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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 December 30, 2022

or

☐ **TRANSITION REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**
For the transition period from to

Commission File Number: 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 has filed a report on and attestation to its management's assessment of the effectiveness of its internal control over financial reporting under Section 404(b) of the Sarbanes-Oxley Act (15 U.S.C. 7262(b)) by the registered public accounting firm that prepared or issued its audit report. ☒

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: $6,831,299,691. Excludes shares of the registrant's common stock held by persons who were directors and/or executive officers of the registrant at July 1, 2022 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 January 30, 2023: 324,087,337

DOCUMENTS INCORPORATED BY REFERENCE

Certain portions of the registrant's definitive proxy statement to be filed with the Securities and Exchange Commission pursuant to Regulation 14A, not later than April 29, 2023, in connection with the registrant's 2023 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
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SPECIAL NOTE REGARDING FORWARD LOOKING STATEMENTS

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 under the heading "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.

In addition, statements that "we believe" and similar statements reflect our beliefs and opinions on the relevant subject. These statements are based upon information available to us as of the date of this report, and while we believe such information forms a reasonable basis for such statements, such information may be limited or incomplete, and our statements should not be read to indicate that we have conducted an exhaustive inquiry into, or review of, all potentially available relevant information. These statements are inherently uncertain and investors are cautioned not to unduly rely upon these statements.

RISK FACTOR SUMMARY

Investing in our securities involves a high degree of risk. Below is a summary of material factors that make an investment in our securities speculative or risky. Importantly, this summary does not address all of the risks that we face. Additional discussion of the risks summarized in this risk factor summary, as well as other risks that we face, can be found under the heading "Item 1A. Risk Factors" below.

- Our ability to grow our company is dependent upon the commercial success of CABOMETYX in its approved indications and the continued clinical development, regulatory approval, clinical acceptance and commercial success of the cabozantinib franchise in additional indications.
- *If we are unable to obtain or maintain coverage and reimbursement for our products from third-party payers, our business will suffer.*
- *Pricing for pharmaceutical products, both in the U.S. and in foreign countries, has come under increasing attention and scrutiny by federal, state and foreign national governments, legislative bodies and enforcement agencies. Initiatives arising from this scrutiny may result in changes that have the effect of reducing our revenue or harming our business or reputation.*
- *The timing of the entrance of generic competitors to CABOMETYX and legislative and regulatory action designed to reduce the barriers to the development, approval and adoption of generic drugs in the U.S. could limit the revenue we derive from our products, most notably CABOMETYX, which could have a material adverse impact on our business, financial condition and results of operations.*
- *We may be unable to expand our discovery and development pipeline, which could limit our growth and revenue potential.*
- *Clinical testing of cabozantinib for new indications, or of new product candidates, is a lengthy, costly, complex and uncertain process that may fail ultimately to demonstrate safety and efficacy data for those products sufficiently differentiated to compete in our highly competitive market environment.*
- *The regulatory approval processes of the U.S. Food and Drug Administration and comparable foreign regulatory authorities are lengthy, uncertain and subject to change, and may not result in regulatory approvals for additional cabozantinib indications or for our other product candidates, which could have a material adverse impact on our business, financial condition and results of operations.*
- *Our profitability could be negatively impacted if expenses associated with our extensive clinical development, business development and commercialization activities, both for the cabozantinib franchise and our other product candidates, grow more quickly than the revenues we generate.*

- *Our clinical, regulatory and commercial collaborations with major companies make us reliant on those companies for their continued performance and investments, which subjects us to a number of risks. For example, we rely on Ipsen and Takeda for the commercial success of CABOMETYX in its approved indications outside of the U.S., and we 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. In addition, our growth potential is dependent in part upon companies with which we have entered into research collaborations, in-licensing arrangements and similar business development relationships.*
- *We are subject to healthcare laws, regulations and enforcement, as well as laws and regulations relating to privacy, data collection and processing of personal data; our failure to comply with those laws could have a material adverse impact on our business, financial condition and results of operations.*
- *Data breaches, cyber attacks and other failures in our information technology operations and infrastructure could compromise our intellectual property or other sensitive information, damage our operations and cause significant harm to our business and reputation.*
- *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.*
- *If the COVID-19 pandemic is further prolonged or becomes more severe, our business operations and corresponding financial results could suffer, which could have a material adverse impact on our prospects for growth.*
- *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.*

BASIS OF PRESENTATION

We have adopted a 52- or 53-week fiscal year policy that ends on the Friday closest to December 31st. Fiscal year 2022, which was a 52-week fiscal year, ended December 30, 2022, fiscal year 2021, which was a 52-week fiscal year, ended on December 31, 2021 and fiscal year 2020, which was a 52-week fiscal year, ended January 1, 2021. For convenience, references in this report as of and for the fiscal years ended December 30, 2022, and January 1, 2021 are indicated as being as of and for the years ended December 31, 2022 and 2020, respectively.

PART I

Item 1. Business

Overview

Exelixis, Inc. (Exelixis, we, our or us) is an oncology company innovating next-generation medicines and combination regimens at the forefront of cancer care. Through the commitment of our drug discovery, development and commercialization resources, we have produced four marketed pharmaceutical products, including our flagship molecule, cabozantinib. We continue to evolve our product portfolio, leveraging our investments, expertise and strategic partnerships, to target an expanding range of tumor types and indications with our clinically differentiated pipeline of small molecules, antibody-drug conjugates (ADCs) and other biotherapeutics.

Sales related to cabozantinib account for the majority of our revenues. Cabozantinib is an inhibitor of multiple tyrosine kinases including MET, AXL, VEGF receptors and RET and has been approved by the U.S. Food and Drug Administration (FDA) and in 62 other countries as: CABOMETYX® (cabozantinib) tablets approved both alone and in combination with Bristol-Myers Squibb Company's (BMS) OPDIVO® (nivolumab) for advanced renal cell carcinoma (RCC), for previously treated hepatocellular carcinoma (HCC) and, currently by the FDA and European Commission (EC), for previously treated, radioactive iodine (RAI)-refractory differentiated thyroid cancer (DTC); and COMETRIQ® (cabozantinib) capsules approved for progressive, metastatic medullary thyroid cancer (MTC). For physicians treating these types of cancer, cabozantinib has become or is becoming an important medicine in their selection of effective therapies.

The other two products resulting from our discovery efforts are: COTELLIC® (cobimetinib), an inhibitor of MEK approved as part of multiple combination regimens to treat specific forms of 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). See "—Collaborations and Business Development Activities—Other Collaborations."

The year 2022 was our sixth year of annual profitability, which featured growth in net product revenues of approximately 30% year-over-year as a result of increased sales of our cabozantinib products in the U.S., supplemented by an approximately 16% year-over-year increase in royalties earned pursuant to collaboration agreements with our ex-U.S. partners. We plan to continue leveraging the resulting operating cash flows to support the ongoing investigation of cabozantinib in phase 3 trials for new indications and the advancement of a broad array of diverse biotherapeutics and small molecule programs for the treatment of cancer exploring multiple modalities and mechanisms of action. Of the clinical-stage assets that have emerged from our drug discovery and preclinical activities thus far, the furthest along are zanzalintinib (formerly XL092), a next-generation oral tyrosine kinase inhibitor (TKI) and XB002, an ADC that targets tissue factor (TF). As we continue to bolster our pipeline, we pursue options to acquire other investigational drug candidates from third parties if those assets demonstrate evidence of clinical success. One example of this approach is CBX-12 (alphalex™ exatecan), a clinical-stage peptide-drug conjugate (PDC) invented by Cybrexa Therapeutics (Cybrexa) that utilizes Cybrexa's proprietary alphalex technology to enhance the delivery of exatecan, a highly potent, second-generation topoisomerase I inhibitor, to tumor cells.

Exelixis Marketed Products: CABOMETYX and COMETRIQ

As detailed below, CABOMETYX and COMETRIQ have been approved to treat patients with various forms of cancer by the FDA for the U.S. market, the EC for the European Union (EU) markets and the Japanese Ministry of Health, Labour and Welfare (MHLW), as well as by comparable regulatory authorities across other markets worldwide.

Product	Indication	Approval Date	Regimen	Major Markets
CABOMETYX® (cabozantinib)	**Renal Cell Carcinoma (RCC)**			
	Patients with advanced RCC who have received prior anti-angiogenic therapy	April 25, 2016	Monotherapy	U.S.
	Advanced RCC in adults following prior VEGF-targeted therapy	September 9, 2016	Monotherapy	EU
	Patients with advanced RCC	December 19, 2017	Monotherapy	U.S.
	First-line treatment of adults with intermediate- or poor-risk advanced RCC	May 17, 2018	Monotherapy	EU
	Patients with curatively unresectable or metastatic RCC	March 25, 2020	Monotherapy	Japan
	First-line treatment of patients with advanced RCC	January 22, 2021	Combination with OPDIVO® (nivolumab)	U.S.
	First-line treatment for patients with advanced RCC	March 31, 2021	Combination with OPDIVO	EU
	Patients with unresectable or metastatic RCC	August 25, 2021	Combination with OPDIVO	Japan
	Hepatocellular Carcinoma (HCC)			
	HCC in adults who have previously been treated with sorafenib	November 15, 2018	Monotherapy	EU
	Patients with HCC who have been previously treated with sorafenib	January 14, 2019	Monotherapy	U.S.
	Patients with unresectable HCC that has progressed after cancer chemotherapy	November 27, 2020	Monotherapy	Japan
	Differentiated Thyroid Cancer (DTC)			
	Adult and pediatric patients 12 years of age and older with locally advanced or metastatic DTC that has progressed following prior VEGF receptor-targeted therapy and who are RAI-refractory or ineligible	September 17, 2021	Monotherapy	U.S.
	Adult patients with locally advanced or metastatic DTC, refractory pr not eligible to RAI who have progressed during or after prior systemic therapy	May 3, 2022	Monotherapy	EU
COMETRIQ® (cabozantinib)	**Medullary Thyroid Cancer (MTC)**			
	Patients with progressive, metastatic MTC	November 29, 2012	Monotherapy	U.S.
	Adult patients with progressive, unresectable locally advanced or metastatic MTC	March 25, 2014	Monotherapy	EU

In 2022, 2021 and 2020, we generated $1,401.2 million, $1,077.3 million and $741.6 million, respectively, in net product revenues from sales of CABOMETYX and COMETRIQ. Outside the U.S., we rely on collaboration partners for the commercialization of CABOMETYX and COMETRIQ; Ipsen Pharma SAS (Ipsen) is responsible for all territories outside of the U.S. and Japan, and Takeda Pharmaceutical Company Limited (Takeda) is responsible for the Japanese market. In 2022, 2021 and 2020, we earned $121.4 million, $105.1 million and $78.4 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 and Business Development Activities—Cabozantinib Commercial Collaborations."

Renal Cell Carcinoma - CABOMETYX is a Leading TKI Treatment Option for Patients with Advanced RCC

CABOMETYX has become a standard of care for the treatment of patients suffering from advanced RCC, and a growing number of these patients have been or will be treated with CABOMETYX. In 2022, approximately 32,200 patients with advanced kidney cancer required systemic therapy in the U.S., with over 20,000 patients receiving first-line treatment.

Since CABOMETYX was first approved, we have deployed our promotional and medical affairs teams to educate physicians about CABOMETYX. We believe that the product's success is attributable to the strength of the clinical data reflected in its FDA-approved labeling for advanced RCC. The CABOMETYX label incorporates the results of the METEOR, CABOSUN and CheckMate-9ER clinical trials. 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. These results formed the basis for the FDA's approval in April 2016, following which CABOMETYX became the first and only single-agent therapy approved in the U.S. 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). Subsequently, in October 2016, we announced positive results from CABOSUN, a randomized, open-label, active-controlled phase 2 trial conducted by the Alliance for Clinical Trials in Oncology, comparing cabozantinib with sunitinib in patients with previously untreated advanced RCC with intermediate- or poor-risk disease. These results formed the basis for the FDA's approval in December 2017 of CABOMETYX for previously untreated patients with advanced RCC, and for this patient population, CABOMETYX is the only approved single-agent therapy to demonstrate improved PFS compared with sunitinib, a first-generation TKI that was the previous standard of care.

CABOMETYX has also demonstrated positive clinical results in combination with immune checkpoint inhibitors (ICIs), most notably in CheckMate-9ER, an open-label, randomized, multinational phase 3 pivotal trial evaluating OPDIVO, an ICI developed by BMS, in combination with CABOMETYX versus sunitinib in patients with previously untreated, advanced or metastatic RCC. Results from CheckMate-9ER demonstrated that the combination of CABOMETYX and OPDIVO doubled PFS and ORR and reduced the risk of disease progression or death by 40% compared with sunitinib, and formed the basis for the FDA's approval of the combination in January 2021 as a first-line treatment of patients with advanced RCC. The National Comprehensive Cancer Network (NCCN), the nation's foremost non-profit alliance of leading cancer centers, has included the combination of CABOMETYX with OPDIVO in its Clinical Practice Guidelines for Kidney Cancer as a Category 1 option for the first-line treatment of patients with clear cell RCC. The NCCN also lists single-agent CABOMETYX as a category 1 preferred regimen in subsequent treatments for patients with clear cell RCC, and as a preferred systemic therapy regimen for non-clear cell RCC, supporting CABOMETYX's position in the RCC treatment landscape.

In 2022, in markets outside the U.S., we continued to work closely with our collaboration partner Ipsen in support of its regulatory strategy and commercialization efforts for CABOMETYX as a treatment for advanced RCC, both as a single agent and in combination with OPDIVO, as well as in preparation for submission of applications for approvals of CABOMETYX in combination with other therapies, and similarly with our collaboration partner Takeda with respect to the Japanese market. As a result of the approvals of CABOMETYX and/or the combination of CABOMETYX with OPDIVO for RCC indications in 62 countries outside of the U.S., including the Member States of the EU, Japan, the U.K., Canada, Brazil, Taiwan, South Korea and Australia, CABOMETYX has continued to grow markedly outside the U.S. both in sales revenue and the number of RCC patients benefiting from its clinical effect.

Hepatocellular Carcinoma - CABOMETYX Offers an Important Alternative for Patients with Previously Treated HCC

Liver cancer is a leading cause of cancer death worldwide, accounting for more than 800,000 deaths and 900,000 new cases each year. In the U.S., the incidence of liver cancer more than tripled over the past four decades. Although HCC is the most common form of liver cancer, making up about three-fourths of the more than 41,000 cases of liver cancer estimated to be diagnosed in the U.S. during 2023, this patient population has long been underserved. Prior to 2017, there

was only one approved systemic therapy for the treatment of HCC. Since that time, multiple new therapies were approved in the U.S. for HCC, both for previously untreated patients and for patients previously treated with sorafenib. Given the introduction of new and demonstrably more effective therapies, including ICI combination therapies, we believe the second- and later-line market for HCC therapies has the potential to grow significantly in coming years, as these new treatment options are expected to improve longer-term outcomes, thereby resulting in a greater number of patients receiving multiple lines of therapy. With the approval of CABOMETYX in January 2019 for HCC patients previously treated with sorafenib, we expect to continue to play a key role in the treatment landscape for these patients.

The FDA's approval of CABOMETYX's 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. The NCCN has included 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, providing further support for 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 approvals from Health Canada and the Japanese MHLW brought a much-needed therapy to HCC patients in those countries. In addition to the Member States of the EU, Japan, the U.K. and Canada, CABOMETYX is also approved for previously treated HCC indications in Brazil, Taiwan, South Korea, Australia and Hong Kong, among other countries.

Differentiated Thyroid Cancer - An Opportunity for CABOMETYX to Help an Underserved Patient Population

Approximately 44,000 new cases of thyroid cancer will be diagnosed in the U.S. in 2023. 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 RAI. Approximately 5% to 15% of differentiated thyroid tumors are resistant to RAI 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 December 2020, we announced that COSMIC-311, our phase 3 pivotal trial evaluating cabozantinib in patients with RAI-refractory DTC who have progressed after up to two prior VEGF receptor-targeted therapies, met its co-primary endpoint of demonstrating significant improvement in PFS as compared with placebo. These results formed the basis for the FDA's approval in September 2021 of CABOMETYX for the treatment of adult and pediatric patients 12 years of age and older with locally advanced or metastatic DTC that has progressed following prior VEGF receptor-targeted therapy and who are RAI-refractory or ineligible. We commenced the commercial launch of CABOMETYX in this patient group upon the FDA's approval, and we have seen a strong uptake in prescriptions for CABOMETYX in previously treated DTC during the months that followed.

Outside the U.S., our collaboration partner Ipsen received approval from the EC in May 2022 for CABOMETYX as a monotherapy for the treatment of adult patients with locally advanced or metastatic DTC, refractory or not eligible to RAI who have progressed during or after prior systemic therapy, which followed an approval from Health Canada in April 2022 to market CABOMETYX for a similar DTC indication.

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

Estimates suggest that there will be approximately 950 MTC cases diagnosed in the U.S. in 2023, and COMETRIQ has served as an important treatment option for these patients since January 2013. The FDA's approval of COMETRIQ for progressive, metastatic MTC 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. We are continuing to market COMETRIQ capsules for MTC patients at the labeled dose of 140 mg.

Exelixis Development Programs

We have extensive expertise in the clinical development of oncology products, which we continue to leverage for the investigation of additional clinical uses of cabozantinib in combination with other therapies. Those activities comprise the cabozantinib development program described below. We also apply that expertise to advancing our company's next generation of cancer treatments: innovative therapies that have the potential to help future cancer patients recover stronger and live longer. Accordingly, we have initiated clinical studies for our small molecule drug candidates, zanzalintinib and XL102, as well as for our first biotherapeutics product candidate, XB002, and these activities are described under "—Pipeline Development Programs - Advancing Exelixis' Future Cancer Therapy Candidates."

A summary of our cabozantinib and our pipeline development programs is provided below.

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 multiple individual tumor types investigated in phase 1, 2 and 3 clinical trials to date, reflecting the medicine's broad clinical potential. We are continuing to evaluate cabozantinib in combination with ICIs in late-stage clinical trials that we sponsor, along with our collaboration partners, across RCC and metastatic castration-resistant prostate cancer (mCRPC). Beyond clinical trials that we or our collaboration partners sponsor, independent investigators also conduct trials evaluating cabozantinib 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 have conducted trials in their respective territories through similar independently-sponsored programs.

Combination Studies with BMS

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. Based on the data from CheckMate-9ER, the first clinical trial conducted under this collaboration, the FDA approved CABOMETYX in combination with OPDIVO on January 22, 2021 as a first-line treatment of patients with advanced RCC. We continue to evaluate these combinations in COSMIC-313, a phase 3 pivotal trial in previously untreated advanced RCC. Pursuant to our agreements with BMS, each party is responsible for supplying finished drug product for the applicable clinical trial, and responsibility for the payment of costs for each trial is determined on a trial-by-trial basis. For additional information on the terms of the BMS clinical trial collaboration agreement, see "—Collaborations and Business Development Activities—Cabozantinib Development Collaborations—BMS Collaboration."

COSMIC-313 - RCC. 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. Patients were randomized 1:1 to the experimental arm of the triplet combination of cabozantinib, nivolumab and ipilimumab or to the control arm of nivolumab and ipilimumab in combination with matched placebo. We announced top-line results from COSMIC-313 in July 2022, and in September 2022 we presented the data at the Presidential Symposium III at the 2022 European Society for Medical Oncology (ESMO) Congress. The trial met its primary endpoint, demonstrating significant improvement in blinded independent radiology committee (BIRC)-assessed PFS at the primary analysis for the triplet combination, reducing the risk of disease progression or death compared with the doublet combination of nivolumab and ipilimumab (hazard ratio: 0.73; 95% confidence interval [CI]: 0.57-0.94; P=0.01). Median PFS for the triplet combination was not reached (95% CI: 14.0-not estimable) versus 11.3 months for the doublet combination of nivolumab and ipilimumab (95% CI: 7.7-18.2). At a prespecified interim analysis for the secondary endpoint of OS, the triplet combination did not demonstrate a significant benefit, and therefore, the trial will continue to the next analysis of OS, expected in 2023. The safety profile observed in the trial was reflective of the known safety profiles for each single agent, as well as the combination regimens used in this study. Based on feedback from the FDA, we do not intend to submit a supplemental new drug application (sNDA) for the combination regimen based on the currently available data, and we plan to discuss a potential regulatory submission with the FDA when the results of the next OS analysis are available. We are sponsoring COSMIC-313, and BMS is providing nivolumab and ipilimumab for the study free of charge.

Combination Studies with Roche

We have entered into collaborations with F. Hoffmann-La Roche Ltd. (Roche) for the purpose of evaluating the combination of cabozantinib and Roche's anti-PD-L1 ICI, atezolizumab, diversifying our exploration of cabozantinib combinations with ICIs.

COSMIC-021 - Locally Advanced or Metastatic Solid Tumors. In February 2017, we entered into a master clinical supply agreement with Roche. As part of the clinical supply agreement, in June 2017, we initiated COSMIC-021, a large phase 1b dose escalation study that is evaluating the safety and tolerability of the cabozantinib and atezolizumab combination 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. Enrollment in the expansion phase of this study

includes 20 combination therapy tumor expansion cohorts in non-small cell lung cancer (NSCLC), mCRPC, RCC and various other tumor types.

