy, without the disclosure of such information to Roche.

2. APPROVALS BY IPSEN AND EXELIXIS

2.1 Combined Therapy Trial Approvals. Ipsen and Exelixis have agreed to the division of responsibilities for the Initial Trials, including but not limited to Roche's right to be the Conducting Party and holder of the IND, or Combined Therapy IND as necessary, as identified in Exhibit A to the Agreement. Ipsen and Exelixis have agreed to amend the Global Development Plan (as that term is defined in the Ipsen-Exelixis Agreements) to include the Combined Therapy Trials as described in Exhibit A of the Agreement and the Protocols for such trials. Consistent with its agreement to

said Exhibit A, Ipsen agrees to consider, in good faith, Protocol(s) for such additional Combined Therapy Trials as may be approved by the Exelixis-Roche JPT, and if acceptable and approved by the Exelixis-Ipsen Joint Steering Committee under the Ipsen-Exelixis Agreement, those Combined Therapy Trials will be added to the Ipsen-Exelixis Global Development Plan under the Ipsen-Exelixis Agreement in due course. If a Combined Therapy Trial is not approved by the Exelixis-Ipson Joint Steering Committee, Exelixis shall act to effectuate its obligations under the Agreement independent of Ipsen.

2.2 Approved Protocols. With respect to Combined Therapy Trials for which the Protocols are: (a) reviewed and approved by the Exelixis-Roche JPT under the Agreement; and (b) approved by the Exelixis-Ipsen Joint Steering Committee and added to the Global Development Plan under the Ipsen-Exelixis Agreements; the rights and obligations of Exelixis, Roche, and Ipsen under such Protocol, this Supplement and the Agreement will prevail over any conflicting terms in the Ipsen-Exelixis Agreements (and for any amendments to the Agreement, provided that Ipsen will have reviewed any such amendments in full).

2.3 Ipsen's participation in the Exelixis-Roche JPT. If a Combination Therapy is approved by the Exelixis-Ipsen Joint Steering Committee as set forth in Section 2.1 above, Ipsen's representatives having expertise in development activities and regulatory affairs will have the right to participate in and contribute to the Exelixis-Roche JPT for the relevant Combination Therapy as a non-voting attendee, as approved by the JPT pursuant to Section 3.4(c) of the Agreement. Exelixis shall ensure to inform Ipsen of the date of such Exelixis-Roche JPT meeting and invite Ipsen's identified representatives who will participate in the Exelixis-Roche JPT as soon as Exelixis and Roche would have agreed to convene such JPT meeting. Exelixis shall also ensure that relevant agendas of the Exelixis-Roche JPT for the above-mentioned meetings are circulated to such Ipsen's identified representative at least [*] prior to such meetings.

3. GRANTS, REPRESENTATIONS, AND WARRANTIES BY IPSEN

3.1 License Grant. Ipsen hereby grants, and shall cause its Affiliates to grant, to Roche a non-exclusive, worldwide, non-transferable, free of charge and royalty-free license (and for the avoidance of doubt, free and clear of any payment by Roche to Ipsen and/or Exelixis) under Ipsen's interest in the Exelixis Independent Patent rights, Exelixis Technology, and Exelixis Regulatory Documentation and under the Licensee Technology (as the term is defined in the Ipsen-Exelixis Agreement) in the Ipsen Territory to use the Exelixis Compound, solely to the extent necessary to discharge Roche's obligations under the Agreement with respect to the conduct of the Combined Therapy Trials.

3.2 Sublicenses. Roche shall further have the right to grant sublicenses, under the licenses granted to it under Section 3.1 above, to Affiliates and to Third Parties, solely to the extent required for a an Affiliate or Third Party to perform its duties with respect to the conduct of the Combined Therapy Trials, solely as necessary to assist Roche in carrying out its responsibilities with respect to the Combined Therapy Trials, and otherwise in accordance with the Agreement.