CONTACT trials. The encouraging efficacy and safety data that emerged from COSMIC-021 have been instrumental in guiding our clinical development strategy for cabozantinib in combination with ICIs. Informed by these data, we also entered into a joint clinical research agreement with Roche in December 2019, pursuant to which we are evaluating the cabozantinib and atezolizumab combination in two late-stage clinical trials: CONTACT-03, which focuses on patients with inoperable, locally advanced or metastatic RCC who have progressed during or following treatment with an ICI as the immediate preceding therapy; and CONTACT-02, which focuses on patients with mCRPC who have been previously treated with one novel hormonal therapy (NHT). A third trial, CONTACT-01, which focused on patients with metastatic NSCLC who have been previously treated with an ICI and platinum-containing chemotherapy, did not meet its primary endpoint of OS at final analysis. For additional information on the terms of the Roche joint clinical research agreement, see "–Collaborations and Business Development Activities–Cabozantinib Development Collaborations–Roche Collaboration."

CONTACT-03 - RCC. Taking into account the rapidly evolving treatment landscape for RCC and based on positive early-stage results from COSMIC-021, in July 2020, we and Roche initiated CONTACT-03, a global, multicenter, randomized, open-label phase 3 pivotal trial evaluating cabozantinib in combination with atezolizumab versus cabozantinib alone in patients with inoperable, locally advanced or metastatic RCC who progressed during or following treatment with an ICI as the immediate preceding therapy. Patients are randomized 1:1 to the experimental arm of cabozantinib in combination with atezolizumab or to the control arm of cabozantinib alone. The two primary efficacy endpoints for CONTACT-03 are PFS per Response Evaluation Criteria in Solid Tumors (RECIST) v. 1.1 as assessed by BIRC and OS, and secondary efficacy endpoints include PFS, ORR and duration of response (DOR) as assessed by the investigators. CONTACT-03 is sponsored by Roche and co-funded by us. In addition, both Ipsen and Takeda have the right to opt in and co-fund the trial and if doing so, they will have access to the results to support potential future regulatory submissions in their respective territories outside of the U.S. In January 2022, we announced the completion of enrollment of 523 patients at 168 sites globally. Based on current event rates, we anticipate announcing results of the primary PFS analysis in the first half of 2023. We intend to use the data from CONTACT-03 to further study the therapeutic potential of cabozantinib in this patient population, both as a single agent and in combination with ICIs.

CONTACT-02 - mCRPC. According to the American Cancer Society, in 2023, approximately 288,000 new cases of prostate cancer will be diagnosed in the U.S., and 34,000 people will die from the disease. Prostate cancer that has spread beyond the prostate and does not respond to androgen-suppression therapies—a common treatment for prostate cancer—is known as mCRPC. Researchers estimate that in the U.S. in 2020, 43,000 men were diagnosed with mCRPC, which has a median survival of less than two years. In response to this significant unmet need and based on positive early-stage results from Cohort 6 of COSMIC-021, in June 2020, we and Roche initiated CONTACT-02, a global, multicenter, randomized, open-label phase 3 pivotal trial evaluating cabozantinib in combination with atezolizumab in patients with mCRPC who have been previously treated with one NHT. The trial aims to enroll approximately 580 patients at approximately 280 sites globally, and we expect to complete enrollment in the second half of 2023. Patients are being randomized 1:1 to the experimental arm of cabozantinib in combination with atezolizumab or to the control arm of a second NHT (either abiraterone and prednisone or enzalutamide). The two primary efficacy endpoints for CONTACT-02 are PFS per RECIST v. 1.1 as assessed by BIRC and OS, and secondary efficacy endpoints include ORR, prostate-specific antigen response rate and DOR. CONTACT-02 is sponsored by us and co-funded by Roche. In addition, both Ipsen and Takeda have opted into and are co-funding the trial, and both companies will have access to the results to support potential future regulatory submissions in their respective territories outside of the U.S. Based on current event rates, we anticipate announcing results of the primary PFS analysis in the second half of 2023.

CONTACT-01 - NSCLC. In June 2020, we and Roche initiated CONTACT-01, a global, multicenter, randomized, open-label phase 3 pivotal trial evaluating cabozantinib in combination with atezolizumab versus docetaxel in patients with metastatic NSCLC who have been previously treated with an ICI and platinum-containing chemotherapy. Patients were randomized 1:1 to the experimental arm of cabozantinib in combination with atezolizumab and the control arm of docetaxel. In December 2022, we announced that the trial did not meet its primary efficacy endpoint of OS at final analysis. The safety profile of the combination of cabozantinib and atezolizumab was consistent with the known safety profiles for each single agent, and no new safety signals were identified. Detailed findings from CONTACT-01 will be submitted for presentation at a future medical meeting.

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

Pipeline Development Programs - Advancing Exelixis' Future Cancer Therapy Candidates

To continue growing our pipeline, we are investing heavily in the identification, exploration and advancement of new approaches to treating cancer. Several product candidates have progressed into clinical trials, including both small molecules and an assortment of multi-modal biotherapeutics that we have discovered or in-licensed and believe have the potential to treat a variety of cancers. The following table summarizes our current and planned clinical development activities outside of the cabozantinib franchise:

CLINICAL DEVELOPMENT PROGRAM FOR PIPELINE			
Product Candidate	**Mechanism of Action**	**Setting**	**Status Update**
Zanzalintinib	Next-generation tyrosine kinase inhibitor (TKI) targeting MET/VEGFR/AXL/MER	Advanced or metastatic solid tumors	Phase 1b trials evaluating zanzalintinib as a single-agent and in combination with immune checkpoint inhibitors (ICIs) combination regimens ongoing • In combination with atezolizumab and with avelumab (STELLAR-001) • In combination with nivolumab, with nivolumab and ipilimumab and with a fixed dose of nivolumab and relatlimab (STELLAR-002)
		Colorectal cancer (CRC)	Phase 3 trial evaluating zanzalintinib in combination with atezolizumab ongoing (STELLAR-303)
		Non-clear cell renal cell carcinoma (RCC)	Phase 3 trial evaluating zanzalintinib in combination with nivolumab ongoing (STELLAR-304)
XB002	Next-generation tissue factor (TF)-targeting antibody-drug conjugate (ADC)	Advanced solid tumors	Phase 1 trial evaluating single-agent and ICI combination regimens ongoing (JEWEL-101) • In combination with nivolumab, with bevacizumab, and potentially with additional ICIs or other targeted therapies
XL102	Potent, selective, orally bioavailable cyclin-dependent kinase 7 (CDK7) inhibitor	Advanced or metastatic solid tumors	Phase 1 trial evaluating single-agent ongoing and combination regimens planned (QUARTZ-101) • In combination with fulvestrant, with abiraterone and prednisone and potentially with other anti-cancer regimens
CBX-12	Peptide-drug conjugate (PDC) enhancing delivery of exatecan, a highly potent, second-generation topoisomerase I inhibitor, to tumor cells	Advanced or metastatic refractory solid tumors	Phase 1/2 evaluating CBX-12 as a single-agent ongoing (sponsored by Cybrexa)

Zanzalintinib Development Program

The first compound discovered at Exelixis to enter the clinic following our re-initiation of drug discovery activities in 2017 was zanzalintinib, a next-generation oral TKI that targets VEGF receptors, MET, AXL, MER and other kinases implicated in cancer's growth and spread. In designing zanzalintinib, we sought to build upon our experience with cabozantinib, retaining a similar target profile while improving key characteristics, including the pharmacokinetic half-life. We are evaluating zanzalintinib in a growing clinical development program across various tumor types.

STELLAR-001 - Advanced Solid Tumors. Following the FDA's acceptance of our Investigational New Drug (IND) for zanzalintinib, in February 2019, we initiated STELLAR-001, a multicenter phase 1b clinical trial evaluating the pharmacokinetics, safety, tolerability and preliminary anti-tumor activity of zanzalintinib. STELLAR-001 is divided into dose-escalation and expansion phases. In October 2020, we presented data at the 32nd EORTC-NCI-AACR Symposium (the 2020 ENA Symposium) that suggest zanzalintinib has a desirable therapeutic profile. We believe it pairs the potential for significant anti-tumor activity with a much shorter clinical pharmacokinetic half-life than cabozantinib, and also presents the potential for synergistic effects in combination with ICIs. In consideration of these data, we amended the phase 1 study protocol in October 2020 to include dose-escalation and expansion cohorts for zanzalintinib in combination with atezolizumab, and again in March 2021 to include dose-escalation and expansion cohorts for zanzalintinib in combination with avelumab, an ICI developed by Merck KGaA, Darmstadt, Germany (Merck KGaA) and Pfizer Inc. (Pfizer). We have established a recommended dose of 100 mg for both single-agent zanzalintinib and zanzalintinib in combination with atezolizumab, and we have begun enrolling expansion cohorts for patients with clear cell RCC, non-clear cell RCC, hormone-receptor positive breast cancer, mCRPC and colorectal cancer (CRC). The dose-escalation stage for zanzalintinib in combination with avelumab is ongoing, with expansion cohorts planned initially in urothelial carcinoma (UC). We presented data from STELLAR-001 during poster sessions at the most recent ESMO Congress in September 2022, which showed zanzalintinib has demonstrated preliminary, clinical activity similar to that observed with cabozantinib in phase 1 across a range of solid tumors and dose levels, with a manageable safety profile. The primary efficacy endpoints for the expansion phase may include ORR per RECIST v. 1.1 and PFS per RECIST v. 1.1, in each case as assessed by the investigator.

STELLAR-002 - Advanced Solid Tumors. In December 2021, we initiated STELLAR-002, a multicenter phase 1 clinical trial evaluating the safety, tolerability and efficacy of zanzalintinib in combination with either nivolumab, nivolumab and ipilimumab, or a fixed dose of nivolumab and relatlimab, a lymphocyte activation gene-3-blocking antibody developed by BMS (which replaced Nektar Therapeutics' bempegaldesleukin in the original trial protocol, which we announced in October 2022). STELLAR-002 is divided into dose-escalation and expansion phases. We have established a recommended dose of 100 mg for zanzalintinib in combination with nivolumab, and we have begun enrolling expansion cohorts for patients with clear cell RCC. The dose-escalation stage for zanzalintinib in the other combination regimens is ongoing and is continuing to enroll patients with advanced solid tumors. Depending on the dose-escalation results, STELLAR-002 may enroll additional expansion cohorts for patients with clear cell and non-clear cell RCC, mCRPC, UC, HCC, NSCLC, CRC and squamous cell cancers of the head and neck (SCCHN). The primary efficacy endpoint of the expansion phase will be ORR, except for the cohort of patients with mCRPC, for which the primary efficacy endpoint will be duration of radiographic PFS. To better understand the individual contribution of the therapies, treatment arms in the expansion cohorts may include zanzalintinib as a single agent in addition to the ICI combination regimens.

STELLAR-303 - CRC. CRC is the third most common cancer and the third-leading cause of cancer-related deaths in the U.S. According to the American Cancer Society, approximately 153,000 new cases will be diagnosed in the U.S. and around 52,000 people will die from the disease in 2023. Colorectal cancer is most frequently diagnosed among people aged 65-74 and is more common in men and those of African American descent. Nearly a quarter of colorectal cancer cases are diagnosed at the metastatic stage, at which point the five-year survival rate is just 15%. It has been estimated that approximately 43-45% of metastatic colorectal cancer cases exhibit a RAS mutation. In June 2022, we initiated STELLAR-303, a global, multicenter, randomized, open-label phase 3 pivotal trial evaluating zanzalintinib in combination with atezolizumab versus regorafenib in patients with metastatic non-microsatellite instability-high or non-mismatch repair-deficient CRC who have progressed after, or are intolerant to, the current standard of care. The trial aims to enroll approximately 600 patients with documented RAS status at approximately 137 sites globally. Patients are being randomized 1:1 to the experimental arm of zanzalintinib in combination with atezolizumab or to the control arm of regorafenib. The primary objective of STELLAR-303 is to evaluate the efficacy of the combination in patients with RAS wild-type disease, and outcomes in patients with RAS-mutated disease will also be evaluated. The primary efficacy endpoint of STELLAR-303 is OS, and additional efficacy endpoints include PFS, ORR and DOR per RECIST v. 1.1, in each case as assessed by the investigator.

STELLAR-304 - Non-Clear Cell RCC. In December 2022, we initiated STELLAR-304, a global, multicenter, randomized, open-label phase 3 pivotal trial evaluating zanzalintinib in combination with nivolumab versus sunitinib in previously

untreated patients with advanced non-clear cell RCC. The trial aims to enroll approximately 291 patients at approximately 170 sites globally. Patients are being randomized 2:1 to the experimental arm of zanzalintinib in combination with nivolumab or to the control arm of sunitinib. The primary efficacy endpoints of STELLAR-304 are PFS and ORR per RECIST v 1.1., in each case as assessed by BIRC. The secondary efficacy endpoint is OS.

Beyond STELLAR-303 and STELLAR-304, we intend to explore a series of early-stage and/or pivotal trials evaluating zanzalintinib in novel combination regimens across a broad array of future potential indications.

XB002 Development Program

XB002 (formerly ICON-2) is our lead TF-targeting ADC program, in-licensed from Iconic Therapeutics, Inc. (Iconic), now a wholly owned subsidiary of Endpoint Health, Inc. XB002 is an ADC composed of a human monoclonal antibody (mAb) against TF that is conjugated to a cytotoxic agent. TF is highly expressed on tumor cells and in the tumor microenvironment, and TF overexpression, while not oncogenic itself, facilitates angiogenesis, metastasis and other processes important to tumor development and progression. After binding to TF on tumor cells, XB002 is internalized, and the cytotoxic agent is released, resulting in targeted tumor cell death. XB002 is a rationally designed next-generation ADC that leverages proprietary linker-payload technology. Based on promising preclinical data, we exercised our exclusive option to license XB002 in December 2020, resulting in our assuming responsibility for all subsequent clinical development of XB002. In December 2021, we amended our agreement with Iconic to acquire broad rights to use the anti-TF antibody used in XB002 for any application, including conjugated to other payloads, as well as rights within oncology to a number of other anti-TF antibodies developed by Iconic, including for use in ADCs and multispecific biotherapeutics. For additional information on our business development activities with Iconic, see "—Collaborations and Business Development Activities—Research Collaborations and In-licensing Arrangements—Iconic."

JEWEL-101 - Advanced Solid Tumors. In June 2021, we initiated JEWEL-101, a multicenter phase 1, open-label clinical trial evaluating the safety, tolerability, pharmacokinetics and preliminary anti-tumor activity of XB002 in patients with advanced solid tumors for which therapies are unavailable, ineffective or intolerable. The trial is divided into dose-escalation and cohort-expansion phases and aims to enroll approximately 450 patients with advanced solid tumors, with the primary objective of determining the maximum tolerated dose or recommended dose levels for intravenous infusion of XB002 as a single agent and in combination with either nivolumab or bevacizumab, a mAb developed by Roche. In October 2022, we announced promising initial dose-escalation results from JEWEL-101 during the Antibody-drug Conjugates Poster Session at the 34th EORTC-NCI-AACR Symposium (2022 ENA Symposium). The data demonstrated that XB002 was well-tolerated at multiple dose levels, and pharmacokinetic analyses showed that XB002 remains stable after infusion with low levels of free payload in circulation. The planned cohort-expansion phase, which we expect to initiate during 2023, is designed to further explore the selected dose of XB002, both as a single agent and in combination with either nivolumab or bevacizumab, in individual tumor cohorts, which may include forms of NSCLC, cervical cancer, ovarian cancer, UC, SCCHN, pancreatic cancer, esophageal cancer, mCRPC, triple negative breast cancer and hormone-receptor positive breast cancer, and will evaluate ORR per RECIST v. 1.1 as a primary endpoint as well as XB002's safety, tolerability and pharmacokinetic profile. We also intend to initiate additional dose-escalation and expansion cohorts to evaluate the potential of XB002 in combination with additional ICIs and other targeted therapies across a wide range of tumor types, including indications other than those currently addressed by commercially available TF-targeted therapies.

XL102 Development Program

XL102 (formerly AUR102) is the lead compound under our research collaboration with Aurigene Oncology, Ltd. (Aurigene). It is a potent, selective, irreversible and orally bioavailable covalent inhibitor of CDK7, which is an important regulator of the cellular transcriptional and cell cycle machinery. Based on encouraging preclinical data for XL102, which we presented, along with Aurigene, at the 2020 ENA Symposium in October 2020, we exercised our exclusive option to license XL102 in December 2020, resulting in our assuming responsibility for all subsequent clinical development of XL102. For additional information on our collaboration with Aurigene, see "—Collaborations and Business Development Activities—Research Collaborations and In-licensing Arrangements —Aurigene."

QUARTZ-101 - Advanced Solid Tumors. In January 2021, we initiated QUARTZ-101, a multicenter phase 1, open-label clinical trial evaluating the safety, tolerability, pharmacokinetics and preliminary anti-tumor activity of XL102, both as a single agent and in combination with other anti-cancer therapies, in patients with inoperable, locally advanced or metastatic solid tumors. The trial is divided into dose-escalation and cohort-expansion phases and aims to enroll approximately 298 patients with advanced solid tumors, with the primary objective of determining the maximum tolerated dose or recommended dose levels for daily oral administration of XL102 as a single agent, as well as in combination with

fulvestrant for patients with hormone-receptor positive breast cancer and with abiraterone and prednisone for patients with mCRPC. Combinations with other agents may also be evaluated in the future. In December 2022, we announced initial dose-escalation results from QUARTZ-101 during the Poster Session at the 2022 San Antonio Breast Cancer Symposium. The data demonstrated that XL102 was well-tolerated at multiple dose levels, and a pharmacokinetic analysis showed rapid absorption of XL102 and an elimination half-life of 5-9 hours and supported adding investigation of twice-daily oral dosing. We are continuing to evaluate the efficacy of XL102 in additional patients during this initial dose-escalation phase. The subsequent cohort-expansion phase is designed to further explore the selected dose of XL102 as a single agent and in combination regimens in individual tumor cohorts, including ovarian cancer, triple-negative breast cancer, hormone-receptor positive breast cancer and mCRPC, and will evaluate ORR per RECIST v. 1.1 as assessed by the investigator, as well as XL102's safety, tolerability and pharmacokinetic profile.

Development of CBX-12

In November 2022, we executed an exclusive collaboration agreement with Cybrexa providing us with the right to acquire CBX-12, a clinical-stage, first-in-class PDC that utilizes Cybrexa's proprietary alphalex technology to enhance delivery of exatecan to tumor cells. CBX-12 is currently being evaluated in a phase 1 clinical trial to explore its pharmacokinetics, safety, tolerability and preliminary anti-tumor activity in patients with advanced or metastatic refractory solid tumors. The trial is divided into dose-escalation and cohort-expansion phases, with the primary objective of determining the recommended dose levels for intravenous infusion of CBX-12 as a single agent. Data from this trial reported in an oral presentation during a plenary session at the 2022 ENA Symposium demonstrated preliminary anti-tumor activity in a heavily pretreated patient population, including a complete response in a patient with ovarian cancer. The subsequent cohort-expansion phase is designed to further explore the selected dose of CBX-12 as a single agent in individual tumor cohorts, including forms of ovarian cancer, breast cancer, NSCLC and small cell lung cancer, and will evaluate ORR per RECIST v. 1.1 as assessed by the Investigator, as well as CBX-12's safety, tolerability and pharmacokinetic profile. For more information on the Cybrexa option arrangement, see "—Collaborations and Business Development Activities—Research Collaborations and In-licensing Arrangements—Cybrexa."

XL114 Development Program

XL114 (formerly AUR104) is a novel anti-cancer compound that inhibits activation of the CARD11-BCL10-MALT1 (CBM) complex, a key component of signaling downstream of B- and T-cell receptors, which promotes B- and T-cell lymphoma survival and proliferation. At the American Association of Cancer Research Annual Meeting in April 2021, Aurigene presented preclinical data (Abstract 1266) demonstrating that XL114 exhibited potent anti-proliferative activity in a large panel of cancer cell lines ranging from hematological cancers to solid tumors with excellent selectivity over normal cells. We exercised our exclusive option to in-license XL114 in October 2021, resulting in our assuming responsibility for all subsequent clinical development, manufacturing and commercialization of XL114. For additional information on our collaboration with Aurigene, see "—Collaborations and Business Development Activities—Research Collaborations and In-licensing Arrangements—Aurigene."

In April 2022 we initiated a first-in-human, phase 1 clinical trial evaluating the safety, tolerability, pharmacokinetics and preliminary anti-tumor activity of XL114 as a monotherapy in patients with non-Hodgkin's lymphoma (NHL). Based on initial findings in this phase 1 trial and the evolving treatment landscape for NHL, we have discontinued development of XL114 as of January 2023.

Expansion of the Exelixis Pipeline

Increasing our access to novel anti-cancer agents is essential to our pipeline strategy and overall business goals. We are working to expand our oncology product pipeline through drug discovery efforts, which encompass our diverse biotherapeutics and small molecule programs exploring multiple modalities and mechanisms of action. This approach provides a high degree of flexibility with respect to target selection and allows us to prioritize those targets that we believe have the greatest chance of yielding impactful therapeutics. As part of our strategy, our drug discovery activities have included research collaborations, in-licensing arrangements and other strategic transactions that increase our discovery bandwidth and allow us to access a wide range of technology platforms. In November 2022, we executed an option agreement with Sairopa, B.V. (Sairopa) to develop ADU-1805, a potentially best-in-class mAb that targets SIRPα. For more information on the Sairopa option arrangement, see "—Collaborations and Business Development Activities—Research Collaborations and In-licensing Arrangements."

In addition to discovering or in-licensing antibodies and other biotherapeutics or small molecule drug candidates aimed at specific targets, we are building our portfolio of potential cancer therapies through various business development arrangements with other companies that expand our capability to identify new targets using their proprietary technology platforms. One example is our exclusive option and license agreement with BioInvent International AB (BioInvent), described in more detail below, which is focused on the identification and development of novel antibodies for use in immuno-oncology therapeutics utilizing BioInvent's proprietary n-CoDeR® antibody library and patient-centric F.I.R.S.T™.

We have also continued our efforts to increase our laboratory space during 2022, both by expanding our leased space at our Alameda headquarters and as part of our planned new Exelixis East facilities in the Greater Philadelphia area, which are intended to further enhance the capacity and capability of our biotherapeutics and small molecule discovery efforts. As of the date of this Annual Report on Form 10-K, we are currently advancing more than 10 discovery programs and expect to progress up to five new development candidates into preclinical development during 2023. In addition, we will continue to engage in business development initiatives with the goal of acquiring and in-licensing promising oncology platforms and assets and then further characterize and develop them utilizing our established preclinical and clinical development infrastructure.

Biotherapeutics Programs

Much of our drug discovery activities focuses on discovering and advancing various biotherapeutics that have the potential to become anti-cancer therapies, such as bispecific antibodies, ADCs and other innovative treatments. ADCs in particular present a unique opportunity for new cancer treatments, given their capabilities to deliver anti-cancer payload drugs to targets with increased precision while minimizing impact on healthy tissues. This biotherapeutic approach has been validated by multiple regulatory approvals for the commercial sale of ADCs in the past several years. To facilitate the growth of these programs, we have established multiple research collaborations and in-licensing arrangements and entered into other strategic transactions that provide us with access to antibodies and binders, which are the starting point for use with additional technology platforms that we employ to generate next-generation ADCs or multispecific antibodies. In addition to the option deals with Cybrexa and Sairopa, some of our active research collaborations for biotherapeutics programs include collaborations with:

- Adagene Inc. (Adagene), which is focused on using Adagene's SAFEbody™ technology to develop novel masked ADCs or other innovative biotherapeutics with potential for improved therapeutic index;
- BioInvent, which is intended to expand our portfolio of antibody-based therapies and will utilize BioInvent's proprietary n-CoDeR antibody library and patient-centric F.I.R.S.T screening platform, which together are designed to allow for parallel target and antibody discovery;
- Catalent, Inc.'s wholly owned subsidiaries Redwood Bioscience, Inc., R.P. Scherer Technologies, LLC and Catalent Pharma Solutions, Inc. (individually and collectively referred to as Catalent), which is focused on the discovery and development of multiple ADCs using Catalent's proprietary SMARTag® site-specific bioconjugation technology;
- Invenra, Inc. (Invenra), which is focused on the discovery and development of novel binders and multispecific antibodies for the treatment of cancer; and
- NBE-Therapeutics AG (NBE), which is focused on the discovery and development of multiple ADCs by leveraging NBE's unique expertise and proprietary platforms in ADC discovery, including NBE's SMAC-Technology™ (a site-specific conjugation technology) and novel payloads.

We have already made significant progress under these and other research collaborations and in-licensing arrangements and believe we will continue to do so in 2023 and future years. For example, based on promising preclinical data for XB002, we exercised our exclusive option to license XB002 from Iconic in December 2020 and initiated the JEWEL-101 phase 1 clinical trial in June 2021. For additional information on XB002, see "—Exelixis Development Programs—Pipeline Development Programs - Advancing Exelixis' Future Cancer Therapy Candidates—XB002 Development Program." Also, as a direct result of these arrangements, we are advancing three biotherapeutics development candidates: XB010, XB014 and XB628. XB010, our first ADC advanced internally, targets the tumor antigen 5T4, incorporates an antibody sourced from Invenra and was constructed using Catalent's SMARTag site-specific bioconjugation platform.

XB014 and XB628 are bispecific antibodies; XB014 combines a PD-L1 targeting arm with a CD47 targeting arm to block a macrophage checkpoint; and XB628 targets PD-L1 and natural killer cell receptor group 2A (NKG2A), identified as an emerging immune checkpoint that may mediate resistance to classical checkpoint inhibition. Both XB014 and XB628 were developed through our collaboration with Invenra. For additional information on these specific research collaborations and

in-licensing arrangements related to our biotherapeutics programs, see "—Collaborations and Business Development Activities—Research Collaborations and In-licensing Arrangements."

Small Molecule Programs

Since its formation in 2000, our drug discovery group has advanced 25 compounds to the IND-stage, either independently or with collaboration partners, and today we deploy our drug discovery expertise to advance small molecule drug candidates toward and through preclinical development. These efforts are led by our experienced scientists, including some of the same scientists who led the efforts to discover cabozantinib, cobimetinib and esaxerenone, each of which are now commercially distributed drug products. We augment our small molecule discovery activities through research collaborations and in-licensing arrangements with other companies engaged in small molecule discovery, including:

- STORM Therapeutics LTD (STORM), which is focused on the discovery and development of inhibitors of novel RNA modifying enzymes, including ADAR1;
- Aurigene, which is focused on the discovery and development of novel small molecules as therapies for 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) and the Notch pathway.

For additional information on these research collaborations and in-licensing arrangements related to our small molecule programs, see "—Collaborations and Business Development Activities—Research Collaborations and In-licensing Arrangements."

Amongst our small molecule programs, furthest along are zanzalintinib, which was discovered at Exelixis, and XL102 which was discovered at Aurigene. Zanzalintinib first entered the clinic in 2019, and we initiated the first two phase 3 pivotal studies evaluating zanzalintinib in 2022, and XL102 entered the clinic in 2021. For additional information on these clinical trial programs, see "—Exelixis Development Programs—Pipeline Development Programs - Advancing Exelixis' Future Cancer Therapy Candidates." In addition, we continue to make progress on multiple, additional lead optimization programs for inhibitors of a variety of targets that we believe play significant roles in tumor growth, and we anticipate that some of these other programs could reach development candidate status in 2023.

Collaborations and Business Development Activities

We have established multiple collaborations with leading biopharmaceutical companies for the commercialization and further development of the cabozantinib franchise. Additionally, we have made considerable progress under our existing research collaborations and in-licensing arrangements to further enhance our early-stage pipeline and expand our ability to discover, develop and commercialize novel therapies with the goal of providing new treatment options for cancer patients and their physicians. We expect to enter into additional, external collaborative relationships around assets and technologies that complement our drug discovery and clinical development efforts. Under our commercial 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. Under our research collaborations and in-licensing arrangements, we are obligated to pay milestones and royalties to our various partners.

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. Under 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 four 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, 2022, we achieved aggregate milestone payments of $489.5 million related to regulatory and commercial

progress by Ipsen since the inception of the collaboration agreement, including two regulatory milestone payments during 2022 totaling $27.0 million upon approval by the EC and Health Canada of CABOMETYX as monotherapy for the treatment of adult patients with locally advanced or metastatic DTC.

We are also eligible to receive future development and regulatory milestone payments from Ipsen, totaling an aggregate of $19.5 million upon additional approvals of cabozantinib in future indications and/or jurisdictions, as well as contingent payments of up to $350.0 million and CAD$26.5 million associated with future sales milestones. We will further receive royalties on net sales of cabozantinib by Ipsen outside of the U.S. and Japan. 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. As of December 31, 2022, we have earned royalties of $382.1 million on net sales of cabozantinib by Ipsen since the inception of the collaboration agreement.

We received notification that, effective January 1, 2021, Royalty Pharma plc (Royalty Pharma) acquired from GlaxoSmithKline (GSK) all rights, title and interest in royalties on total net sales of any product containing cabozantinib for non-U.S. markets for the full term of the royalty and for the U.S. market through September 2026, after which time U.S. royalties will revert back to GSK. Accordingly, and consistent with our historical agreement with GSK, we are required to pay a 3% royalty to Royalty Pharma on total 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 certain clinical trials, including: CheckMate-9ER, COSMIC-021, COSMIC-311, COSMIC-312, CONTACT-01 and CONTACT-02.

We remain responsible for manufacturing and supply of cabozantinib for all development and commercialization activities under the collaboration agreement. Relatedly, we entered into a supply agreement with Ipsen to supply finished and labeled drug product 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 earlier terminated, 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 on three occasions 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, as well as modify certain cost sharing obligations related to the Japan-specific development costs associated with CONTACT-01 and CONTACT-02. Under the 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, 2022, we have also achieved regulatory and development milestones in the aggregate of $127.0 million related to regulatory and commercial progress by Takeda since the inception of the collaboration agreement. We are 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 $119.0 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. As of December 31, 2022, we have earned royalties of $21.5 million on net sales of cabozantinib by Takeda since the inception of the collaboration agreement.

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

Except for CONTACT-01 and CONTACT-02, 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, certain cohorts of COSMIC-021, CONTACT-01 and CONTACT-02.

Under the collaboration agreement, we are responsible for the manufacturing and supply of cabozantinib for all development and commercialization activities under the collaboration agreement. Relatedly, 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. 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 Collaboration

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 the triplet combination of cabozantinib, nivolumab and ipilimumab as a treatment option for RCC in the COSMIC-313 trial. For a description of the COSMIC-313 trial, see "—Exelixis Development Programs—Cabozantinib Development Program—Combination Studies with BMS."

Under the collaboration agreement with BMS, each party granted to the other a non-exclusive, worldwide (within the collaboration territory as defined in the collaboration agreement and its supplemental agreements), non-transferable, royalty-free license to use the other party's compounds in the conduct of each clinical trial. The parties' efforts are governed through a joint development committee established to guide and oversee the collaboration's operation. Each trial is conducted under a combination IND application, unless otherwise required by a regulatory authority. Each party is 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. Following the FDA's approval of CABOMETYX in combination with OPDIVO as a first-line treatment of patients with advanced RCC, we and BMS commenced the commercial launch of the combination and have agreed to pursue commercialization and marketing efforts independently.

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. Under this agreement with Roche, in June 2017, we initiated COSMIC-021 and in December 2018, we initiated COSMIC-312. We were the sponsor of both trials, and Roche provided atezolizumab free of charge. 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 the CONTACT-01, CONTACT-02 and CONTACT-03 studies. If a party to the joint clinical research agreement proposes any additional combined therapy trials beyond these three ongoing 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.

Under 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 are governed through a joint steering committee established to guide and oversee the collaboration and the conduct of the combined therapy trials. Each party is 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 are 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 are borne by the proposing party, except that the cost of clinical supply for all combined therapy trials are 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.

Zanzalintinib Clinical Collaborations

In an effort to diversify our exploration of the therapeutic potential of zanzalintinib, we have also entered into multiple collaboration and supply agreements to evaluate zanzalintinib in various combination trials, including with Roche's atezolizumab, Merck KGaA and Pfizer's avelumab, and BMS' nivolumab, ipilimumab and relatlimab. These agreements facilitate the efficient exploration of the safety and efficacy of zanzalintinib in combinations with a variety of established cancer therapies as we continue to build a broad development program for zanzalintinib. For descriptions of our ongoing clinical trials evaluating zanzalintinib in combination with other therapies, see "—Exelixis Development Programs—Pipeline Development Programs - Advancing Exelixis' Future Cancer Therapy Candidates—Zanzalintinib Development Program."

Research Collaborations and In-licensing Arrangements

As part of our pipeline expansion efforts, we have entered into several research collaborations and in-licensing arrangements, as well other strategic transactions that collectively serve to increase our discovery bandwidth and allow us to access a wide range of technology platforms. More recently, we have focused our business development activities on late preclinical and early-stage clinical assets that align with our oncology development expertise and have immediate potential as product candidates to treat cancer patients, including the following:

- *Cybrexa*. In November 2022, we entered into an agreement with Cybrexa that provides us the right to acquire CBX-12. Under the agreement, we made an upfront payment to Cybrexa in exchange for the right to acquire CBX-12 pending certain phase 1 results and to fund certain development and manufacturing expenses incurred by Cybrexa to advance CBX-12 according to an agreed development plan. Cybrexa may also be eligible to receive additional potential development, regulatory and commercial milestone payments, as well as a fee for the acquisition of CBX-12 upon evaluation of a pre-specified clinical data package to be delivered by Cybrexa.
- *Sairopa*. In November 2022, we entered into an exclusive option and license agreement and clinical development collaboration with Sairopa to develop ADU-1805. The collaboration is intended to expand our clinical pipeline with an IND filing for ADU-1805 anticipated in early 2023 to explore its applicability across multiple tumor types, as well as the potential to combine ADU-1805 with zanzalintinib and approved ICIs. Under the agreement, we made an upfront payment to Sairopa, including additional payments for near-term milestones, in exchange for an option to obtain an exclusive, worldwide license to develop and commercialize ADU-1805 and other anti-SIRPα antibodies, and for certain expenses to be incurred by Sairopa in conducting prespecified phase 1 clinical studies of ADU-1805 during the option period. Sairopa is eligible to receive additional development milestone payments during the option period. Following the completion of the prespecified clinical studies, we have the right to exercise our option upon payment of an option exercise fee. Upon option exercise, Sairopa will be eligible to receive additional development and commercial milestone payments, as well as royalties on potential sales.

In addition, we are continuing to make progress on our various research collaborations and in-licensing arrangements focused on our early-stage pipeline with the goal of advancing new biotherapeutics and small molecule development candidates towards the clinic, including the following:

- *Catalent*. In September 2020, we entered into a collaboration and license agreement with Catalent to develop multiple ADCs using Catalent's proprietary SMARTag site-specific bioconjugation technology. Under the September 2020 agreement, we made an upfront payment in exchange for an exclusive option to license up to four targets using Catalent's ADC platform over a three-year period. In addition, in August 2022 we exercised our right to extend the target selection term to five years and nominate up to two additional targets for an additional payment. For each option we decide to exercise, we will be required to pay an exercise fee, and we would then assume responsibility for all subsequent clinical development, manufacturing and commercialization for that program. Catalent would then become eligible for potential development, regulatory and commercial milestone payments, as well as royalties on potential sales. We have also committed to contribute research funding to Catalent for discovery and preclinical development work. In November 2022, we entered into a separate license agreement with Catalent for three target programs with lead antibody and/or ADC candidates. The ADC candidates were developed using Catalent's SMARTag technology, and each of the licensed antibodies has potential for development as an ADC or other biologic therapy using a variety of technologies to which we have access through our partnership network. Under the November 2022 agreement, we made an upfront payment in exchange for rights to the three biotherapeutics programs. We will fund the development work conducted by Catalent until development candidate selection is complete, after which we will assume responsibility for all subsequent preclinical, clinical and commercial activities. Catalent will be eligible for potential development and commercial milestone payments, as well as royalties on potential sales.
- *BioInvent*. In June 2022, we entered into an exclusive option and license agreement with BioInvent to identify and develop novel antibodies for use in immune-oncology therapeutics. The collaboration is intended to expand our portfolio of antibody-based therapies and will utilize BioInvent's proprietary n-CoDeR antibody library and patient-centric F.I.R.S.T screening platform, which together are designed to allow for parallel target and antibody discovery. Under the agreement, we made an upfront payment in exchange for rights to select three targets identified using BioInvent's proprietary F.I.R.S.T platform and n-CoDeR library. BioInvent is responsible for initial target and antibody discovery activities, and characterization of antibody mechanism of action. We may exercise an option to in-license any of the target programs upon identification of a development candidate directed to that target. Upon option exercise, we will pay an option exercise fee and will assume responsibility for all future

development and commercialization activities for the development candidate, including potential ADC and bispecific antibody engineering activities. In addition, BioInvent will be eligible for potential development and commercial milestone payments, as well as royalties on potential sales.

- *STORM.* In October 2021, we entered into an exclusive collaboration and license agreement with STORM to discover and advance novel drug candidates intended for the treatment of cancer. Our collaboration focuses initially on the RNA modifying enzyme ADAR1, building on early work by STORM applying its proprietary RNA epigenetic platform, as well as exploring an additional undisclosed target. Under the agreement, we made an upfront payment in exchange for exclusive licenses to these two discovery programs. STORM is responsible for discovery and generation of lead candidates for both target programs, and we will assume responsibility for IND-enabling studies and all subsequent clinical development, manufacturing and commercialization activities. STORM is eligible for potential development, regulatory and commercial milestone payments, as well as royalties on potential sales. We have also committed to contribute research funding to STORM for discovery and preclinical development work for each program.
- *Adagene.* In February 2021, we entered into a collaboration and license agreement with Adagene to utilize Adagene's SAFEbody technology platform to generate masked versions of mAbs from our growing preclinical pipeline for the development of ADCs or other innovative biotherapeutics against Exelixis-nominated targets. Under the agreement, we made an upfront payment in exchange for an exclusive, worldwide license to develop and commercialize any potential ADC products generated by Adagene with respect to an initial target, as well as a second target we may nominate during the collaboration term. For each target that we nominate, we would then assume responsibility for all subsequent clinical development, manufacturing and commercialization for that program. Adagene is eligible for potential development, regulatory and commercial milestone payments, as well as royalties on potential sales.
- *NBE.* In September 2020, we entered into a collaboration and license agreement with NBE to discover and develop multiple ADCs for oncology applications by leveraging NBE's unique expertise and proprietary platforms in ADC discovery, including NBE's SMAC-Technology and novel payloads. Under the agreement, we made an upfront payment in exchange for exclusive options to nominate four targets using NBE's ADC platform over a two-year period. For each option we decide to exercise, we will be required to pay an exercise fee, and we would then assume responsibility for all subsequent clinical development, manufacturing and commercialization connected with any resulting program. NBE would then become eligible for potential development, regulatory and commercial milestone payments, as well as royalties on potential sales. We have also committed to contribute research funding to NBE for discovery and preclinical development work.
- *Aurigene.* In July 2019, we entered into an exclusive collaboration, option and license agreement with Aurigene to in-license as many as six oncology target programs to discover and develop small molecules as therapies for cancer, and in April 2021, we expanded the collaboration to include three additional early discovery programs for a total of nine programs. Under the agreement, we made upfront payments in exchange for exclusive options to license eight of the nine programs to date, and we will pay an additional upfront payment upon the nomination of the ninth program. Based on encouraging preclinical data for XL102, the lead Aurigene program targeting CDK7, we exercised our exclusive option to license XL102 in December 2020, resulting in our assuming responsibility for all subsequent clinical development, manufacturing and commercialization of XL102 and payment of an exercise fee to Aurigene, and we initiated the QUARTZ-101 phase 1 clinical trial evaluating XL102 in January 2021. For additional information on XL102, see "—Exelixis Development Programs—Pipeline Development Programs - Advancing Exelixis' Future Cancer Therapy Candidates—XL102 Development Program." In addition, we exercised our exclusive option to in-license XL114, Aurigene's novel CBM inhibitor, in October 2021, resulting in our assuming responsibility for all subsequent clinical development, manufacturing and commercialization of XL114 and payment of an option exercise fee to Aurigene. Based on initial findings in this phase 1 trial and the evolving treatment landscape for NHL, we have discontinued development of XL114 as of January 2023. For additional information on XL114, see "—Exelixis Development Programs —Pipeline Development Programs - Advancing Exelixis' Future Cancer Therapy Candidates—XL114 Development Program." With respect to XL102, Aurigene is eligible for potential development, regulatory and commercial milestone payments, as well as royalties on potential sales. Beyond XL102, we are continuing to work with Aurigene to advance the other small molecule programs through preclinical development. For each additional option we decide to exercise, we will be required to pay an exercise fee, and we would then assume responsibility for all subsequent clinical development, manufacturing and commercialization for that program. Aurigene would then become eligible for potential development, regulatory and commercial milestone payments, as well as royalties on potential sales. We are also responsible for research funding for the discovery and preclinical development

work on these programs. Under the agreement, Aurigene retains limited development and commercial rights for India and Russia.