3.3 Right of Reference. Ipsen hereby grants, and shall cause its Affiliates to grant, to Roche a Right of Reference to the relevant Regulatory Documentation Controlled by Ipsen and its Affiliates for the Exelixis Compound and the Combined Therapy (i) for the conduct of any Combined Therapy Trial, and (ii) with respect to regulatory filings and approvals, solely to the extent required to submit regulatory filings and seek approvals for the Roche Compound as part of a Combined Therapy or if required by the relevant Regulatory Authority (which right shall survive any expiration or termination of this Supplement and the Agreement). In such case, Ipsen shall reasonably cooperate with Exelixis and Roche and make written authorizations and other filings with the applicable Regulatory Authority required to effect such Right of Reference.

[*] = Certain confidential information contained in this document, marked by brackets, has been omitted because it is both (I) not material and (II) would be competitively harmful if publicly disclosed.

3.4 No Implied Licenses. Except as specifically set forth in this Supplement, no right or license or other intellectual property interest, shall be granted to Roche by Ipsen by implication or otherwise in any intellectual property of Ipsen, including any Patent Rights controlled by Ipsen or its Affiliates not specifically licensed herein.

3.5 Representations and Warranties. Ipsen represents and warrants that: (a) it has the corporate power and authority and the legal right to enter into this Supplement and perform its obligations hereunder; (b) it has the corporate power and authority and the legal right to assist in the performance of the obligations under the Agreement that are agreed to by Exelixis, but require further licenses, rights, and/or assistance from Ipsen; (c) it has reviewed the Agreement in full, and to the extent not otherwise provided for under this Supplement, it shall grant all licenses and rights that are necessary and desirable, and provide such assistance as is reasonably necessary, for Exelixis and Roche to exercise their rights and to fulfill their obligations under the Agreement and/or this Supplement.

4. GRANTS, REPRESENTATIONS, AND WARRANTIES BY EXELIXIS

4.1 License Grant.

(a) Subject to the terms and conditions of the Agreement, Exelixis hereby grants to Ipsen a non-exclusive, non-transferable, free of charge and royalty-free sublicense (and for the avoidance of doubt, free and clear of any payment by Ipsen to Roche) under the Roche Independent Patents, Roche Technology, and Roche Regulatory Documentation, solely to the extent that Exelixis has been granted license rights to the Roche Independent Patent rights, Roche Technology, Roche Regulatory Documentation, and Right of Reference to Roche Regulatory Documentation under the Agreement. Such sublicense rights are limited to use of any portion of the Combined Therapy Study Data and Right of Reference reasonably needed to support regulatory filing and approval of a Combined Therapy, or if required by relevant Regulatory Authority, in the Ipsen Territory in accordance with and under the Ipsen-Exelixis Agreement (which right shall survive any expiration or termination of this Supplement and the Agreement). In such case, Roche and Exelixis shall reasonably cooperate with Ipsen to make written authorizations and other filings with the applicable Regulatory Authority reasonably required to effect such Right of Reference.

(b) Subject to the terms and conditions of the Agreement, Exelixis hereby grants, and shall cause its Affiliates to grant, to Ipsen an exclusive, non-transferable, royalty-free sublicense under (i) Exelixis' interest in the Combined Therapy Patents and Combined Therapy Inventions, (ii) Exelixis Technology, (iii) Exelixis Independent Patents, (iv) Exelixis Study Inventions, (v) Exelixis Study Patents and (vi) Exelixis Regulatory Documentation, in the Ipsen Territory for purposes of using any portion of the Combined Therapy Study Data to support Ipsen's regulatory approval of a Combined Therapy in the Ipsen Territory, or if required by the relevant Regulatory Authority, and performing Ipsen's obligations under the Ipsen-Exelixis Agreement, including conducting development, regulatory, and commercialization activities in accordance with the Ipsen-Exelixis Agreement.

4.2 Sublicenses. Ipsen shall further have the right to grant sublicenses, under the licenses granted to it under Section 4.1 above, to Affiliates and to Third Parties, solely to the extent required for an Affiliate or Third Party to perform its duties, solely as necessary to assist Ipsen in carrying out its responsibilities with respect to using any portion of the Combined Therapy Study Data to support Ipsen's regulatory filing and approval for a Combined Therapy in the Ipsen Territory, or if required by the relevant Regulatory Authority.

4.3 No Implied Licenses. Except as specifically set forth in this Supplement, no right or license or other intellectual property interest, shall be granted by Exelixis to Ipsen by implication or otherwise in any intellectual property of Roche, including any Patent Rights controlled by Roche or its Affiliates not specifically licensed herein.

4.4 Additional Combined Therapy Trials. In the event Exelixis and Roche decide to conduct further Combined Therapy Trials beyond the Initial Trials as set forth in Section 6.5 of the Agreement, Exelixis shall ensure that Ipsen is

granted access to any data arising from such additional Combined Therapy Trials, subject to Ipsen agreeing to amend the Global Development Plan of the Ipsen-Exelixis Agreement to include such additional Combined Therapy Trials and the Protocol for such Trials.

4.5 Representations and Warranties.

(a) Exelixis represents and warrants that: (a) it has the corporate power and authority and the legal right to enter into this Supplement and perform its obligations hereunder; (b) it has the corporate power and authority and the legal right to assist in the performance the obligations under the Agreement that are agreed to with Roche, but require further licenses, rights, and/or assistance from Roche; (c) to the extent not otherwise provided for under this Supplement, it shall grant all licenses and rights that are necessary and desirable, and provide such assistance as is reasonably necessary, for Ipsen to exercise its rights and to fulfill its obligations under this Supplement.

(b) Roche represents and warrants that: (a) it has the corporate power and authority and the legal right to enter into this Supplement and perform its obligations hereunder; (b) it has the corporate power and authority and the legal right to assist in the performance the obligations under the Agreement that are agreed to with Exelixis, but require further licenses, rights, and/or assistance from Exelixis; (c) to the extent not otherwise provided for under this Supplement, it shall grant all licenses and rights that are necessary and desirable, and provide such assistance as is reasonably necessary, for Ipsen to exercise its rights and to fulfill its obligations under this Supplement.

5. CONDUCT AND COOPERATION

5.1 Conduct. Each of Exelixis, Roche, and Ipsen shall use Commercially Reasonable Efforts to perform and fulfill its respective activities under this Supplement, and shall do so in accordance with Applicable Law.

5.2 Cooperation. In the event that Roche, Exelixis, or Ipsen receives questions or requests from Regulatory Authorities in relation to obtaining or maintaining regulatory approvals for the Combination Therapy, Roche, Exelixis, and Ipsen shall cooperate with each other in the applicable Party's effort to obtain and maintain such regulatory approvals.

6. CONFIDENTIALITY

6.1 Confidential Information. Except to the extent expressly authorized by the Agreement or otherwise agreed in writing by the Parties, the Parties agree that, during the Term and for [*] thereafter, the receiving Party shall keep confidential and shall not publish or otherwise disclose, and shall not use for any purpose other than as expressly provided for in the Agreement, any Confidential Information of the other Party, and both Parties shall keep confidential and, subject to the remainder of this Article 6 shall not publish or otherwise disclose the terms of this Agreement. Each Party may use the other Party's Confidential Information only to the extent required to accomplish the purposes of this Agreement, including exercising its rights or performing its obligations under this Agreement. Each Party will use at least the same standard of care as it uses to protect proprietary or confidential information of its own (but no less than reasonable care) to ensure that its employees, agents, consultants, contractors, and other representatives do not disclose or make any unauthorized use of the other Party's Confidential Information. Each Party will promptly notify the other upon discovery of any loss or unauthorized use or disclosure of the other Party's Confidential Information. For clarity, Combined Therapy Study Data shall be treated as Confidential Information of both Parties and shall not be disclosed to Third Parties unless it falls within the exceptions set forth in Section 6.2 below or is reasonably necessary to be disclosed in order for a Party to exercise its rights under Section Article 6.