- *Iconic.* 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 TF in solid tumors. Under the original May 2019 agreement, we gained an exclusive option to license XB002, Iconic's lead TF ADC program, in exchange for an upfront payment to Iconic and a commitment for preclinical development funding. Based on encouraging preclinical data, we exercised our exclusive option to license XB002 in December 2020, resulting in our assuming responsibility for all subsequent clinical development, manufacturing and commercialization for XB002 and payment of an option exercise fee to Iconic. Following the FDA's acceptance of our IND for XB002 in April 2021, we initiated a phase 1 clinical trial of XB002 in June 2021 designed to evaluate its pharmacokinetics, safety, tolerability and preliminary efficacy as a monotherapy in patients with advanced solid tumors. For additional information on XLB002, see "—Exelixis Development Programs—Pipeline Development Programs - Advancing Exelixis' Future Cancer Therapy Candidates—XB002 Development Program." In January 2022, we announced an amendment to our agreement with Iconic, which we entered into in December 2021, to acquire broad rights to use the anti-TF antibody used in XB002 for any application, including conjugated to other payloads, as well as rights within oncology to a number of other anti-TF antibodies developed by Iconic, including for use in ADCs and multispecific biotherapeutics. Under the amended agreement, we made a final payment to Iconic and will not owe Iconic any further payments, but we will continue to be responsible for milestone payments and royalties owed to other companies pursuant to prior agreements between Iconic and those companies.
- *Invenra.* 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 multiple additional discovery projects across three different programs during the term of the collaboration. 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. We amended the agreement again in March 2020 and January 2021 to enable the use of target binders in non-Invenra platform-based modalities, such as ADC platforms, and to enable the development of biparatopic antibodies, respectively. Then in August 2021, we further expanded our collaboration to include an additional 20 targets for biotherapeutics discovery and development, for which we agreed to pay Invenra exclusivity payments and research program funding over a three-year period. Under the collaboration, Invenra is eligible for project initiation fees and potential development, regulatory and commercial milestone payments, as well as tiered royalties on net sales of any approved products. We also have the right to exercise options with respect to certain of Invenra's other research programs in exchange for an option exercise payment, and Invenra is eligible for milestone payments and royalties for any products that arise from these optioned research programs.
- *StemSynergy.* 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, including in colorectal cancers. One such compound, EXEL-4329, reached development candidate status in 2021. In May 2021, we amended the agreement to provide for an additional research platform to explore inhibitors of the Notch pathway, a major developmental pathway that regulates cancer stem cells in Notch-driven cancers, such as certain types of T-cell lymphomas and esophageal adenocarcinomas. Under the agreement, we paid StemSynergy upfront payments in each of 2018 and 2021, and StemSynergy is eligible for additional research and development funding on an as needed basis. StemSynergy is also eligible for potential development, regulatory and commercial milestone payments, as well as royalties on potential 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 are representative of this historical

strategy. Under our collaboration agreement with Genentech we out-licensed the further development and commercialization of COTELLIC, and under our collaboration agreement with Daiichi Sankyo we granted Daiichi Sankyo an exclusive, worldwide license to certain intellectual property, including MINNEBRO. 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 the cabozantinib franchise and drug discovery efforts. While these historical collaboration agreements have the potential to provide future revenue, and while we have received some collaboration revenues from these arrangements, we do not expect to receive significant revenues from these historical collaboration agreements.

Manufacturing and Product Supply

We do not own or operate manufacturing or distribution facilities for chemistry, manufacturing and control (CMC) development activities, preclinical, clinical or commercial production and distribution for our current products and new product candidates. Instead, we rely on various third-party contract manufacturing organizations to conduct these operations on our behalf. As our operations continue to grow in these areas, we continue to expand our supply chain through additional third-party contract manufacturers, distributors and suppliers. Specifically with respect to CABOMETYX, we entered into agreements with secondary contract manufacturing organizations to produce additional commercial supplies of CABOMETYX tablets and cabozantinib drug substance, which bolsters our commercial supply chain and serves to mitigate the risk of supply chain interruptions or other failures. For our portfolio of biotherapeutics and small molecules, we continue to expand our network through well-established and reputable global third-party contract manufacturers for our CMC development and manufacturing that have good regulatory standing, suitable manufacturing capacities and capabilities. We anticipate that this network will meet our future commercial manufacturing and supply needs for our product candidates currently in development, should such programs advance to regulatory approval and subsequent commercialization. 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) and its foreign equivalents where applicable.

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 other supply chain partners, 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, Europe and North America. 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.

In addition to having expanded our commercial supply chain to include secondary contract manufacturing organizations, we have established and continue to maintain substantial safety stock inventories for 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. Our response to the COVID-19 pandemic has included more frequent engagement with our vendors to maintain the consistency and effectiveness of our third-party contract manufacturers and other supply chain partners, however we have not experienced significant production delays or seen significant impairment to our supply chain as a result of the COVID-19 pandemic or the ongoing Russo-Ukrainian War. We believe that our current manufacturing network has the appropriate capacity to produce sufficient commercial quantities of CABOMETYX to support the currently approved RCC, HCC and DTC indications, and also 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 our products and product candidates to our collaboration partners for global commercial and development purposes.

Marketing and Sales

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. We market our products in the U.S. and concentrate our efforts on oncologists, oncology nurses, pharmacists and other healthcare professionals. In addition to using customary in-person pharmaceutical company practices, we also utilize digital marketing technologies to expand our engagement opportunities with customers.

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 parties, such as advertising agencies, market research firms and vendors providing other sales-support related services as needed, including digital marketing and other non-personal promotion. 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.

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. Beyond financial assistance, patients who participate in EASE also receive treatment coordination through a dedicated case manager, as well as clinical outreach and support from a network of oncology nurses or other healthcare professionals who help many of these patients better understand how to take their medication and mitigate side effects.

Environmental, Health and Safety

Our research and development processes involve the controlled use of certain hazardous materials and chemicals. In the U.S., at the federal, state and local levels, and in other foreign countries, we are subject to environmental, health and workplace safety laws and regulations governing the use, manufacture, storage, handling and disposal of hazardous materials. While we have incurred, and will 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.

Laboratory Safety Program

Due to the focus of our business in discovering and developing drug products, many of our employees work in our on-site laboratory facilities. All laboratory staff are trained on chemical hygiene, the use of personal protective equipment, and certain other relevant laboratory safety topics, such as working with blood-borne pathogens, and current staff are retrained regularly. We also extend these trainings to facilities staff and others who support our work in the labs. In an effort to maintain a safe environment for all staff, we regularly perform thorough safety inspections of our laboratories, and continuously update our procedures based on the observations made during these inspections. Additionally, we conduct periodic industrial hygiene monitoring to ensure lab staff working with certain known hazardous chemicals do not exceed regulated exposure limits, regularly test and certify fume hoods, biosafety cabinets and other individual pieces of equipment on which employees rely, and adhere to the standards set by the Environmental Protection Agency, the Occupational Safety and Health Administration, Cal-OSHA and Bay Area Air Quality Management District, among other governing bodies, to ensure compliance with laws and regulations and to maintain a safe work environment.

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 Practices (GLP);
- submission of an IND, which contains results of nonclinical studies (*e.g.*, laboratory evaluations of the chemistry, formulation, stability and toxicity of the product candidate), together with manufacturing information, analytical data, any available clinical data or literature and a proposed clinical protocol, and must become effective before human clinical trials may begin;
- approval by an independent institutional review board or ethics committee at each clinical trial site before each trial may be initiated;
- adequate and well-controlled human clinical trials conducted in accordance with the protocol, IND and Good Clinical Practice (GCP) 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 an sNDA, for approval of a new indication if the product is already approved for another indication;
- for biotherapeutic 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, clinical trial sites and/or Exelixis as the clinical trial sponsor for their compliance with GMP and GCP, respectively;
- payment of user fees for FDA review of an NDA or BLA unless a fee waiver applies;
- agreement with the FDA on the final labeling for the product and design and implementation of any required Risk Evaluation and Mitigation Strategy;
- if the FDA convenes an advisory committee, satisfactory completion of the advisory committee review; and
- FDA approval of the NDA or sNDA, or BLA or sBLA.

For purposes of NDA approval, human clinical trials are typically conducted in three sequential phases that may overlap or be combined:

- *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 at least one 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.
- *Phase 3 studies* are conducted to gather the additional information about effectiveness and safety across a higher number of patients and evaluate the overall benefit-risk relationship of the product candidate following

earlier phase evaluations, which will have provided preliminary evidence suggesting an effective dosage range and acceptable safety profile for the product candidate. Phase 3 trials are also intended to provide an adequate basis for physician labeling of the product if it is approved.

The FDA may require, or companies may pursue, additional clinical trials after a product is approved. These so-called post-marketing or "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 the labeling of an approved drug, including new indications, 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 FDA may initially issue a Refuse to File letter for an incomplete NDA or sNDA, or it may deny approval of an NDA or sNDA by way of a Complete Response letter if the applicable regulatory criteria are not satisfied, or alternatively require additional clinical and/or nonclinical data and/or an additional phase 3 pivotal clinical trial. 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. 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. In particular, the FDA has developed and implemented, and continues to develop and implement, various guidance, programs and initiatives specific to oncology products that can affect product development and the data necessary for 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, and interruptions in the manufacture of, 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 biotherapeutic 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 drug must have the potential to treat such rare disease or condition as described above. In addition, 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.

Expedited FDA Approval Pathways

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 the application within six months as compared to a standard review time of 10 months. Sponsors may also obtain a priority review voucher upon approval of an NDA for certain qualifying diseases and conditions that can be applied to a subsequent NDA submission
- 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 provides a meaningful advantage over available therapies and demonstrates an effect on a surrogate endpoint, or an intermediate clinical endpoint, which is considered reasonably likely to predict clinical benefit. As a condition of approval, the FDA requires that a sponsor of a product candidate receiving accelerated approval perform post-marketing clinical trials or provide data on established clinical endpoints from the same trial to confirm the clinical benefit as predicted by the surrogate marker trial. The FDA may require such trials to be underway prior to approval, or within a specific period thereafter, and will specify the conditions for such trials. Further, sponsors must provide reports on post-marketing trial progress no later than 180 days after approval and every 180 days thereafter until such trials are completed. The failure to conduct required post-marketing trials with due diligence and or to submit the required reports are prohibited acts, and these failures by sponsor in administering such trials, or the failure of such trials to confirm the clinically meaningful outcome, may result in withdrawal of the approval of the drug or the indication approved under accelerated approval. The FDA can also withdraw an accelerated approval on an expedited basis provided it follows certain procedures.

Specifically, with respect to oncology products, the FDA may review applications under the Real-Time Oncology Review (RTOR) program established by the FDA's Oncology Center of Excellence. The RTOR program, which allows an applicant to pre-submit components of the application to allow the FDA to review clinical data before the complete filing is submitted, aims to explore a more efficient review process to ensure that safe and effective treatments are available to patients as early as possible, while maintaining and improving review quality. Drugs considered for review under the RTOR program must be likely to demonstrate substantial improvements over available therapy, which may include drugs previously granted breakthrough therapy designation for the same or other indications, and must have straight-forward study designs and endpoints that can be easily interpreted.

Abbreviated FDA Approval Pathways and Generic Products

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 through clinical development. 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 drug products.

- 505(b)(2) NDAs. A 505(b)(2) NDA is an application 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) NDA 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) NDA applicant establishes that reliance on the 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 an ANDA or a 505(b)(2) NDA 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 sNDA for a product that is not an NCE but rather where the application contains new clinical studies conducted or sponsored by the sponsor and 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) NDA 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) NDA product). The three-year "changes" exclusivity generally bars the FDA from approving any ANDA or 505(b)(2) NDA 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.

Both Congress and the FDA are considering, and have enacted, 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 Ensuring Innovation Act, enacted in April 2021, amended the FDA's statutory authority for granting NCE exclusivity to reflect the agency's existing regulations and longstanding interpretation that award NCE exclusivity based on a drug's active moiety, as opposed to its active ingredient, which is intended to limit the applicability of NCE exclusivity, thereby potentially facilitating generic competition. In addition, the Further Consolidated Appropriations Act, 2020, which incorporated the framework from the Creating and Restoring Equal Access To Equivalent Samples (CREATES) legislation, allowed ANDA, 505(b)(2) NDA or biosimilar developers to obtain access to branded drug and biotherapeutic product samples. Further, Section 3222 of the Consolidated Appropriations Act, 2023, enacted on December 29, 2022 (the 2023 Appropriations Act), requires the FDA to make therapeutic equivalence determinations for 505(b)(2) NDAs at the time of approval, or up to 180 days thereafter, if requested by the applicant. Additionally, Section 3224 of the 2023 Appropriations Act allows the FDA to approve an ANDA even if there are differences between the generic drug's proposed labeling and that of the listed drug due to the FDA approving a change to the listed drug's label (excluding warnings) within 90 days of when the ANDA is otherwise eligible for approval, provided that the ANDA applicant agrees to submit revised labeling for the generic drug within 60 days of approval.

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) NDA 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) NDA applicant. The ANDA or 505(b)(2) NDA also will not receive final approval until any applicable non-patent exclusivity listed in the Orange Book for the RLD has expired.

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 has undergone a major change with the application of Regulation (EU) 536/2014, repealing the existing Directive 2001/20/EC. This new regulation harmonizes the assessment and supervision processes for clinical trials throughout the EU, via an EU portal and database, which the EMA will maintain in collaboration with the Member States and the EC. Following the EC's confirmation of full functionality of the Clinical Trials Information System (CTIS) through an independent audit, which was published in the Official Journal of the European Union in August 2021, Regulation (EU) 536/2014 became applicable concurrent with the CTIS "go-live" date on January 31, 2022. While existing clinical trials could continue to be conducted under the rules of Directive 2001/20/EC until January 31, 2025, any clinical trial initiated on or after January 31, 2023 must comply with the rules of the new regulation.

Under EU regulatory systems, a company may submit a marketing authorization application (MAA) 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 or reject it on the basis of potential serious risk to public health. If 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.

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 affecting a larger number of persons but 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 designation of a product as an orphan drug in the EU 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 govern 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 in January 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. These protections were expanded by the California Privacy Rights Act (CPRA), which became effective in most key respects in January 2023 and will be enforceable in most key respects beginning on July 1, 2023. Privacy laws in other states may also impact our operations, including both comprehensive and sector specific legislation, and Congress is considering additional federal privacy legislation. In addition, most healthcare professionals and facilities who may prescribe our products and from whom we may 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 considered to be a covered entity or business associate under HIPAA with respect to our clinical and commercial activities, we could be subject to penalties if we 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. The CCPA, as amended by the CPRA, 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 (CMS) annually certain payments and other transfers of value provided to physicians (defined to include doctors, dentists, optometrists, podiatrists and chiropractors), other healthcare professionals (such as physician assistants and nurse practitioners) and teaching hospitals, as well as ownership interests held by such physicians and their immediate family during the previous calendar year.

Because our products are covered in the U.S. by the Medicaid program, 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 (the 340B Program)). CMS continues to issue guidance and rulemaking governing our participation in the Medicaid Drug Rebate Program, and we cannot predict how future guidance or rules would affect our profitability (including due the potential for increases in our overall Medicaid rebate liability and the obligation to charge greatly reduced prices to covered entities. 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 countries 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 and rules, as well as executive orders, designed to, among other things: reduce or limit the prices of drugs and make them more affordable for patients (including, for example, by tying drug prices to the prices of drugs in other countries); reform the structure and financing of Medicare Part D pharmaceutical benefits; implement additional data collection and transparency reporting regarding drug pricing, rebates, fees and other remuneration provided by drug manufacturers; enable the government to negotiate prices under Medicare; revise rules associated with the calculation of average manufacturer price and best price under Medicaid; eliminate the AKS discount safe harbor protection for manufacturer rebate arrangements with Medicare Part D plan sponsors; create new AKS safe harbors applicable to certain point-of-sale discounts to patients and fixed fee administrative fee payment arrangements with pharmacy benefit managers; and revise the rebate methodology under the Medicaid Drug Rebate Program. For instance, in August 2022, President Biden signed the Inflation Reduction Act, which among other things: allows for CMS to impose price controls for certain single-source drugs and biotherapeutics reimbursed under Medicare Part B and Part D; subjects drug manufacturers to civil monetary penalties and a potential excise tax for offering a price that is not equal to or less than the government-imposed "maximum fair price" under the law; imposes additional rebates for price increases that exceed inflation; and redesigns the funding and benefit structure of the Medicare Part D program, potentially increasing manufacturer liability while capping annual out-of-pocket drug expenses for Medicare beneficiaries. These provisions have started taking effect incrementally beginning in 2022 and may be subject to various legal challenges. As of the date of this Annual Report on Form 10-K, CMS has commenced public rulemaking and issued guidance addressing certain aspects of the Inflation Reduction Act, and overtime the Inflation Reduction Act could reduce the revenues we are able to collect from sales of our

products and increase our government discount and rebate liabilities; however, the degree of impact that the Inflation Reduction Act will ultimately have upon our business remains unclear.

At the state level, legislatures have increasingly passed legislation and implemented regulations designed to control pharmaceutical and biotherapeutic 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. 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.

The U.S. pharmaceutical industry has already been significantly impacted by major legislative initiatives and related political contests. For instance, efforts to repeal, substantially modify or invalidate some or all of the provisions of the PPACA, some of which have been successful, create considerable uncertainties for all businesses involved in healthcare, including our own. In addition, there have been, and may in the future be, initiatives at both the federal and state-level that could significantly modify the terms and scope of 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. Although such attempts to reform the U.S. healthcare system have not significantly impacted our business to date, it is possible that additional legislative, executive and judicial activities in the future could have a material adverse impact on our business, financial condition and results of operations.

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. These entities could refuse, limit or condition coverage for our products, such as by using tiered reimbursement or pressing for new forms of contracting, or alternatively for patients who rely on our co-pay assistance program, implement co-pay accumulators or maximizers that exempt such co-pay assistance from deductibles (or otherwise modify benefit designs in a manner that takes into account the availability of co-pay assistance), which has increased and could further increase the costs of our co-pay assistance program or cause patients to abandon CABOMETYX or COMETRIQ therapy due to higher out-of-pocket costs. Due to general uncertainty in the current regulatory and healthcare policy environment, and specifically regarding positions that the Biden Administration may take with respect to these issues, 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, it is also possible that CMS could issue new rulemaking or guidance that would affect the amount of rebates owed under the Medicaid Drug Rebate Program.

In addition, in some foreign countries, 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 or otherwise provide data that seeks to establish the cost effectiveness of a new drug compared with other available established therapies. Other cost-control initiatives are similarly focused on affordability and accessibility, such as the Regulation on Health Technology Assessment (HTA Regulation) adopted in December 2021 and entering into application in 2025, as well as other upcoming legislative and policy changes aimed at increasing cooperation between EU Member States, and once enacted these initiatives may further impact the price and reimbursement status of many medicinal products. 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 EU Member States and other non-U.S. jurisdictions 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, antibodies and other treatments 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, deeper regulatory expertise and more extensive product manufacturing and commercial capabilities than we do, which may afford them 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, both alone and in combination with other therapies;
- 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, both alone and in combination with other therapies;
- our ability to manufacture and sell commercial quantities of cabozantinib product to the market;
- our ability to successfully commercialize cabozantinib, both as a single agent and as part of any combination therapy regimen, 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, or any combination therapy regimen that includes cabozantinib, in territories where they are approved;
- 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.

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. While we have had success in adapting our development strategy for the cabozantinib franchise to address the competitive landscape, including through evaluation of therapies that combine ICIs with other targeted agents, it is uncertain whether current and future clinical trials, including those evaluating cabozantinib in combination with an ICI in HCC, NSCLC and mCRPC, will lead to regulatory approvals, or whether physicians will prescribe regimens containing cabozantinib instead of competing product combinations in approved indications.

Below is a summary of the principal competition for cabozantinib in the indications for which it is approved or for which it has been or is currently being evaluated in potentially label-enabling trials, both as a single agent and in combination with other therapies. The information below does not include all competitor products, but rather those approved products that have or we believe may capture significant market share within their respective indications, or with respect to therapies still in development, those that are likely to overlap with patient populations that are or may be treated with cabozantinib or a combination therapy regimen that includes cabozantinib.

Competition in Approved Cabozantinib Indications

CABOMETYX - RCC: We believe the principal competition for CABOMETYX in advanced RCC includes: the combination of Merck & Co.'s pembrolizumab and Pfizer's axitinib; the combination of BMS's ipilimumab and nivolumab; and the combination of Merck & Co.'s pembrolizumab and Eisai's lenvatinib. Additionally, there are a variety of therapies being developed for advanced RCC, including: the combination of Peloton Therapeutics' (a wholly owned subsidiary of Merck & Co.) belzutifan (also known as MK-6482) and Eisai's lenvatinib; the combination of Merck & Co.'s pembrolizumab, Eisai's lenvatinib and Peloton Therapeutics' belzutifan; the combination of Merck & Co.'s pembrolizumab and quavonlimab and Eisai's lenvatinib; and Peloton Therapeutics' belzutifan.

The competitive landscape for RCC is evolving rapidly, especially given the entrance and increased adoption of ICI and ICI-TKI combination therapies into the RCC treatment landscape, particularly in the first-line setting. This has led to changing trends in prescribing and sequencing of certain drugs and combinations across different lines of therapy. It is difficult to predict how these changes will affect sales of CABOMETYX during 2023 and going forward.

CABOMETYX - HCC: We believe the principal competition for CABOMETYX in previously treated HCC includes: Bayer's regorafenib; and Eisai's lenvatinib. Additionally, there are a variety of therapies being developed for previously treated HCC, including the combination of Roche's atezolizumab and either Eisai's lenvatinib or Bayer's sorafenib.