6.2 Exceptions. The obligations of confidentiality and restriction on use under Section 6.1 will not apply to any information that the receiving Party can prove by competent written evidence:

[*] = Certain confidential information contained in this document, marked by brackets, has been omitted because it is both (I) not material and (II) would be competitively harmful if publicly disclosed.

(a) is now, or hereafter becomes, through no act or failure to act on the part of the receiving Party, generally known or available to the public;

(b) is known by the receiving Party at the time of receiving such information, other than by previous disclosure of the disclosing Party, or its Affiliates, employees, agents, consultants, or contractors;

(c) is hereafter furnished to the receiving Party without restriction by a Third Party who has no obligation of confidentiality or limitations on use with respect thereto, as a matter of right; or

(d) is independently discovered or developed by the receiving Party without the use of the disclosing Party's Confidential Information.

6.3 Authorized Disclosure. Notwithstanding any other provision of this Agreement, each Party may disclose Confidential Information belonging to the other Party to the extent such disclosure is reasonably necessary in the following instances:

(a) prosecuting or defending litigation as permitted by this Agreement;

(b) complying with Applicable Law (including regulations promulgated by any securities exchange);

(c) disclosure, in connection with the performance of this Agreement, to Affiliates, permitted sublicensees, contractors, manufacturers, ethics committees and IRBs, academic institutions, consultants, agents, investigators, and employees engaged in connection with the performance of a Combined Therapy Trial, each of whom prior to disclosure must be bound by similar terms of confidentiality and non-use at least equivalent in scope to those set forth in this Article 6;

(d) disclosure of the Combined Therapy Study Data, Combined Therapy Inventions, and Combined Therapy Patents to Regulatory Authorities in connection with the development of the Combined Therapy, the Exelixis Compound, or the Roche Compound; and

(e) disclosure of relevant safety information contained within the Combined Therapy Study Data to investigators, IRBs, and/or ethics committees and Regulatory Authorities that are involved in other clinical trials of the Exelixis Compound with respect to Exelixis, and the Roche Compound with respect to Roche, and (in the event of a Material Safety Issue) to Third Parties that are collaborating with Exelixis or Roche, respectively in the conduct of such other clinical trials of the Exelixis Compound or the Roche Compound, in each case solely to the extent necessary for the conduct of such clinical trials and/or to comply with Applicable Law and regulatory requirements.

6.4 Notwithstanding the foregoing, in the event that a Party is required to make a disclosure of the other Party's Confidential Information pursuant to Section 6.3(a) or (b), it will, except where impracticable, give reasonable advance notice to the other Party of such disclosure and use efforts to secure confidential treatment of such Confidential Information at least as diligent as such Party would use to protect its own confidential information of a similar nature, but in no event less than reasonable efforts. In any event, the Parties agree to take all reasonable action to avoid disclosure of Confidential Information. Any information disclosed pursuant to any of Sections 10.3(a)-(e) shall remain Confidential Information and subject to the restrictions set forth in this Agreement.

7. MISCELLANEOUS

7.1 Full Force and Effect. This Supplement is deemed incorporated into, and governed by all other terms of, the Agreement. The provisions of the Agreement remain in full force and effect.

7.2 Term; Survival. This Supplement shall be effective as of the Effective Date and expire or terminate upon expiration or termination of the Agreement. The following Sections of this Supplement, all definitions relating thereto,

[*] = Certain confidential information contained in this document, marked by brackets, has been omitted because it is both (I) not material and (II) would be competitively harmful if publicly disclosed.

and any other provisions of this Supplement that by their nature are intended to survive expiration or termination of this Supplement shall survive any expiration or termination of this Supplement for any reason: Sections 1.3, 2.2, 3.3, 4.1, 4.2, 4.3, 4.5, 5.2, 6.1-6.4, 6.2, 6.3, 7.5 through 7.12, 7.14, and 7.16.