The competitive landscape for HCC has significantly changed with the increased adoption of ICI combination therapies in the first-line setting, which may lead to an increase in prescribing and sequencing of TKIs in subsequent lines of therapy. It is difficult to predict how these changes will affect sales of CABOMETYX during 2023 and going forward.

CABOMETYX - DTC: We believe the principal competition for CABOMETYX in its previously treated DTC indication includes two treatments that are also approved for previously untreated DTC: Bayer's sorafenib; and Eisai's lenvatinib. In addition, we believe there is also competition for CABOMETYX from therapies approved to treat patients with advanced or metastatic RET fusion-positive thyroid cancer who require systemic therapy and who are RAI-refractory (if RAI is appropriate), including: Blueprint Medicine's and Roche's pralsetinib; and Loxo Oncology's (a wholly owned subsidiary of Eli Lilly) selpercatinib.

Other than the approvals of RET inhibitors to treat certain DTC patients, there has been little change in the competitive landscape for RAI-refractory DTC treatments during recent years.

COMETRIQ - MTC: 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, as well as other therapies that have been recently approved to treat patients with advanced or metastatic RET-mutant MTC who require systemic therapy, including: Blueprint Medicines' and Roche's pralsetinib; and Loxo Oncology's selpercatinib.

Other than the recent approvals of RET inhibitors to treat certain MTC patients, there has been little change in the treatment landscape for progressive, metastatic MTC during recent years, and due to the limited number of ongoing late-stage clinical trials in this indication, we do not expect many additional competitors to emerge in 2023.

Competition in Potential Cabozantinib Indications

Cabozantinib in combination with ICI – mCRPC: CONTACT-02 is a phase 3 pivotal trial evaluating the combination of cabozantinib and atezolizumab in patients with mCRPC who have been previously treated with one NHT. Should the combination of cabozantinib and atezolizumab be approved for the treatment of these mCRPC patients, 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; Sanofi's docetaxel; the combination of Merck & Co.'s pembrolizumab and Astellas Pharma's and Pfizer's enzalutamide; the combination of BMS' nivolumab and Sanofi's docetaxel; Veru Pharma's sabizabulin; and generic versions of abiraterone and docetaxel. In addition, we believe there may be competition for the combination of cabozantinib and atezolizumab in mCRPC from approved therapies or therapies in late-stage development focused on the subset of mCRPC patients who are prostate-specific membrane antigen positive, including: Novartis' ^{177}Lu-PSMA-617; POINT Biopharma's ^{177}Lu-PNT2002; Telix International's ^{177}Lu-DOTA-rosopatamab; and Curium US LLC's ^{177}Lu-PSMA-I&T.

Competition for Zanzalintinib

Zanzalintinib in combination with ICI - CRC: STELLAR-303 is a phase 3 pivotal trial evaluating the combination of zanzalintinib and atezolizumab in patients with metastatic non-microsatellite instability-high or non-mismatch repair-deficient CRC who have progressed after, or are intolerant to, the current standard of care. Should the combination of zanzalintinib and atezolizumab be approved for the treatment of these CRC patients, we believe its principal competition may include: Bayer's regorafenib; the combination of Ipsen's irinotecan and either Eli Lilly's cetuximab or Merck & Co.'s pembrolizumab; the combination of Eisai's lenvatinib and Merck & Co.'s pembrolizumab; the combination of Merck & Co.'s pembrolizumab and favezelimab; and the combination of Taiho Oncoloy's trifluridine/tipiracil and Roche's bevacizumab.

Zanzalintinib in combination with ICI - RCC: STELLAR-304 is a phase 3 pivotal trial evaluating zanzalintinib in combination with nivolumab in previously untreated patients with advanced non-clear cell RCC. Should the combination of zanzalintinib and nivolumab be approved for the treatment of these RCC patients, we believe its principal competition may include similar therapies that compete with cabozantinib or combination regimens containing cabozantinib in their various approved RCC indications.

Competition for Cobimetinib and Esaxerenone

There is competition for both cobimetinib and esaxerenone in the specific indications and territories where they are approved, and there are regular new entrants and developments in all aspects of these markets. However, given the relatively lesser degree of adoption of these therapies within the broader markets in which they compete and their minimal contribution to our total revenues as out-licensed products, we do not believe changes in the competitive landscape in these indications will have a material impact on our business.

Patents and Proprietary Rights

We actively seek patent protection in the U.S., EU and selected other foreign jurisdictions 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. To our knowledge, we own all global patents necessary for the continued sale and development of cabozantinib and cobimetinib, and we either own or have in-licensed all global patents for our other drug candidates, as further described below.

Cabozantinib

Cabozantinib is covered by more than 15 issued patents in the U.S., building from U.S. Patent No. 7,579,473, for the composition of matter of cabozantinib and pharmaceutical compositions thereof. This composition of matter patent would expire in September 2024, but we have been granted a patent term extension to extend the term to August 2026. The following table describes the US patents that cover our marketed cabozantinib products, and which are listed in the Orange Book. Except as otherwise noted, the stated expiration dates include any patent term extensions already granted. In addition to the composition of matter patent referenced above, the table includes patents directed to, among other things, particular salts, polymorphs, formulations, or use of the compound in the treatment of specified diseases or conditions. We continue to pursue additional patents and patent term extensions in the U.S. and other territories covering various aspects of our cabozantinib products that may, if issued, extend exclusivity beyond the expiration of the patents listed in the table.

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
	10,034,873	Methods of treatment	2031
	10,039,757	Methods of treatment	2031
	11,091,439	Crystalline salt forms of cabozantinib	2030
	11,091,440	Pharmaceutical composition	2030
	11,098,015	Methods of treatment	2030
	11,298,349	Pharmaceutical composition	2032
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
	11,091,439	Crystalline salt forms of cabozantinib	2030
	11,091,440	Pharmaceutical composition	2030
	11,098,015	Methods of treatment	2030
	11,298,349	Pharmaceutical composition	2032

Given the importance of our intellectual property portfolio to our business operations, we vigorously enforce our rights and defend against challenges that have arisen or may arise with respect to patents and patent applications required for the commercialization of medicines containing cabozantinib. For example, in September 2019, we received a Paragraph IV notice letter regarding an ANDA submitted to the FDA by MSN Pharmaceuticals, Inc. (MSN), requesting approval to market a generic version of CABOMETYX tablets, which MSN then amended with additional Paragraph IV certifications in May 2020, January 2022 and June 2022. In response, we have filed a total of four patent infringement lawsuits against MSN in the United States District Court for the District of Delaware (the Delaware District Court): the first two lawsuits filed in October 2019 and May 2020 were later consolidated into a single case (referred to as MSN I) and adjudicated at a bench trial in May 2022; and the third and fourth lawsuits filed in February 2022 and July 2022, respectively, were also consolidated into a single case (referred to as MSN II) and will be adjudicated at another bench trial scheduled for October 2023. In January 2023, the Delaware District Court issued a ruling in the MSN I case, rejecting MSN's invalidity challenge to U.S. Patent No. 7,759,473, which expires in 2026, but also ruled that MSN's proposed ANDA product does not infringe U.S. Patent No. 8,877,776, which expires in 2030. This ruling in MSN I does not address the parties' claims in the MSN II lawsuit. In addition, in May 2021, we received Paragraph IV certification notice letters regarding an ANDA submitted to the FDA by Teva Pharmaceutical Industries Limited, Teva Pharmaceuticals Development, Inc. and Teva Pharmaceuticals USA, Inc. (individually and collectively referred to as Teva), requesting approval to market a generic version of CABOMETYX tablets, which Teva then amended with additional Paragraph IV certifications in July 2022. In response, we have filed two patent infringement lawsuits against Teva in the Delaware District Court in June 2021 and September 2022, which were consolidated into a single case, and all proceedings in our litigation against Teva were stayed pursuant to an order of the Delaware District Court in October 2022. Most recently, on February 6, 2023, we received a Paragraph IV certification notice letter regarding an ANDA submitted to the FDA by Cipla Limited (Cipla) requesting approval to market a generic version of CABOMETYX tablets. We cannot predict the ultimate outcome of these ANDA submissions and/or any related lawsuits or provide assurance that these lawsuits 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 these litigation matters, see "Legal Proceedings" in Part I, Item 3 of this Annual Report on Form 10-K.

In the EU, 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 the EU to extend the term to 2029. In addition to the composition of matter patent, the table below includes certain 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 issued patents covering the composition of matter, and salts thereof, as well as pharmaceutical compositions and related methods of use, and Takeda has applied 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 2037. Outside the U.S. and Japan, cabozantinib is licensed to Ipsen, and 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.

Zanzalintinib and Other Drug Candidates

We also have issued patents and pending patent applications, and will continue to file new patent applications, in the U.S., the EU and other selected countries covering our other drug candidates in clinical and/or preclinical development, including zanzalintinib, XB002 and XL102. Zanzalintinib in particular is covered by U.S. Patent No. 11,542,259, and we have pending patent applications in the U.S. and other selected countries covering the composition of matter, certain synthetic methods, salts, polymorphs, formulations and combinations of zanzalintinib that, if issued, are anticipated to expire between 2039 and 2043, excluding any potential patent term adjustments and/or extensions.

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.

Human Capital Management

Our Employees and Commitment to Diversity, Equity and Inclusion

As of December 31, 2022, we had 1,223 employees, representing a 28% increase in our employee workforce as compared to December 31, 2021. Of these employees, 600 are members of our research and development teams and 623 are members of our commercial, general and administrative teams. Of these employees, 215 hold Ph.D. degrees, 23 hold M.D. (or foreign equivalent) degrees, 32 hold PharmD degrees and 111 hold other professional degrees such as a J.D. or M.B.A. None of our employees are represented by a labor union, and we consider our employee relations to be good.

During the past five years, our employee turnover has remained consistently below average for the U.S. life sciences industry generally. Given our expanding operations and need to further grow our headcount to support our business, we continually assess employee turnover, recruitment initiatives, compensation and benefits programs, safety in

performing critical laboratory work, diversity and other matters relevant to human capital management, and we review results with our Board of Directors on a periodic basis.

We are an equal opportunity employer and maintain policies that prohibit unlawful discrimination based on race, color, religion, gender, sexual orientation, gender identity/expression, national origin/ancestry, age, disability, marital and veteran status. We are proud to employ a diverse workforce that, as of December 31, 2022, was 59% non-white and 52% women. In addition, as of December 31, 2022, 54% of our positions that manage other employees directly were held by non-whites and 44% were held by women, and women made up 33% of our senior leadership team. We strive to build and nurture a culture where all employees feel empowered to be their authentic selves. We respect and appreciate each employee's unique perspective and experiences, and value their contributions to our mission. It is important that we celebrate, encourage and support similarities and differences to drive innovation for the benefit of our employees, patients and community.

Culture, Compensation and Benefits

At Exelixis, we value being exceptional in what we do and how we lead, excelling for patients by going the extra mile to care for them and exceeding together as a business and contributor to the scientific community. We strive to live these values every day across the company, integrating them into everything from our interview, hiring and onboarding processes, to our performance evaluation, rewards and promotion programs.

We provide generous compensation packages designed to attract and retain high-quality employees, and all of our employees are eligible for cash bonuses and grants of long-term incentive awards. We regularly evaluate our compensation programs with an independent compensation consultant and utilize industry benchmarking in an effort to ensure they are competitive with the biotechnology and biopharmaceutical companies against which we compete for talent, as well as fair and equitable across our workforce with respect to gender, race and other personal characteristics. We utilize a third-party firm to conduct an annual pay equity analysis; for 2022, the fourth year in a row, this analysis demonstrated no gender or ethnicity-based disparities. In addition, we are proud to provide a variety of programs and services to help employees meet and balance their needs at work, at home and in life, including an attractive mix of healthcare, insurance and other benefit plans. We deliver a benefits program that is designed to keep our employees and their families mentally, physically and emotionally healthy, which includes not only medical, dental and vision benefits, but also dependent care, mental health and other wellness benefits. For a discussion of workplace safety measures we have taken, see "—Environmental, Health and Safety."

Beyond compensation and benefits, we also value career development for all employees, and we offer a tuition reimbursement program, as well as professional development courses ranging from technical training, competency-based workshops and leadership development programs facilitated by external partners who are experts in their respective fields. Direct managers also take an active role in identifying individualized development plans to assist their employees in realizing their full potential and creating opportunities for promotions and added responsibilities that enhance the engagement and retention of our workforce.

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 make an investment in our securities speculative or risky, and 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 and the value of your investment in our company could be harmed.

Risks Related to the Commercialization of Our Products

Our ability to grow our company is dependent upon the commercial success of CABOMETYX in its approved indications and the continued clinical development, regulatory approval, clinical acceptance and commercial success of the cabozantinib franchise 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, both alone and in combination with other therapies, as a treatment for the highly competitive indications for which it is approved, and possibly for other indications for which cabozantinib is currently being evaluated in potentially label-enabling clinical trials, if warranted by the data generated from these trials. In this regard, part of our strategy is to pursue additional indications for CABOMETYX and increase the number of cancer patients who could potentially benefit from this medicine. However, we cannot be certain that the clinical trials we and our collaboration partners are conducting 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 the required regulatory approvals to market CABOMETYX for additional indications are achieved, 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 number of labeled indications for which CABOMETYX is approved, or if we or our collaboration partners 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.

Our ability to grow revenues from sales of CABOMETYX depends upon the degree of market acceptance among physicians, patients, healthcare 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, foreign and U.S. government healthcare payers such as Medicare and Medicaid, commercial healthcare plans and the medical community. Market acceptance for CABOMETYX could be impacted by numerous factors, including the effectiveness and safety profile, or the 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 patients in its approved 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 current and future product candidates.

The biopharmaceutical industry is competitive and characterized by constant technological change and diverse offerings of products, particularly in the area of 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 biopharmaceutical 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. Even if our current and future clinical trials, including those evaluating cabozantinib in combination with an ICI in mCRPC or evaluating zanzalintinib in combination with an ICI in CRC and RCC, produce positive results sufficient to obtain marketing approval by the FDA and other global regulatory authorities, it is uncertain whether physicians will choose to prescribe regimens containing our products instead of competing products and product combinations in approved indications.

If we are unable to maintain or increase our 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 our 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 precommercial-stage, oncology-focused biopharmaceutical companies seeking to build out and maintain their commercial organizations, as well as larger biopharmaceutical 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 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 foreign and U.S. 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. These entities could refuse, limit or condition coverage for our products, such as by using tiered reimbursement or pressing for new forms of contracting, or alternatively for patients who rely on our co-pay assistance program, implement co-pay accumulators or maximizers that exempt such co-pay assistance from patient deductibles (or otherwise modify benefit designs in a manner that takes into account the availability of co-pay assistance), which has increased and could further increase the costs of our co-pay assistance program or cause patients to abandon CABOMETYX or COMETRIQ therapy due to higher out-of-pocket costs. If third-party payers do not provide or increase limitations on coverage or reimbursement for CABOMETYX or COMETRIQ, our revenues and results of operations may 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.

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 and expanding patient access. The life sciences 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. In addition, there have been, and may in the future be, initiatives at both the federal and state level that could significantly modify the terms and scope of government-provided health insurance coverage, ranging from changes to some or all of the provisions of the PPACA to establishing a single-payer, national health insurance system to more limited “buy-in” options to existing public health insurance programs, any of which could have a significant impact on the healthcare industry. Although such attempts to reform the U.S. healthcare system have not significantly impacted our business to date, it is possible that additional legislative, executive and judicial activities in the future could have a material adverse impact on our business, financial condition and results of operations.

Furthermore, because we participate in the 340B Program to sell a portion of our marketed products, changes in the administration of the program could have a material adverse impact on our revenues. Some manufacturers are currently involved in ongoing litigation regarding the legality of contract pharmacy arrangements under the 340B Program,

which may affect the way in which manufacturers are required to extend discounts to covered entities through contract pharmacies. Effective July 2022, we implemented a 340B Program Integrity Initiative, pursuant to which we request all hospital covered entities (i.e., hospitals that participate in the 340B Program) to provide claims-level data for CABOMETYX and COMETRIQ dispensed by contract pharmacies. A covered entity that elects not to provide this limited claims data and that does not have an in-house pharmacy may designate a single contract pharmacy location within our authorized specialty pharmacy network. We believe this initiative will provide much-needed transparency and promote compliance with program requirements, and at the same time, should not restrict patient access to our medicines. HHS has notified us that it is reviewing our policy, and we have responded to HHS' request for information. Since 2021, numerous manufacturers that previously implemented similar contract pharmacy integrity programs have received enforcement letters from HHS stating that those manufacturers' actions restricted contract pharmacy transactions in violation of the 340B Program statute, which may subject them to repayment of overcharges and civil monetary penalties. As mentioned above, certain of these manufacturers are now in litigation with the government over the legality of these programs, and depending on the outcome of such litigation, we may be required to modify or suspend our 340B Program Integrity Initiative. Further, it is possible that HHS could seek to implement administrative proceedings to recover overcharges and/or impose civil monetary penalties against us regarding our 340B Program Integrity Initiative. If such proceedings were implemented against us, a negative ruling could have a material adverse effect on our business, financial condition and results of operations. Due to general uncertainty with respect to this litigation and in the current regulatory and healthcare policy environment, and specifically regarding positions that the Biden Administration may take with respect to these issues, 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, we and any third parties we might engage may be unable to adapt to any changes implemented as a result of such measures, and we could face difficulties in maintaining or increasing profitability or otherwise experience 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. Initiatives arising from this scrutiny may result in changes that have the effect of reducing our revenue or harming our business or reputation.

There continue to be U.S. Congressional inquiries, hearings and proposed and enacted federal legislation and rules, as well as executive orders, designed to, among other things: reduce or limit the prices of drugs and make them more affordable for patients (including, for example, by tying drug prices to the prices of drugs in other countries); reform the structure and financing of Medicare Part D pharmaceutical benefits; implement additional data collection and transparency reporting regarding drug pricing, rebates, fees and other remuneration provided by drug manufacturers; enable the government to negotiate prices under Medicare; revise rules associated with the calculation of average manufacturer price and best price under Medicaid; eliminate the AKS discount safe harbor protection for manufacturer rebate arrangements with Medicare Part D plan sponsors; create new AKS safe harbors applicable to certain point-of-sale discounts to patients and fixed fee administrative fee payment arrangements with pharmacy benefit managers; and revise the rebate methodology under the Medicaid Drug Rebate Program. For instance in August 2022, President Biden signed the Inflation Reduction Act, which among other things: allows for CMS to impose price controls for certain single-source drugs and biotherapeutics reimbursed under Medicare Part B and Part D; subjects drug manufacturers to civil monetary penalties and a potential excise tax for offering a price that is not equal to or less than the government-imposed "maximum fair price" under the law; imposes Medicare rebates for price increases that exceed inflation; and redesigns the funding and benefit structure of the Medicare Part D program, potentially increasing manufacturer liability while capping annual out-of-pocket drug expenses for Medicare beneficiaries. These provisions have started taking effect incrementally in late 2022 and may be subject to various legal challenges. As of the date of this Annual Report on Form 10-K, CMS has commenced public rulemaking and issued guidance addressing certain aspects of the Inflation Reduction Act, and overtime the Inflation Reduction Act could reduce the revenues we are able to collect from sales of our products and increase our government discount and rebate liabilities; however, the degree of impact that the Inflation Reduction Act will ultimately have upon our business remains unclear. In addition, we cannot know the final form or timing of any other legislative, regulatory and/or administrative measures, and some of these pending and enacted legislative proposals or executive rulemaking, if implemented without successful legal challenges, 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.

At the state level, legislatures have increasingly passed legislation and implemented regulations designed to control pharmaceutical and biotherapeutic 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. In particular, the obligation to provide notices of price increases to purchasers under laws such as California's SB-17 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 these drug pricing transparency regulations, and our associated compliance obligations, may increase our general and administrative costs and/or diminish our revenues. Implementation of these federal and/or state cost-containment measures or other healthcare reforms may limit our ability to generate product revenue or commercialize our products, and in the case of drug pricing transparency regulations, may result in fluctuations in our results of operations.

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., including major markets in the EU and Japan, the pricing and reimbursement of prescription pharmaceuticals is generally subject to significant governmental control. In these 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 partners Ipsen and Takeda may also be required to conduct a study or otherwise provide data 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 and accessibility, as well as post-marketing assessments of the added value of CABOMETYX and COMETRIQ as compared to existing treatments, could influence the prices paid for and net revenues we realize from CABOMETYX and COMETRIQ, or the indications for which we are able to obtain reimbursement, which would result in lower license revenues to us. Recent legislative changes and ongoing policy changes in the EU are aimed at increasing cooperation between the EU Member States. Such initiatives, particularly the HTA Regulation adopted in December 2021, may further impact the price and reimbursement status of CABOMETYX and COMETRIQ when it enters into application 2025.