7.3 Governing Law. This Supplement shall be governed and construed in accordance with the internal laws of the State of California, USA, excluding any choice of law rules that may direct the application of the laws of another jurisdiction.

7.4 Force Majeure. The parties shall be excused from the performance of their obligations under this Supplement to the extent such performance is prevented by force majeure and the non-performing party promptly provides notice of the prevention to each other party. Such excuse shall be continued so long as the condition constituting force majeure continues and the non-performing party takes reasonable efforts to remove the condition. For purpose of this Supplement, force majeure means acts of God, strikes or other concerted acts of workers, civil disturbances, fires, earthquakes, acts of terrorism, floods, explosions, riots, war, rebellion, sabotage, or failure or default of public utilities or common carriers or similar conditions beyond the control of the parties.

7.5 No Waiver; Modifications. It is agreed that no waiver by a party hereto of any breach or default of any of the covenants or agreements herein set forth shall be deemed a waiver as to any subsequent and/or similar breach or default. No amendment, modification, release or discharge shall be binding upon the parties unless in writing and duly executed by authorized representatives of all parties.

7.6 No Strict Construction. This Supplement has been prepared jointly and shall not be strictly construed against any party. No presumption as to construction of this Supplement shall apply against any party with respect to any ambiguity in the wording of any provision(s) of this Supplement irrespective of which party may be deemed to have authored the ambiguous provision(s).

7.7 Independent Contractor. The parties are independent contractors of each other, and the relationship between the parties shall not constitute a partnership, joint venture, or agency. No party shall be the agent of another party or have any authority to act for, or on behalf of, another party in any manner.

7.8 Assignment. No party may assign or transfer this Supplement or any rights or obligations hereunder without prior written consent of each other party, *except* that a party may make such assignment without each other party's consent (a) to an Affiliate, (b) to a Third Party that merges with, consolidates with, or acquires substantially all of the assets or voting control of the assigning party or (c) to a Third Party that acquires all the rights to Exelixis Compound, in the case of Exelixis or the case of Ipsen, or the Roche Compound, in the case of Roche. Any assignment or attempted assignment by any party in violation of the terms of this Section shall be null and void and of no legal effect.

7.9 Headings. The captions to the several Sections and Articles hereof are not a part of this Supplement, but are included merely for convenience of reference only and shall not affect its meaning or interpretation.

7.10 Counterparts. This Supplement may be executed in three (3) or more counterparts, each of which shall be deemed an original, but all of which together shall constitute one (1) and the same instrument. This Agreement may be executed by electronic (e.g., .pdf) signatures and such signatures shall be deemed to bind each Party hereto as if they were original signatures, provided that ink originals will be promptly exchanged.

7.11 Severability. If any provision of this Supplement is held to be illegal, invalid, or unenforceable under any present or future law, and if the rights or obligations of a party under this Supplement will not be materially and adversely affected thereby, (a) such provision shall be fully severable, (b) this Supplement shall be construed and enforced as if such illegal, invalid, or unenforceable provision had never comprised a part hereof, (c) the remaining

provisions of this Supplement shall remain in full force and effect and shall not be affected by the illegal, invalid, or unenforceable provision or by its severance herefrom and (d) in lieu of such illegal, invalid, or unenforceable provision, there shall be added automatically as a part of this Supplement a legal, valid, and enforceable provision as similar in terms to such illegal, invalid, or unenforceable provision as may be possible and reasonably acceptable to the parties.

7.12 No Benefit to Third Parties. The representations, warranties, and agreements set forth in this Supplement are for the sole benefit of the parties and their successors and permitted assigns, and they shall not be construed as conferring any rights on any other parties.

7.13 The Agreement. Roche and Exelixis shall execute the Agreement concurrently with the execution of this Supplement by Roche, Exelixis, and Ipsen, and if the Agreement is not so executed concurrently with this Supplement, this Supplement shall be null and void and of no force or effect.