The timing of the entrance of generic competitors to CABOMETYX and legislative and regulatory action designed to reduce barriers to the development, approval and adoption of generic drugs in the U.S. could limit the revenue we derive from our products, most notably CABOMETYX, 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 part on the agency's findings of safety and/or effectiveness for a previously approved drug, where at least some of the information required for approval comes from studies not conducted by or for the applicant and for which the applicant has not obtained a right of reference or use. Both the ANDA and 505(b)(2) NDA processes are discussed above in "Item 1. Business—Government Regulation—FDA Review and Approval—Abbreviated FDA Approval Pathways and Generic Products" in this Annual Report on Form 10-K. In either case, if an ANDA or 505(b)(2) NDA 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 substantial costs, divert the attention of management, and could have an adverse impact on our stock price. For example, MSN, Teva and Cipla have separately submitted ANDAs to the FDA requesting approval to market their respective generic versions of CABOMETYX tablets, and we have subsequently filed patent enforcement lawsuits against both companies. For a more detailed discussion of these litigation matters, see "Legal Proceedings" in Part I, Item 3 of this Annual Report on Form 10-K. It is possible that MSN, Teva, Cipla or other companies, following FDA approval of an ANDA or 505(b)(2) NDA, could introduce generic or otherwise competitor 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. Regardless of the regulatory approach, the introduction of a generic version of cabozantinib would likely decrease our revenues derived from the U.S. sales of CABOMETYX and thereby materially harm our business, financial condition and results of operations. There are also equivalent procedures in the EU permitting authorization of generic versions and biosimilars of medicinal products authorized in the EU once related data and market exclusivity periods have expired.

The U.S. federal government has also taken numerous legislative and regulatory actions to expedite the development and approval of generic drugs and biosimilars. Both Congress and the FDA are considering, and have enacted, 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 Ensuring Innovation Act, enacted in April 2021, amended the FDA's statutory authority for granting NCE exclusivity to reflect the agency's existing regulations and longstanding interpretation that award NCE exclusivity based on a drug's active moiety, as opposed to its active ingredient, which is intended to limit the applicability of NCE exclusivity, thereby potentially facilitating generic competition. In addition, the Further Consolidated Appropriations Act, 2020, which incorporated the framework from the CREATES legislation, allowed ANDA, 505(b)(2) NDA or biosimilar developers to obtain access to branded drug and biotherapeutic product samples. Further, Section 3222 of the of the 2023 Appropriations Act requires the FDA to make therapeutic equivalence determinations for 505(b)(2) NDAs at the time of approval, or up to 180 days thereafter, if requested by the applicant. Additionally, Section 3224 of the 2023 Appropriations Act allows the FDA to approve an ANDA even if there are differences between the generic drug's proposed labeling and that of the listed drug due to the FDA approving a change to the listed drug's label (excluding warnings) within 90 days of when the ANDA is otherwise eligible for approval, provided that the ANDA applicant agrees to submit revised labeling for the generic drug within 60 days of approval. While the full impact of these provisions is unclear at this time, its provisions do have the potential to facilitate the development and future approval and market success of generic versions of our products, introducing generic competition that could have a material adverse impact on our business, financial condition and results of operations.

Risks Related to Growth of Our Product Portfolio and Research and Development

We may be unable to expand our discovery and 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 drug discovery activities with the goal of identifying new product candidates to advance into clinical trials. Notwithstanding this investment, many programs that initially show promise will 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 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 and technologies. However, the in-licensing and acquisition of product candidates and technologies is a highly competitive area, and many other companies are pursuing the same or similar product candidates and technologies 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 and technologies on acceptable terms that would allow us to realize an appropriate return on our investment. Even if we succeed in our efforts to obtain rights to suitable product candidates and technologies, the competitive business environment may result in higher acquisition or licensing costs, and our investment in these potential products and technologies 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 company, or retain key personnel of the acquired business. Furthermore, we could assume unknown or contingent liabilities or otherwise 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. If our drug discovery efforts, including research collaborations, in-licensing arrangements and other business development activities, do not result in suitable product candidates, our business and prospects for growth could suffer.

Clinical testing of cabozantinib for new indications, or of new product candidates, is a lengthy, costly, complex and uncertain process that may fail ultimately to demonstrate safety and efficacy data for those products sufficiently differentiated to compete in our highly competitive market environment.

Clinical trials are inherently risky and may reveal that cabozantinib, despite its approval for certain indications, or a new 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 of a product candidate or of an approved product for a new 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 investigations, that could delay or prevent commercialization of cabozantinib in new indications or of zanzalintinib or other new product candidates. These events may include:

- lack of acceptable 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 clinical trial sites;
- lower-than-anticipated patient registration or enrollment in our clinical testing;
- additional complexities posed by clinical trials evaluating cabozantinib, zanzalintinib or our other product candidates in combination with other therapies, including extended timelines to provide for collaboration on clinical development planning, the 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
- reduced staffing or shortages in laboratory supplies and other resources necessary to complete the trials;
- 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, variations, 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.

The ongoing Russo-Ukrainian War has had a modest impact on our clinical development operations, particularly with respect to patient recruitment, potentially delaying our ability to complete enrollment in a timely manner. In addition, this conflict has had and may continue to have an adverse impact on the ability of clinical sites and their patients to adhere to trial protocols for in-office clinical visits and other procedures, our ability to supply clinical sites with cabozantinib or other study drugs and to pay clinical sites and investigators for work performed, as well as our ability to collect data and conduct site monitoring visits, all of which could undermine the data quality for patients enrolled at these clinical sites. The need to shift enrollment of patients away from these clinical sites or close certain sites entirely, or to replace patients in affected territories should investigators be unable to continue treating and monitoring them, could further impact our anticipated timelines for completing the trials and achieving clinical endpoints, as well as increase our clinical development expenses.

If there are further delays in or termination of the clinical testing of cabozantinib, zanzalintinib or our other product candidates due to 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 cabozantinib 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 the cabozantinib franchise 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 the cabozantinib franchise, zanzalintinib 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 otherwise may not result in an approvable product. The duration and the cost of clinical trials vary significantly as a result of factors relating to a particular clinical trial, including, among others: the 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 trial; 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.

The regulatory approval processes of the FDA and comparable foreign regulatory authorities are lengthy, uncertain and subject to change, and may not result in regulatory approvals for additional cabozantinib indications or for 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 the cabozantinib franchise, zanzalintinib 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 regulatory authorities in other territories. 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 marketing authorization application to the EMA or any application or submission to comparable 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. 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 zanzalintinib or our other product candidates. For example, the FDA launched Project Optimus in 2021 as an initiative to reform the dose optimization and dose selection paradigm in oncology drug development, which was driven by the FDA's concerns that the current paradigm for dose selection may result in doses and schedules of molecularly targeted therapies that are inadequately characterized before initiating pivotal trials. Through collaboration with the biopharmaceutical industry, academia and other stakeholders, the FDA's goal for this initiative is to advance an oncology dose-finding and dose optimization paradigm that emphasizes dose selections that maximize efficacy as well as safety and tolerability. In support of this initiative, the FDA may request sponsors of oncology product candidates to conduct dose optimization studies pre- or post-approval, and the FDA also continues to develop and finalize guidance documents and implement initiatives regarding the development and clinical research of oncology product candidates. Recently, in part due to questions raised by the process underlying the approval of an Alzheimer's disease drug, government authorities and other stakeholders have been scrutinizing the accelerated approval pathway, with some stakeholders advocating for reforms. Even prior to this, the FDA has held Oncologic Drugs Advisory Committee meetings to discuss accelerated approvals for which confirmatory trials have not verified clinical benefit. Such scrutiny, among other factors, has resulted in voluntary withdrawals of certain products and indications approved on an accelerated basis. Spurred by the Alzheimer's drug controversy, the HHS Office of Inspector General has also initiated an assessment of how the FDA implements the accelerated approval pathway. In addition, Section 3210 of the 2023 Appropriations Act revised the accelerated approval pathway. Although this legislation did not change the standard for accelerated approval, it, among other things: requires the FDA to specify the conditions for required post-marketing trials; permits the FDA to require such trials to be underway prior to approval, or within a specific period after approval; requires sponsors to provide reports on post-marketing trial progress no later than 180 days after approval and every 180 days thereafter until such trials are completed; makes the failure to conduct required post-marketing trials with due diligence and the failure to submit the required reports prohibited acts; and details procedures the FDA must follow to withdraw an accelerated approval on an expedited basis. While it is not clear at this time how these legislative and regulatory initiatives will affect our plans to pursue accelerated approval for one or more of our product candidates, these developments may have a material adverse impact on our business, financial condition and results of operations.

Even if the FDA or a comparable authority in another jurisdiction approves cabozantinib for one or more new indications or approves one of our other product candidates, including zanzalintinib, for use, 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-marketing 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, zanzalintinib or our other product candidates in any new indications. Failure to complete post-marketing requirements of the FDA in connection with a specific approval 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, zanzalintinib or another product candidate in the approved indication. Regulatory agencies could also impose various administrative, civil or criminal sanctions for failure to comply with regulatory requirements, including withdrawal of product approval. Further, current or any future laws or executive orders governing FDA or foreign regulatory approval processes that may be enacted or executed could have a material adverse impact on our business, financial condition and results of operations.

Risks Related to Financial Matters

Our profitability could be negatively impacted if expenses associated with our extensive clinical development, business development and commercialization activities, both for the cabozantinib franchise and our other product candidates, grow more quickly than the revenues we generate.

Although we reported net income of $182.3 million and $231.1 million for the fiscal years ended December 31, 2022 and 2021, 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.; our achievement of development, regulatory and commercial milestones, if any, under our collaboration agreements; the amount of royalties from sales of CABOMETYX and COMETRIQ outside of the U.S. under our collaboration agreements; other collaboration revenues; and the level of our expenses, including those associated with our extensive drug discovery, clinical development and business development activities, both for the cabozantinib franchise and our other product candidates, as well as our general business expansion plans. Our expected future expenses in particular may also be increased by inflationary pressures, which could increase the costs of outside services, labor, raw materials and finished drug product. We expect to continue to spend substantial amounts to fund the continued development of the cabozantinib franchise for additional indications and of our other product candidates, as well as the commercialization of our approved products. In addition, we intend to continue to expand our oncology product pipeline through our drug discovery efforts, including research collaborations, in-licensing arrangements and other 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.

Risks Related to Our Relationships with Third Parties

We rely on Ipsen and Takeda for the commercial success of CABOMETYX in its approved indications outside of the U.S., and we 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 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. If our collaboration partners are unable or unwilling to invest the resources necessary to commercialize CABOMETYX successfully in the EU, Japan 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 clinical, regulatory and commercial collaborations with major companies make us reliant on those companies for their continued performance and investments, which subjects us to a number of risks.

We have established clinical and commercial collaborations with leading biopharmaceutical companies for the development and commercialization of our products, and our dependence on these collaboration partners subjects us to a number of risks, including, but not limited to:

- our collaboration partners' decision to terminate our collaboration, or their failure to comply with the terms of our collaboration agreements and related ancillary agreements, either intentionally or as a result of negligence or other insufficient performance;
- our inability to control the amount and timing of resources that our collaboration partners devote to the development or commercialization of our products;
- the possibility that our collaboration partners may stop or delay clinical trials, fail to supply us on a timely basis with product required for a combination trial, or deliver product that fails to meet appropriate quality and regulatory standards;
- disputes that may arise between us and our collaboration partners that result in the delay or termination of the 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 that prevent them from fulfilling their obligations under our agreements;
- our collaboration partners' inability to obtain regulatory approvals in a timely manner, or at all;
- our collaboration partners' failure to comply with legal and regulatory requirements relevant to the authorization, marketing, distribution and supply of our marketed products in the territories outside the U.S. where they are approved; and
- 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.

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 and prospects for growth could be delayed or disrupted, all of which could have a material adverse impact on our business, financial condition and results of operations.

Our growth potential is dependent in part upon companies with which we have entered into research collaborations, in-licensing arrangements and similar business development relationships.

To expand our early-stage product pipeline, we have augmented our drug discovery activities with multiple research collaborations and in-licensing arrangements with other companies. Our dependence on our relationships with these research and in-licensing partners subjects us to numerous risks, including, but not limited to:

- our research and in-licensing partners' decision to terminate our relationship, or their failure to comply with the terms of our agreements, either intentionally or as a result of negligent performance;
- disputes that may arise between us and our research and in-licensing partners that result in the delay or termination of research activities with respect to any in-licensed assets or supporting technology platforms;
- the possibility that our research and in-licensing partners may experience financial difficulties that prevent them from fulfilling their obligations under our agreements;
- the possibility that our research and in-licensing partners may be acquired and that any acquiring entity may not honor our partners' research commitments or otherwise fail to continue fulfilling their obligations under our agreements;
- our research and in-licensing partners' failure to properly maintain or defend their intellectual property rights or their use of third-party intellectual property rights or proprietary information in such a way as to invite litigation that could jeopardize or invalidate our license to develop these assets or utilize technology platforms;
- laws, regulations or practices imposed by countries outside the U.S. that could impact or inhibit scientific research or the development of healthcare products by foreign competitors or otherwise disadvantage healthcare products made by foreign competitors, as well as general political or economic instability in those countries, any of which could complicate, interfere with or impede our relationships with our ex-U.S. research, development and in-licensing partners; and

- our research and in-licensing partners' failure to comply with applicable healthcare laws, as well as established guidelines, laws and regulations related to GMP and GLP.

If any of these risks materialize, we may not be able to expand our product pipeline or otherwise realize a return on the resources we will have invested to develop these early-stage assets, which could have a material adverse impact on our financial condition and prospects for growth.

If third parties upon which we rely to perform clinical trials for cabozantinib in new indications or for new 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, 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 trial or data security 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 beyond currently approved indications or obtain regulatory approval for zanzalintinib or our other product candidates. 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 help advance our drug discovery efforts, which would impede our ability to identify, develop and commercialize our potential product candidates.

We lack our own manufacturing and distribution capabilities necessary for us to produce materials required for certain preclinical activities and to produce and distribute our products for clinical development or for commercial sale, and our reliance on third parties for these services subjects us to various risks.

We do not own or operate manufacturing or distribution facilities for CMC development activities, preclinical, clinical or commercial production and distribution for our current products and new product candidates. Instead, we rely on various third-party contract manufacturing organizations to conduct these operations on our behalf. As our operations continue to grow in these areas, we continue to expand our supply chain through additional third-party contract manufacturers, distributors 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 or deliver material on a timely basis or manufacture material with the required quality standards, or in the quantity required to meet our preclinical, clinical development and commercial needs and applicable regulatory requirements. Although we have not yet experienced significant production delays or seen significant impairment to our supply chain as a result of the COVID-19 pandemic or the ongoing Russo-Ukrainian War, our third-party contract manufacturers, distributors and suppliers could experience operational delays due to lack of capacity or resources, facility closures and other hardships as a result of these types of global events, which could impact our supply chain by potentially causing delays to or disruptions in the supply of our preclinical, clinical or commercial products. If our third-party contract manufacturers, distributors 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 manufacturing, distribution and supply arrangements, we may not have adequate remedies for any breach. Furthermore, their failure to supply us could impair or preclude meeting commercial or clinical product supply requirements for us or our partners, which could delay product development and future commercialization 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 and its foreign equivalents where applicable. If our third-party contract manufacturers or data service providers fail to support our efforts to continue to comply with DSCSA and its foreign equivalents, as well as any future electronic pedigree requirements, we may face legal penalties or be restricted from selling our products.

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 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, their ability to perform services may be impacted by increased demand for such services from other companies or by other external factors, such as reduced capacity to perform services. If we experience additional delays in the receipt of services, lose work performed by these scientific advisors and contractors or are unable to engage them in the first place, 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 Healthcare Regulatory and Other Legal Compliance Matters

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 federal and state healthcare laws and regulations, which laws and regulations are enforced 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 business conduct or inaccurate reporting, we could be subject to enforcement of the following, including, without limitation:

- the federal AKS;
- the FDCA and its implementing regulations;
- federal civil and criminal false claims laws, including the civil False Claims Act, and the Civil Monetary Penalties Law;
- 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, as amended;
- state law equivalents of each of the above federal laws;
- the Open Payments program of the PPACA;
- 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; and
- state and federal pharmaceutical price and price reporting laws and regulations.

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 drug marketing practices, including off-label promotion, and also impact our current and future business arrangements with third parties, including various healthcare entities. If our operations are found, or even alleged, to be in violation of the laws described above or 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 through a Corporate Integrity Agreement or other monitoring agreement, any of which would adversely affect our ability to sell our products and operate our business and also adversely affect our financial results. Furthermore, responding to any such allegation or investigation

and/or defending against any such enforcement actions can be time-consuming and would require significant financial and personnel resources. Therefore, if any state or the federal government initiates an enforcement action against us, our business may be impaired, and even if we are ultimately successful in our defense, litigating these actions could result in substantial costs and divert the attention of management.

Enhanced governmental and private scrutiny over, or investigations or litigation involving, pharmaceutical manufacturer patient assistance programs and donations to patient assistance foundations created by charitable organizations 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 HHS Office of Inspector General established 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. In the event we make such donations but are found not to have complied with these guidelines and other laws or regulations respecting the operation of these programs, we could be subject to significant damages, fines, penalties or other criminal, civil or administrative sanctions or enforcement actions. Moreover, in December 2020, the CMS finalized changes to Medicaid Drug Rebate Program pricing calculations regarding the provision of co-payment assistance to patients that may be impacted by private insurer accumulator programs. The portion of this rule dealing with manufacturer co-payment assistance (and related support programs) was challenged and vacated by a federal court in May 2022 (and CMS did not appeal). However, it is possible that CMS could issue new rulemaking or guidance that would affect the amount of rebates owed under the Medicaid program or otherwise limit our ability to support our patient co-pay assistance program. We also rely on a third-party hub provider and exercise oversight to monitor patient assistance program activities. Hub providers are generally hired by manufacturers to assist patients with insurance coverage, financial assistance and treatment support after the patients receive a prescription from their healthcare professional. For manufacturers of specialty pharmaceuticals (including our marketed products), the ability to have a single point of contact for their therapies helps ensure efficient medication distribution to patients. Accordingly, our hub activities are also subject to scrutiny and may create risk for us if not conducted appropriately. A variety of entities, including independent charitable foundations and pharmaceutical manufacturers, but not including our company, have received subpoenas from the U.S. Department of Justice (DOJ) and other enforcement authorities seeking information related to their patient assistance programs and support, and certain of these entities have entered into costly civil settlement agreements with DOJ and other enforcement authorities that include requirements to maintain complex corporate integrity agreements that impose significant reporting and other requirements. Should we or our hub providers receive a subpoena or other process, regardless of whether we are ultimately found to 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 in the U.S. and other jurisdictions around the world. For example, the CPRA went into operation in 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. These protections were expanded by the CPRA, which became effective in January 2023 and will be enforceable in most key respects beginning on July 1, 2023. Privacy laws in other states may also impact our operations, including both comprehensive and sector-specific legislation, and Congress is also considering additional federal privacy legislation. In addition, most healthcare professionals and facilities are subject to privacy and security requirements under HIPAA with respect to our clinical and commercial activities. Although we are not considered to be a covered entity or business associate under HIPAA, we could be subject to penalties if we 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, in the EU, 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 places restrictions on 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, including the CCPA, as amended by the CPRA, as well as the GDPR, we could be subject to sanctions or other penalties, litigation, an increase in our cost of doing business and questions concerning the validity of our data processing activities, including clinical trials.

Risks Related to Our Information Technology and Intellectual Property

Data breaches, cyber-attacks and other failures in our information technology operations and 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 and our third-party service providers, such as contract research organizations, 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 critical business operations, expend key information technology resources and divert the attention of management.

Although the aggregate impact of cyber-attacks on our operations and financial condition has not been material to date, we and our third-party service providers have frequently been the target of threats of this nature and expect them to continue. Any future data breach and/or 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 and result in harm to 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 third-party service providers 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, we received Paragraph IV certification notice letters from MSN, Teva and Cipla concerning the respective ANDAs that each had filed with the FDA seeking approval to market their respective generic versions of CABOMETYX tablets. Should MSN, Teva, Cipla 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. They may also be negatively impacted by the decisions of foreign courts, which could limit the protection contemplated by the original regulatory approval and our ability to thwart the development of competing products that might otherwise have been determined to infringe our intellectual property rights. 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 the EU, have compulsory licensing laws based on related EU rules, 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 Russian Federation has and may further limit protections on patents originating from "unfriendly countries" (including the U.S.) in response to sanctions relating to the ongoing Russo-Ukrainian War, and in general, 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 also rely on trade secret protection for some of our confidential and proprietary information, and we are taking security measures to protect our proprietary information and trade secrets, particularly in light of recent instances of data loss and misappropriation of intellectual property in the biopharmaceutical industry. However, these measures may not provide adequate protection, and while we seek to protect our proprietary information by entering into confidentiality agreements with employees, partners and consultants, as well as maintain cybersecurity protocols within our information technology infrastructure, 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, we may be subject to claims that our employees or independent contractors have inadvertently or otherwise used or disclosed trade secrets or other proprietary information of their former employers, or that they used or sought to use patent inventions belonging to their former employers. Furthermore, 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 and divert the attention of management and key technical personnel in defending ourselves against any such claims or enforcing our own patents. In the event of any third party's successful claim of patent infringement or misappropriation of trade secrets, we may lose valuable intellectual property rights or personnel, which could impede or prevent the achievement of our product development goals, or 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.

Risks Related to Our Operations, Managing Our Growth and Employee Matters

If the COVID-19 pandemic is further prolonged or becomes more severe, our business operations and corresponding financial results could suffer, which could have a material adverse impact on our financial condition and prospects for growth.

To date, the COVID-19 pandemic has had a modest impact on our business operations, in particular with respect to our clinical trial, drug discovery and commercial activities. We anticipate that a further prolonged, or more severe, global public health crisis could limit our ability to identify and work with clinical investigators at clinical trial sites globally to enroll, initiate and maintain treatment per protocol of patients for our ongoing clinical trials. Disruptions to medical and administrative operations at clinical trial sites, including staffing and materials shortages and the implementation of crisis management initiatives, have and may continue to reduce personnel and other resources necessary to conduct our clinical trials, which could further delay some of our clinical trial plans or may require certain trials to be temporarily suspended. We are also reliant on laboratory materials manufactured and distributed from areas that continue to be impacted by both the COVID-19 pandemic and other natural disasters, for which supply has become limited. If we are unable to obtain the requisite materials to conduct our planned drug discovery activities, we may be required to redirect the focus of, or even suspend, such activities. Should the COVID-19 pandemic be further prolonged or grow in severity, we may ultimately be unable to achieve our drug discovery and preclinical development objectives within the previously disclosed timelines, which could have a material adverse impact on our prospects for growth.

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, in particular as we continue to grow our pipeline of product candidates. 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 continue 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 we 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 programs for the cabozantinib franchise and our other product candidates, successfully executing upon our commercialization plan for the cabozantinib franchise and our 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.

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. Such liability may exceed our insurance coverage and our total assets, and 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. We maintain limited product liability insurance coverage for our clinical trials and commercial activities for cabozantinib. However, our insurance 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.

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 it may remain highly volatile or fluctuate substantially due to factors such as the following, many of which we cannot control:

- the announcement of FDA or other regulatory approval or non-approval, or delays in the FDA or other regulatory review process with respect to cabozantinib, zanzalintinib or our other product candidates, our collaboration partners' product candidates being developed in combination with either cabozantinib, zanzalintinib or our other product candidates, 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 the cabozantinib franchise, zanzalintinib or any of our other product candidates or programs;
- our ability to make future investments in the expansion of our pipeline through drug discovery, including future research collaborations, in-licensing arrangements and other strategic transactions;
- 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, zanzalintinib and our other product candidates;
- actions taken by regulatory agencies, both in the U.S. and abroad, with respect to cabozantinib or our clinical trials for cabozantinib, zanzalintinib or our other product candidates;
- 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, Teva's and Cipla's respective ANDAs, 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;
- 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 biopharmaceutical 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; and
- general market, macroeconomic and political conditions and other factors, including factors unrelated to our operating performance or the operating performance of our competitors.

These and other 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 macroeconomic conditions, including historically high inflation, as well as policies governing foreign trade and healthcare spending and delivery, or the ongoing Russo-Ukrainian War, the financial markets could continue to experience significant volatility that could also continue to 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 initiated. A securities class action suit against us could result in substantial costs and divert the attention of management, 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 approximately 610,000 square feet of office and laboratory space under multiple leases. Approximately 100,000 square feet of leased laboratory space in Alameda is under construction and anticipated to be available for operations in 2025. Also in 2022, we established a presence for Exelixis East in the Greater Philadelphia area and signed intermediate-term office and laboratory space. We believe these leased facilities are sufficient to accommodate our current and near-term needs.

Item 3. Legal Proceedings

MSN I ANDA Litigation

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. MSN's initial notice letter included a Paragraph IV certification with respect to our U.S. Patents No. 8,877,776 (salt and polymorphic forms), 9,724,342 (formulations), 10,034,873 (methods of treatment) and 10,039,757 (methods of treatment), which are listed in the Orange Book, for CABOMETYX. MSN's initial notice letter did not provide a Paragraph IV certification against U.S. Patents No. 7,579,473 (composition of matter) or 8,497,284 (methods of treatment), each of which is listed in the Orange Book. On October 29, 2019, we filed a complaint in the Delaware District Court for patent infringement against MSN asserting infringement of U.S. Patent No. 8,877,776 arising from MSN's ANDA filing with the FDA. On November 20, 2019, MSN filed its response to the complaint, alleging that the asserted claims of U.S. Patent No. 8,877,776 are invalid and not infringed. On May 5, 2020, we received notice from MSN that it had amended its ANDA to include additional Paragraph IV certifications. In particular, the May 5, 2020 amended ANDA requested approval to market a generic version of CABOMETYX tablets prior to expiration of two previously unasserted CABOMETYX patents: U.S. Patents No. 7,579,473 and 8,497,284. On May 11, 2020, we filed a complaint in the Delaware District Court for patent infringement against MSN asserting infringement of U.S. Patents No. 7,579,473 and 8,497,284 arising from MSN's amended ANDA filing with the FDA. Neither of our complaints have alleged infringement of U.S. Patents No. 9,724,342, 10,034,873 and 10,039,757. On May 22, 2020, MSN filed its response to the complaint, alleging that the asserted claims of U.S. Patents No. 7,579,473 and 8,497,284 are invalid and not infringed. On March 23, 2021, MSN filed its First Amended Answer and Counterclaims (amending its prior filing from May 22, 2020), seeking, among other things, a declaratory judgment that U.S. Patent No. 9,809,549 (salt and polymorphic forms) is invalid and would not be infringed by MSN if its generic version of CABOMETYX tablets were approved by the FDA. U.S. Patent No. 9,809,549 is not listed in the Orange Book. On April 7, 2021, we filed our response to MSN's First Amended Answer and Counterclaims, denying, among other things, that U.S. Patent No. 9,809,549 is invalid or would not be infringed. The two lawsuits comprising the MSN I litigation, numbered Civil Action Nos. 19-02017 and 20-00633, were consolidated in April 2021.

On October 1, 2021, pursuant to a stipulation between us and MSN, the Delaware District Court entered an order that (i) MSN's submission of its ANDA constitutes infringement of certain claims relating to U.S. Patents No. 7,579,473 and 8,497,284, if those claims are not found to be invalid, and (ii) upon approval, MSN's commercial manufacture, use, sale or offer for sale within the U.S., and importation into the U.S., of MSN's ANDA product prior to the expiration of U.S. Patents No. 7,579,473 and 8,497,284 would also infringe certain claims of each patent, if those claims are not found to be invalid. Then, on October 12, 2021, pursuant to a separate stipulation between us and MSN, the Delaware District Court entered an order dismissing MSN's counterclaims with respect to U.S. Patent No. 9,809,549. In our MSN I complaints, we sought, among other relief, an order that the effective date of any FDA approval of MSN's ANDA be a date no earlier than the expiration of all of U.S. Patents No. 7,579,473, 8,497,284 and 8,877,776, the latest of which expires on October 8, 2030, and equitable relief enjoining MSN from infringing these patents. In an effort to streamline the case, the parties narrowed their assertions. On April 8, 2022, MSN withdrew its validity challenge to U.S. Patent No. 8,877,776. On April 14, 2022, we agreed not to assert U.S. Patent No. 8,497,284 at trial and MSN, correspondingly, agreed to withdraw its validity challenges to U.S. Patent No. 8,497,284, as well as claims 1-4 and 6-7 of U.S. Patent No. 7,579,473. As a result of this narrowing, the trial addressed two issues: (1) infringement of claim 1 of the U.S. Patent No. 8,877,776; and (2) validity of claim 5 of the U.S. Patent No. 7,579,473. A bench trial for MSN I occurred in May 2022, and on January 19, 2023, the Delaware District Court issued a ruling rejecting MSN's invalidity challenge to U.S. Patent No. 7,759,473. The Delaware District Court also ruled that MSN's proposed ANDA product does not infringe U.S. Patent No. 8,877,776 and entered judgment that the effective date of any final FDA approval of MSN's ANDA shall not be a date earlier than August 14, 2026, the expiration date of U.S. Patent No. 7,759,473. This ruling in MSN I does not impact our separate and ongoing MSN II lawsuit. At this time, we are evaluating the next course of action, but we intend to vigorously defend our intellectual property rights, including through potential appeal.

MSN II ANDA Litigation

On January 11, 2022, we received notice from MSN that it had further amended its ANDA to assert additional Paragraph IV certifications. In particular, the January 11, 2022 amended ANDA requested approval to market a generic version of CABOMETYX tablets prior to expiration of three previously-unasserted CABOMETYX patents that are now listed in the Orange Book: U.S. Patents No. 11,091,439 (crystalline salt forms), 11,091,440 (pharmaceutical composition) and 11,098,015 (methods of treatment). On February 23, 2022, we filed a complaint in the Delaware District Court for patent infringement against MSN asserting infringement of U.S. Patents No. 11,091,439, 11,091,440 and 11,098,015 arising from MSN's further amendment of its ANDA filing with the FDA. On February 25, 2022, MSN filed its response to the complaint, alleging that the asserted claims of U.S. Patents No. 11,091,439, 11,091,440 and 11,098,015 are invalid and not infringed. On June 7, 2022, we received notice from MSN that it had further amended its ANDA to assert an additional Paragraph IV certification. As currently amended, MSN's ANDA now requests approval to market a generic version of CABOMETYX tablets prior to expiration of a previously-unasserted CABOMETYX patent that is now listed in the Orange Book: U.S. Patent No. 11,298,349 (pharmaceutical composition). On July 18, 2022, we filed a complaint in the Delaware District Court for patent infringement against MSN asserting infringement of U.S. Patent No. 11,298,349 arising from MSN's further amendment of its ANDA filing with the FDA. On August 9, 2022, MSN filed its response to the complaint, alleging that the asserted claims of U.S. Patent No. 11,298,349 are invalid and not infringed and amended its challenges to U.S. Patents No. 11,091,439, 11,091,440 and 11,098,015 to allege that these patents are not enforceable based on equitable grounds. The two lawsuits comprising the MSN II litigation, numbered Civil Action Nos. 22-00228 and 22-00945, were consolidated in October 2022 and involve Exelixis patents that are different from those asserted in the MSN I litigation described above.

On June 21, 2022, pursuant to a stipulation between us and MSN, the Delaware District Court entered an order that (i) MSN's submission of its ANDA constitutes infringement of certain claims relating to U.S. Patents No. 11,091,439, 11,091,440 and 11,098,015, if those claims are not found to be invalid, and (ii) upon approval, MSN's commercial manufacture, use, sale or offer for sale within the U.S., and importation into the U.S., of MSN's ANDA product prior to the expiration of U.S. Patents No. 11,091,439, 11,091,440 and 11,098,015 would also infringe certain claims of each patent, if those claims are not found to be invalid. In our MSN II complaints, we are seeking, among other remedies, equitable relief enjoining MSN from infringing the asserted patents, as well as an order that the effective date of any FDA approval of MSN's ANDA would be a date no earlier than the expiration of all of U.S. Patents No. 11,091,439, 11,091,440, 11,098,015 and 11,298,349, the latest of which expires on February 10, 2032. A bench trial for MSN II has been scheduled for October 2023.

Teva ANDA Litigation

In May 2021, we received notice letters from Teva regarding an ANDA Teva submitted to the FDA, requesting approval to market a generic version of CABOMETYX tablets. Teva's notice letters included a Paragraph IV certification with respect to our U.S. Patents No. 9,724,342 (formulations), 10,034,873 (methods of treatment) and 10,039,757 (methods of treatment), which are listed in the Orange Book. Teva's notice letters did not provide a Paragraph IV certification against any additional CABOMETYX patents. On June 17, 2021, we filed a complaint in the Delaware District Court for patent infringement against Teva, asserting infringement of U.S. Patents No. 9,724,342, 10,034,873 and 10,039,757 arising from Teva's ANDA filing with the FDA. On August 27, 2021, Teva filed its answer and counterclaims to the complaint, alleging that the asserted claims of U.S. Patents No. 9,724,342, 10,034,873 and 10,039,757 are invalid and not infringed. On September 17, 2021, we filed an answer to Teva's counterclaims. On July 29, 2022, we received notice from Teva that it had amended its ANDA to assert an additional Paragraph IV certification. As amended, Teva's ANDA now requests approval to market a generic version of CABOMETYX tablets prior to expiration of a previously-unasserted CABOMETYX patent that is now listed in the Orange Book: U.S. Patent No. 11,298,349 (pharmaceutical composition). On September 2, 2022, we filed a complaint in the Delaware District Court for patent infringement against Teva, asserting infringement of U.S. Patent No. 11,298,349 arising from Teva's amended ANDA filing with the FDA. We are seeking, among other relief, an order that the effective date of any FDA approval of Teva's ANDA be a date no earlier than the expiration of all of U.S. Patents No. 9,724,342, 10,034,873, 10,039,757 and 11,298,349, the latest of which expires on July 9, 2033, and equitable relief enjoining Teva from infringing these patents. On September 30, 2022, the parties filed a stipulation to consolidate the two lawsuits, numbered Civil Action Nos. 21-00871 and 22-01168, and to stay all proceedings, which was granted by the Delaware District Court on October 3, 2022. Following a similar order granted by the Delaware District Court on February 9, 2022 to stay all proceedings with respect to Civil Action No. 21-00871, this case remained administratively closed, and Civil Action No. 22-01168 was administratively closed on October 3, 2022.

Other

On February 6, 2023, we received a notice letter regarding an ANDA submitted to the FDA by Cipla, including a Paragraph IV certification with respect to our U.S. Patents No. 8,877,776 (salt and polymorphic forms), 9,724,342 (formulations), 10,039,757 (methods of treatment), 11,098,015 (methods of treatment), 11,091,439 (crystalline salt forms), 11,091,440 (pharmaceutical composition) and 11,298,349 (pharmaceutical composition). Cipla's ANDA requests approval to market a generic version of CABOMETYX tablets prior to the expiration of the aforementioned patents. We have not yet responded to this Paragraph IV certification notice letter but are evaluating it and will vigorously defend our cabozantinib intellectual property estate.

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 January 30, 2023, there were 339 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, 2022.

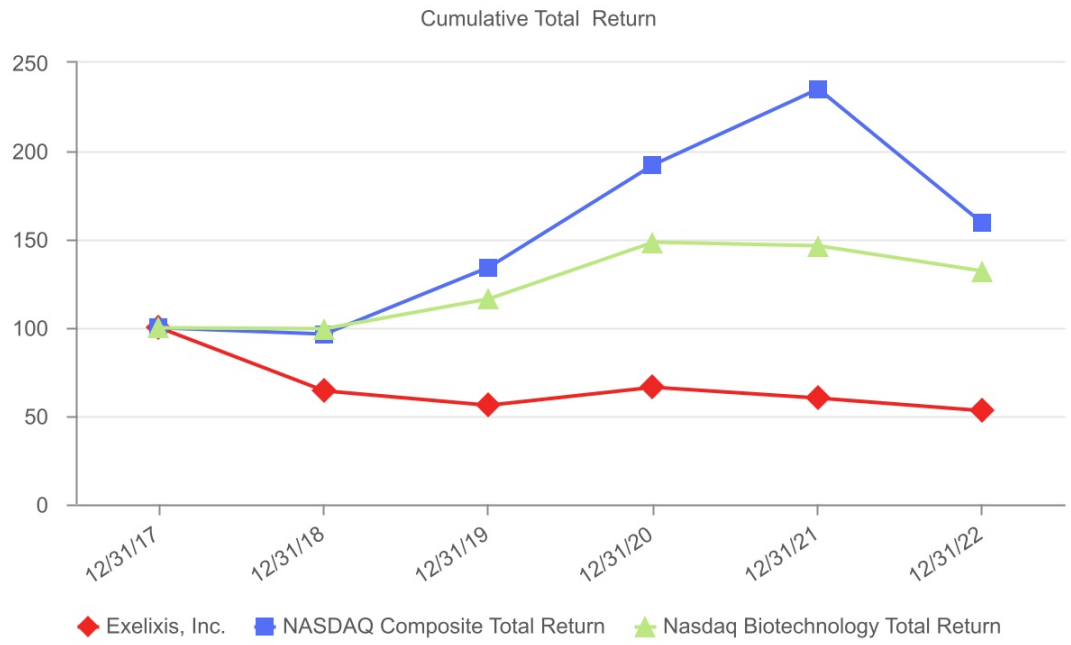
Repurchases of Equity Securities

There were no repurchases of our common stock during the year ended December 31, 2022.

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, 2022, 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, 2017 in each of our common stock, the Nasdaq Composite Total Return Index and the Nasdaq Biotechnology Total Return Index and assumes reinvestment of any dividends. The stock price performance on the following graph is not necessarily indicative of future stock price performance.



	Year Ended December 31,					
	2017	2018	2019	2020	2021	2022
Exelixis, Inc.	100	64	56	66	60	53
Nasdaq Composite Total Return	100	96	134	192	235	159
Nasdaq Biotechnology Total Return	100	99	116	148	146	132

Item 6. Reserved

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

Some of the statements under "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.

Overview

We are an oncology company innovating next-generation medicines and combination regimens at the forefront of cancer care. Through the commitment of our drug discovery, development and commercialization resources, we have produced four marketed pharmaceutical products, including our flagship molecule, cabozantinib. We continue to evolve our product portfolio, leveraging our investments, expertise and strategic partnerships, to target an expanding range of tumor types and indications with our clinically differentiated pipeline of small molecules, ADCs and other biotherapeutics.

Sales related to cabozantinib account for the majority of our revenues. Cabozantinib is an inhibitor of multiple tyrosine kinases including MET, AXL, VEGF receptors and RET and has been approved by the FDA and in 62 other countries as: CABOMETYX tablets, both alone and in combination with BMS' OPDIVO for advanced RCC, for previously treated HCC and, currently by the FDA and EC, for previously treated, RAI-refractory DTC and COMETRIQ capsules approved for progressive, metastatic MTC. For physicians treating these types of cancer, cabozantinib has become or is becoming an important medicine in their selection of effective therapies.

The other two products resulting from our discovery efforts are: COTELLIC, an inhibitor of MEK, approved as part of multiple combination regimens to treat specific forms of advanced melanoma and marketed under a collaboration with Genentech; and MINNEBRO, an oral, non-steroidal, selective blocker of MR, approved for the treatment of hypertension in Japan and licensed to Daiichi Sankyo.

We plan to continue leveraging our operating cash flows to support the ongoing investigation of cabozantinib in phase 3 trials for new indications and the advancement of a broad array of diverse biotherapeutics and small molecule programs for the treatment of cancer exploring multiple modalities and mechanisms of action. Of the clinical-state assets that have emerged from our drug discovery and preclinical activities thus far, the furthest along are zanzalintinib, a next-generation oral TKI, and XB002, an ADC that targets TF. We are also focused on conserving cash and managing risks of clinical failure by securing options to acquire other investigational drug candidates from third parties if those assets demonstrate evidence of clinical success. One example of this approach is CBX-12, a clinical-stage PDC invented by Cybrexa that utilizes Cybrexa's proprietary alphalex technology to enhance the delivery of exatecan, a highly potent, second-generation topoisomerase I inhibitor, to tumor cells.

Cabozantinib Franchise

The FDA first approved CABOMETYX as a monotherapy for previously treated patients with advanced RCC in April 2016, and then for previously untreated patients with advanced RCC in December 2017. In January 2021, the CABOMETYX label was expanded to include first-line advanced RCC in combination with OPDIVO, which was the first CABOMETYX regimen approved for treatment in combination with an ICI. In addition to RCC, in January 2019, the FDA approved CABOMETYX for the treatment of patients with HCC previously treated with sorafenib, and then in September 2021, the FDA approved CABOMETYX for the treatment of adult and pediatric patients 12 years of age and older with locally advanced or metastatic DTC that has progressed following prior VEGF receptor-targeted therapy and who are RAI-refractory or ineligible.

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 the rights to develop and commercialize cabozantinib outside of the U.S. and Japan, and to Takeda we granted the rights to develop and commercialize cabozantinib in Japan. Both Ipsen and Takeda also contribute financially and operationally to the further global development and commercialization of the cabozantinib franchise in other potential indications, and we 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, the United Kingdom and Canada, as a treatment for advanced RCC and for HCC in adults who have previously been treated with sorafenib. In addition, in March 2021, Ipsen and BMS received regulatory approval from the EC for CABOMETYX in combination with OPDIVO as a first-line treatment for patients with advanced RCC, followed by additional regulatory approvals for the combination in other territories beyond the EU. Most recently, in May 2022, we announced that Ipsen received regulatory approval from the EC for CABOMETYX as a monotherapy for the treatment of adult patients with locally advanced or metastatic, RAI-refractory or ineligible DTC and who have progressed during or after prior systemic therapy, which followed an approval from Health Canada in April 2022 for a similar DTC indication. With respect to the Japanese market, Takeda received Manufacturing and Marketing Approvals in 2020 from the Japanese MHLW of CABOMETYX as a treatment of patients with curatively unresectable or metastatic RCC and as a treatment of patients with unresectable HCC who progressed after cancer chemotherapy. In August 2021, Takeda and Ono Pharmaceutical Co., Ltd., BMS' development and commercialization partner in Japan, received Manufacturing and Marketing Approval from the MHLW of CABOMETYX in combination with OPDIVO as a treatment for unresectable or metastatic RCC.