7.14 Construction. Except as otherwise explicitly specified to the contrary, (a) references to a Section, Article, or Exhibit means a Section or Article of, or Exhibit to, this Supplement and all subsections thereof, unless another agreement is specified; (b) references to a particular statute or regulation include all rules and regulations promulgated thereunder and any successor statutes, rules, or regulations then in effect, in each case including the then-current amendments thereto; (c) words in the singular or plural form include the plural and singular form, respectively; (d) the terms “including,” “include(s),” “such as,” and “for example” used in this Supplement mean including the generality of any description preceding such term and will be deemed to be followed by “without limitation”; and (e) the words “hereof,” “herein,” “hereunder,” “hereby” and derivative or similar words refer to this Supplement. No presumption as to construction of this Supplement shall apply against any party with respect to any ambiguity in the wording of any provision(s) of this Supplement irrespective of which party may be deemed to have authored the ambiguous provision(s).

7.15 Further Assurance. Each of Roche, Exelixis, and Ipsen duly execute and deliver or cause to be duly executed and delivered, such further instruments and do and cause to be done such further acts and things, including the filing of such assignments, agreements, documents and instruments, as may be necessary or as another party may reasonably request in order to perfect any license, assignment, or other transfer or any properties or rights under, or pursuant, to this Supplement.

7.16 Entire Agreement. Roche, Exelixis, and Ipsen agree that this Supplement sets forth the complete, final and exclusive agreement between Roche, Exelixis, and Ipsen collectively concerning the subject matter hereof and supersedes all prior agreements and understandings by and between Roche, Exelixis, and Ipsen collectively with respect to such subject matter. For the avoidance of doubt, this Supplement does not supersede the Agreement or the Ipsen-Exelixis Agreement. There are no covenants, promises, agreements, warranties, representations, conditions or understandings, either oral or written, between Roche, Exelixis, and Ipsen collectively with respect to such subject matter other than as are set forth in this Supplement.

7.17 Dispute Resolution. The terms and conditions of Section 14.3 of the Agreement shall be binding upon Ipsen with respect to any dispute, controversy, or claim between Ipsen and Roche and arising out of, relating to, or in connection with this Supplement to the same extent such terms and conditions are binding upon the parties to the Agreement. In the application of Section 14.3 to Ipsen with respect to such dispute, controversy, or claim, the “Alliance Manager” of Ipsen shall be interpreted to mean the representative of Ipsen acting as Alliance Manager, and the “Executive Officer” of Ipsen shall be interpreted to mean the [*] of Ipsen (or his or her designee).

[*Signature page follows*]

[*] = Certain confidential information contained in this document, marked by brackets, has been omitted because it is both (I) not material and (II) would be competitively harmful if publicly disclosed.

IN WITNESS WHEREOF, Roche, Exelixis, and Ipsen, intending to be legally bound hereby, have caused this Supplement to the Agreement to be executed by their duly authorized representatives as of the Effective Date.

Exelixis, Inc.

By: /s/ Michael M. Morrissey, Ph.D.

Name: Michael M. Morrissey, Ph.D.

Title: President and CEO

Date: 18 December 2019

Ipsen Pharma, SAS

By: /s/ François Garnier

Name: François Garnier

Title: EVP, General Counsel

Date: 18 December 2019

F. Hoffmann-La Roche Ltd

By: /s/ Laurence Lehuu

Name: Laurence Lehuu

Title: Operation Program Leader

Date: 18 December 2019

By: /s/ Louis DuPasquier

Name: Louis DuPasquier

Title: Legal Counsel

[*] = Certain confidential information contained in this document, marked by brackets, has been omitted because it is both (I) not material and (II) would be competitively harmful if publicly disclosed.

Exhibit 21.1

SUBSIDIARIES OF EXELIXIS, INC.

Name of Subsidiary	State or Other Jurisdiction of Incorporation or Organization
Exelixis International (Bermuda) Ltd.	Bermuda
Exelixis Patent Company, LLC	Delaware
Exelixis Plant Sciences, Inc.	Delaware
Exelixis U.S., LLC	Delaware

Exhibit 23.1

Consent of Independent Registered Public Accounting Firm

We consent to the incorporation by reference in the Registration Statements (Form S-8 Nos. 333-226493, 333-223225, 333-218236, 333-214766, 333-212866, 333-209824, 333-203758, 333-196761, 333-176674, 333-165389, 333-159280, 333-157825, 333-149834, 333-147063, 333-133237, 333-124536, 333-113472, 333-102770, 333-82724, 333-82722, 333-57026 and 333-35862) of Exelixis, Inc. and the Registration Statement (Form S-3 No. 333-205397) and related Prospectus of Exelixis, Inc. of our reports dated February 25, 2020, with respect to the consolidated financial statements of Exelixis, Inc. and the effectiveness of internal control over financial reporting of Exelixis, Inc., included in this Annual Report (Form 10-K) for the year ended January 3, 2020.

/s/ Ernst & Young LLP

Redwood City, California
February 25, 2020

Exhibit 31.1

CERTIFICATION OF PRINCIPAL EXECUTIVE OFFICER
PURSUANT TO
EXCHANGE ACT RULES 13a-14(a) and 15d-14(a),
AS ADOPTED PURSUANT TO
SECTION 302 OF THE SARBANES-OXLEY ACT OF 2002

I, Michael M. Morrissey, Ph.D., certify that:

1. I have reviewed this Form 10-K of Exelixis, Inc.;

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

4. The registrant's other certifying officer(s) and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:

(a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

(b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, 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;

(c) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

(d) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

5. The registrant's other certifying officer(s) and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):

(a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

(b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

/s/ MICHAEL M. MORRISSEY

Michael M. Morrissey, Ph.D.
President and Chief Executive Officer
(Principal Executive Officer)

Date: February 25, 2020

Exhibit 31.2

CERTIFICATION OF PRINCIPAL FINANCIAL OFFICER
PURSUANT TO
EXCHANGE ACT RULES 13a-14(a) and 15d-14(a),
AS ADOPTED PURSUANT TO
SECTION 302 OF THE SARBANES-OXLEY ACT OF 2002

I, Christopher J. Senner, certify that:

1. I have reviewed this Form 10-K of Exelixis, Inc.;

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

4. The registrant's other certifying officer(s) and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:

(a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

(b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, 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;

(c) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

(d) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

5. The registrant's other certifying officer(s) and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):

(a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

(b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

/s/ CHRISTOPHER J. SENNER

Christopher J. Senner

Executive Vice President and Chief Financial Officer
(Principal Financial Officer)

Date: February 25, 2020

Exhibit 32.1

CERTIFICATIONS OF PRINCIPAL EXECUTIVE OFFICER AND PRINCIPAL FINANCIAL OFFICER
PURSUANT TO
18 U.S.C. SECTION 1350,
AS ADOPTED PURSUANT TO
SECTION 906 OF THE SARBANES-OXLEY ACT OF 2002

Pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002, Michael M. Morrissey, Ph.D., the President and Chief Executive Officer of Exelixis, Inc. (the "Company"), and Christopher J. Senner, the Executive Vice President and Chief Financial Officer of the Company, each hereby certifies that, to the best of his knowledge:

1. The Company's Annual Report on Form 10-K for the period ended January 3, 2020, to which this Certification is attached as Exhibit 32.1 (the "Report"), fully complies with the requirements of Section 13(a) or Section 15(d) of the Securities Exchange Act of 1934, as amended; and

2. The information contained in the Report fairly presents, in all material respects, the financial condition and results of operations of the Company.

In Witness Whereof, the undersigned have set their hands hereto as of the 25th day of February 2020.

/s/ MICHAEL M. MORRISSEY

Michael M. Morrissey, Ph.D.

President and Chief Executive Officer
(Principal Executive Officer)

/s/ CHRISTOPHER J. SENNER

Christopher J. Senner

Executive Vice President and Chief Financial Officer
(Principal Financial Officer)