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 potentially benefit from this medicine. We are continuing to evaluate cabozantinib in combination with ICIs in late-stage clinical trials that we sponsor, along with our collaboration partners, across RCC and mCRPC. Beyond clinical trials that we or our collaboration partners sponsor, independent investigators also conduct trials evaluating cabozantinib through our CRADA with NCI-CTEP or our IST program. Over time, the data we have obtained from these investigator-sponsored clinical trials have helped advance our development program for the cabozantinib franchise by informing subsequent label-enabling trials, including COSMIC-311, our phase 3 pivotal trial evaluating cabozantinib in previously treated patients with RAI-refractory DTC, from which positive results served as the basis for the FDA's and EC's approvals of CABOMETYX for DTC. Moreover, these data sets may also prove valuable by informing our development plans for zanzalintinib.

Building on preclinical and clinical observations that cabozantinib in combination with ICIs may promote a more immune-permissive tumor environment, we initiated numerous pivotal studies to further explore these combination regimens. The first of these studies to deliver results was CheckMate-9ER, a phase 3 pivotal trial evaluating the combination of CABOMETYX and OPDIVO compared to sunitinib in previously untreated, advanced or metastatic RCC, and positive results from CheckMate-9ER served as the basis for the FDA's, EC's and MHLW's approvals of CABOMETYX in combination with OPDIVO as a first-line treatment of patients with advanced RCC in January 2021, March 2021 and August 2021, respectively. We are also collaborating with BMS on 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 announced top-line results from COSMIC-313 in July 2022, and in September 2022 we presented the data at the Presidential Symposium III at the 2022 ESMO Congress. The trial met its primary endpoint, demonstrating significant improvement in BIRC-assessed PFS at the primary analysis for the triplet combination. At a prespecified interim analysis for the secondary endpoint of OS, the triplet combination did not demonstrate a significant benefit, and therefore, the trial will continue to the next analysis of OS, expected in 2023. The safety profile observed in the trial was reflective of the known safety profiles for each single agent, as well as the combination regimens used in this study. Based on feedback from the FDA, we do not intend to submit an sNDA for the combination regimen based on the currently available data, and we plan to discuss a potential regulatory submission with the FDA when the results of the next OS analysis are available.

To diversify our exploration of combinations with ICIs, we also initiated multiple trials evaluating cabozantinib in combination with Roche's ICI, atezolizumab, beginning in 2017 with COSMIC-021, a broad phase 1b study evaluating the safety and tolerability of the cabozantinib and atezolizumab combination with atezolizumab in patients with a wide variety of locally advanced or metastatic solid tumors. The encouraging efficacy and safety data that emerged from COSMIC-021 have been instrumental in guiding our clinical development strategy for cabozantinib in combination with ICIs. We are currently evaluating the cabozantinib and atezolizumab combination in two late-stage trials: CONTACT-03, in which focuses on patients with inoperable, locally advanced or metastatic RCC who have progressed following treatment with an ICI as the immediate proceeding therapy; and CONTACT-02, which focuses on patients with mCRPC who have been previously treated with one NHT. A third trial, CONTACT-01, which focused on patients with metastatic NSCLC who have been previously treated with an ICI and platinum-containing chemotherapy, did not meet its primary endpoint of OS at final analysis. CONTACT-03 is sponsored by Roche and co-funded by us, and we anticipate announcing results of the primary PFS analysis

from CONTACT-03 in the first half of 2023. CONTACT-02 is sponsored by us and co-funded by Roche, and we anticipate completing enrollment and announcing results of the primary PFS analysis in the second half of 2023.

For additional information on our cabozantinib clinical trials, see "Business—Exelixis Development Programs—Cabozantinib Development Program" in Part I, Item 1 of this Annual Report on Form 10-K.

Pipeline Activities

Zanzalintinib

The first compound to enter the clinic following our re-initiation of drug discovery activities in 2017 was zanzalintinib, a next-generation oral TKI that targets VEGF receptors, MET, AXL, MER and other kinases implicated in cancer's growth and spread. In designing zanzalintinib, we sought to build upon our experience with cabozantinib, retaining a similar target profile while improving key characteristics, including the pharmacokinetic half-life. To date, we have initiated two large phase 1b clinical trials studying zanzalintinib: STELLAR-001 and STELLAR-002. STELLAR-001 is a phase 1b clinical trial evaluating zanzalintinib, both as a monotherapy and in combination with either atezolizumab or Merck KGaA's and Pfizer's avelumab. We have established a recommended dose of 100 mg for both single-agent zanzalintinib and zanzalintinib in combination with atezolizumab, and we have begun enrolling expansion cohorts for patients with clear cell RCC, non-clear cell RCC, hormone-receptor positive breast cancer, mCRPC and CRC. The dose-escalation stage for zanzalintinib in combination with avelumab is ongoing, with expansion cohorts planned initially in UC. We presented data from STELLAR-001 during poster sessions at the 2022 ESMO Congress in September 2022, which showed zanzalintinib has demonstrated preliminary, clinical activity similar to that observed with cabozantinib in phase 1 across a range of solid tumors and dose levels, with a manageable safety profile. STELLAR-002 is a phase 1b clinical trial evaluating zanzalintinib in combination with either nivolumab, nivolumab and ipilimumab, or a fixed dose of nivolumab and BMS' relatlimab. We have established a recommended dose of 100 mg for zanzalintinib in combination with nivolumab, and we have begun enrolling patients in expansion cohorts for patients with clear cell RCC. The dose-escalation stage for zanzalintinib in the other combination regimens is ongoing and is continuing to enroll patients with advanced solid tumors in dose-escalation cohorts. Depending on the dose-escalation results, STELLAR-002 may enroll expansion cohorts for patients with clear cell and non-clear cell RCC, mCRPC, UC, HCC, NSCLC, CRC and SCCHN. To better understand the individual contribution of the therapies, treatment arms in the expansion cohorts may include zanzalintinib as a single agent in addition to the ICI combination regimens.

We also initiated two phase 3 pivotal trials evaluating zanzalintinib in combination with ICIs in 2022. The first trial, STELLAR-303, was initiated in June 2022 and is evaluating zanzalintinib in combination with atezolizumab versus regorafenib in patients with metastatic non-microsatellite instability-high or non-mismatch repair-deficient CRC who have progressed after, or are intolerant to, the current standard of care. The trial aims to enroll approximately 600 patients worldwide with documented RAS status at approximately 137 sites globally. The primary objective of STELLAR-303 is to evaluate the efficacy of the combination in patients with RAS wild-type disease, and outcomes in patients with RAS-mutated disease will also be evaluated. The primary efficacy endpoint of STELLAR-303 is OS, and additional efficacy endpoints include PFS, ORR and DOR per RECIST v. 1.1, in each case as assessed by the investigator. The second trial, STELLAR-304, was initiated in December 2022 and is evaluating zanzalintinib in combination with nivolumab versus sunitinib in previously untreated patients with advanced non-clear cell RCC. The trial aims to enroll approximately 291 patients at approximately 170 sites globally. The primary efficacy endpoints of STELLAR-304 are PFS and ORR per RECIST v 1.1, in each case as assessed by BIRC. The secondary efficacy endpoint is OS. Beyond STELLAR-303 and STELLAR-304, we intend to explore a series of early-stage and pivotal trials evaluating zanzalintinib in novel combination regimens across a broad array of future potential indications.

For additional information on our zanzalintinib clinical trials, see "Business—Exelixis Development Programs—Pipeline Development Programs – Advancing Exelixis' Future Cancer Therapy Candidates—Zanzalintinib Development Program" in Part I, Item 1 of this Annual Report on Form 10-K.

Biotherapeutics

Much of our drug discovery activities focuses on discovering and advancing various biotherapeutics that have the potential to become anti-cancer therapies, such as bispecific antibodies, ADCs and other innovative treatments. ADCs in particular present a unique opportunity for new cancer treatments, given their capabilities to deliver anti-cancer payload drugs to targets with increased precision while minimizing impact on healthy tissues. This biotherapeutic approach has been validated by multiple regulatory approvals for the commercial sale of ADCs in the past several years. Furthest along amongst our biotherapeutics programs is XB002, our lead TF-targeting ADC program, in-licensed from Iconic. We are evaluating XB002, both as a single agent and in combination with either nivolumab or Roche's bevacizumab, in JEWEL-101,

a phase 1 study in patients with advanced solid tumors for which therapies are unavailable, ineffective or intolerable. In October 2022, we announced promising initial dose-escalation results from JEWEL-101 during the Antibody-drug Conjugates Poster Session at the 2022 ENA Symposium. The data demonstrated that XB002 was well-tolerated at multiple dose levels, and a pharmacokinetic analysis confirmed that XB002 was stable with low levels of free payload. The planned cohort-expansion phase, which we expect to initiate during 2023, is designed to further explore the selected dose of XB002, both as a single agent and in combination with either nivolumab or bevacizumab, in individual tumor cohorts, which may include forms of NSCLC, cervical cancer, ovarian cancer, UC, SCCHN, pancreatic cancer, esophageal cancer, mCRPC, triple negative breast cancer and hormone-receptor positive breast cancer, and we also intend to initiate additional dose-escalation and expansion cohorts to evaluate the potential of XB002 in combination with additional ICIs and other targeted therapies across a wide range of tumor types, including indications other than those currently addressed by commercially available TF-targeted therapies. For additional information on JEWEL-101 and our development plans for XB002, see "Business—Exelixis Development Programs—Pipeline Development Programs – Advancing Exelixis' Future Cancer Therapy Candidates—XB002 Development Program" in Part I, Item 1 of this Annual Report on Form 10-K.

Most recently, in November 2022, we executed two option deals that highlight our strategic efforts to access clinical- or near-clinical-stage assets: an exclusive collaboration agreement with Cybrexa providing us with the right to acquire CBX-12; and an exclusive clinical development and option agreement with Sairopa to develop ADU-1805, a potentially best-in-class mAb that targets SIRPα. For more information on these arrangements, see "Business—Collaborations and Business Development Activities—Research Collaborations and In-licensing Arrangements" in Part I, Item 1 of this Annual Report on Form 10-K. CBX-12 is currently being evaluated in a phase 1 clinical trial to explore its pharmacokinetics, safety, tolerability and preliminary anti-tumor activity in patients with advanced or metastatic refractory solid tumors. For more information on the current development of CBX-12, see "Business—Exelixis Development Programs—Pipeline Development Programs – Advancing Exelixis' Future Cancer Therapy Candidates—Development of CBX-12" in Part I, Item 1 of this Annual Report on Form 10-K.

To facilitate the growth of our various biotherapeutics programs, we have established multiple research collaborations and in-licensing arrangements and entered into other strategic transactions that provide us with access to antibodies, binders, payloads and conjugation technologies, which are the components employed to generate next-generation ADCs or multispecific antibodies. In addition to the option deals with Cybrexa and Sairopa, some of our active research collaborations for biotherapeutics programs include collaborations with:

- Adagene, which is focused on using Adagene's SAFEbody technology to develop novel masked ADCs or other innovative biotherapeutics with potential for improved therapeutic index;
- BioInvent, which is intended to expand our portfolio of antibody-based therapies and will utilize BioInvent's proprietary n-CoDeR antibody library and patient-centric F.I.R.S.T screening platform, which together are designed to allow for parallel target and antibody discovery;
- Catalent, which is focused on the discovery and development of multiple ADCs using Catalent's proprietary SMARTag site-specific bioconjugation technology;
- Invenra, which is focused on the discovery and development of novel binders and multispecific antibodies for the treatment of cancer; and
- NBE, which is focused on the discovery and development of multiple ADCs by leveraging NBE's unique expertise and proprietary platforms in ADC discovery, including NBE's SMAC-Technology and novel payloads.

We have already made significant progress under these and other research collaborations and in-licensing arrangements and believe we will continue to do so in 2023 and in future years. For example, as a direct result of these arrangements, we are advancing three biotherapeutics development candidates: XB010, XB014 and ZB628. XB010, our first ADC advanced internally, targets the tumor antigen 5T4 and incorporates antibodies sourced from Invenra and was constructed using Catalent's SMARTag site-specific bioconjugation platform. XB014 and XB628 are bispecific antibodies: XB014 combines a PD-L1 targeting arm with a CD47 targeting arm to block a macrophage checkpoint; and XB628 targets PD-L1 and NKG2A, identified as an emerging immune checkpoint that may mediate resistance to classical checkpoint inhibition. Both XB014 and XB628 were developed through our collaboration with Invenra.

For additional information on these specific research collaborations and in-licensing arrangements related to our biotherapeutics programs, see "Business—Collaborations and Business Development Activities—Research Collaborations and In-licensing Arrangements" in Part I, Item 1 of this Annual Report on Form 10-K.

Other Small Molecules

Since its formation in 2000, our drug discovery group has advanced 25 compounds to the IND stage, either independently or with collaboration partners, and today we deploy our drug discovery expertise to advance small molecule drug candidates toward and through preclinical development. These efforts are led by our experienced scientists, including some of the same scientists who led the efforts to discover cabozantinib, cobimetinib and esaxerenone, each of which are now commercially distributed drug products. For example, zanzalintinib, which was discovered at Exelixis, has now entered into phase 3 clinical trials. We augment our small molecule discovery activities through research collaborations and in-licensing arrangements with other companies engaged in small molecule discovery, including:

- STORM, which is focused on the discovery and development of inhibitors of novel RNA modifying enzymes, including ADAR1;
- Aurigene, which is focused on the discovery and development of novel small molecules as therapies for cancer; and
- StemSynergy, which is focused on the discovery and development of novel oncology compounds aimed to inhibit tumor growth by targeting CK1α and the Notch pathway.

For additional information on these research collaborations and in-licensing arrangements related to our small molecule programs, see "Business—Collaborations and Business Development Activities—Research Collaborations and In-licensing Arrangements" in Part I, Item 1 of this Annual Report on Form 10-K.

The most advanced compounds to emerge from these arrangements is XL102, our lead program targeting CDK7, in-licensed from Aurigene. We are evaluating XL102, both as a single agent and in combination with other anti-cancer therapies, in QUARTZ-101, a phase 1 study in patients with inoperable, locally advanced or metastatic solid tumors. In December 2022, we announced initial dose-escalation results from QUARTZ-101 during the Poster Session at the 2022 San Antonio Breast Cancer Symposium. The data demonstrated that XL102 was well-tolerated at multiple dose levels and a pharmacokinetic analysis supported adding investigation of twice-daily oral dosing. We are continuing to evaluate the efficacy of XL102 in additional patients during this initial dose-escalation phase. The subsequent cohort-expansion phase is designed to further explore the selected dose of XL102 as a single agent and in combination regimens in individual tumor cohorts, including ovarian cancer, triple-negative breast cancer, hormone-receptor positive breast cancer and mCRPC. For additional information on QUARTZ-101 and our development plans for XL102, see "Business—Exelixis Development Programs—Pipeline Development Programs – Advancing Exelixis' Future Cancer Therapy Candidates—XL102 Development Program" in Part I, Item 1 of this Annual Report on Form 10-K.

As of the date of this Annual Report on Form 10-K, we are currently advancing more than 10 discovery programs and expect to progress up to five new development candidates into preclinical development during 2023. In addition, we will continue to engage in business development initiatives with the goal of acquiring and in-licensing promising oncology platforms and assets and then further characterize and develop them utilizing our established preclinical and clinical development infrastructure.

2022 Business Updates and Financial Highlights

During 2022, we continued to execute on our business objectives, generating significant revenues 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 2022 and subsequent to year-end include:

Business Updates

- In January 2022, we appointed Vicki L. Goodman, M.D., as Executive Vice President, Product Development & Medical Affairs, and Chief Medical Officer.
- In January 2022, we announced the completion of enrollment for CONTACT-03. Based on current event rates, we anticipate announcing results of the primary PFS analysis in the first half of 2023.
- In January 2022, we announced an amendment to our exclusive option and license agreement with Iconic to acquire broad rights to use the anti-TF antibody incorporated into XB002 for any application, including conjugated to other payloads, as well as rights within oncology to a number of other anti-TF antibodies developed by Iconic, including for use in ADCs and multispecific biotherapeutics.
- In January 2022, cabozantinib in combination with ICIs in patients with forms of previously treated CRC was the subject of multiple data presentations at the 2022 American Society of Clinical Oncology (ASCO) Gastrointestinal Cancers Symposium.

- In February 2022, cabozantinib in patients with forms of RCC and other genitourinary cancers was the subject of multiple data presentations at the 2022 ASCO Genitourinary Cancers Symposium.
- In February 2022, we filed a patent lawsuit in the Delaware District Court against MSN asserting infringement of U.S. Patents No. 11,091,439, 11,091,440 and 11,098,015 arising from MSN's further amendment of its ANDA. This lawsuit, along with a subsequent lawsuit we filed against MSN in July 2022 asserting infringement of U.S. Patent No. 11,298,349, comprise MSN II, a new case against MSN involving Exelixis patents that are different from those asserted previously in the consolidated MSN I patent lawsuits that we filed in 2019 and 2020 and were adjudicated at a bench trial in May 2022. A bench trial for MSN II has been scheduled for October 2023. For a more detailed discussion of the MSN II litigation matter, see "Legal Proceedings" in Part I, Item 3 of this Annual Report on Form 10-K.
- In March 2022, we announced results from the final OS analysis of COSMIC-312 trial, which showed neither improvement nor detriment in OS for cabozantinib in combination with atezolizumab versus sorafenib in patients with previously untreated advanced HCC. Based on this outcome for OS and the rapidly evolving treatment landscape for previously untreated HCC, we do not intend to submit an sNDA to the FDA for the combination regimen.
- In April 2022, we announced the initiation of a phase 1 clinical trial evaluating XL114 as a monotherapy in patients with NHL. Based on initial findings in this phase 1 trial and the evolving treatment landscape for NHL, we have discontinued development of XL114 as of January 2023.
- In May 2022, we announced that Ipsen received regulatory approvals from the EC and Health Canada for CABOMETYX as a monotherapy for patients with previously treated, RAI-refractory DTC.
- In June 2022, cabozantinib in patients with forms of NSCLC, UC, RCC, SCCHN and DTC was the subject of multiple data presentations at the 2022 ASCO Annual Meeting.
- In June 2022, we announced an exclusive option and license agreement with BioInvent to identify and develop novel antibodies for use in immuno-oncology therapeutics utilizing BioInvent's n-CoDeR antibody library and patient-centric F.I.R.S.T screening platform.
- In June 2022, we announced the initiation of STELLAR-303, a global phase 3 pivotal trial evaluating zanzalintinib in combination with atezolizumab in patients with metastatic non-microsatellite instability-high or non-mismatch repair-deficient CRC who have progressed after or are intolerant to the current standard of care.
- In July 2022, we announced an exclusive license agreement with Ryvu to develop novel targeted therapies utilizing Ryvu's STING technology.
- In July 2022, we announced results from the phase 3 COSMIC-313 trial, in which the triplet combination of cabozantinib, nivolumab and ipilimumab met its primary endpoint, demonstrating significant improvement in PFS versus the doublet combination of nivolumab and ipilimumab at the primary analysis. At a prespecified interim analysis for the secondary endpoint of OS, the triplet combination did not demonstrate a significant benefit, and therefore the trial will continue to the next analysis of OS, expected in 2023.
- In September 2022, we filed a patent lawsuit in the Delaware District Court against Teva, asserting infringement of U.S. Patent No. 11,298,349 arising from Teva's amendment of its ANDA, originally filed with the FDA in May 2021. This lawsuit, our second case against Teva, has been consolidated with the prior patent lawsuit we filed in June 2021 and involves an Exelixis patent that is different from those asserted previously in June 2021. All proceedings were stayed pursuant to an order of the Delaware District Court in October 2022. For a more detailed discussion of the Teva litigation matter, see "Legal Proceedings" in Part I, Item 3 of this Annual Report on Form 10-K.
- In September 2022, clinical data from COSMIC-313 were presented as part of Presidential Symposium III at the 2022 ESMO Congress. In addition, cabozantinib in patients with in RCC, DTC and advanced adrenocortical carcinoma was the subject of multiple data presentations, and we also presented phase 1b data from STELLAR-001, in which zanzalintinib demonstrated preliminary clinical activity similar to that observed with cabozantinib in phase 1 across a range of solid tumors with an acceptable safety profile.
- In October 2022, we announced an expansion of our clinical trial collaboration and supply agreement with BMS to include the use of the fixed-dose combination of nivolumab and relatlimab in STELLAR-002, our ongoing phase 1b clinical trial evaluating zanzalintinib in combination with multiple ICIs in advanced solid tumors.
- In October 2022, we announced promising initial dose-escalation results from JEWEL-101, the ongoing phase 1 trial evaluating XB002 in patients with advanced solid tumors, during the Antibody-drug Conjugates Poster

Session at the 2022 ENA Symposium. The data demonstrated that XB002 was well-tolerated at multiple dose levels, and a pharmacokinetic analysis confirmed that XB002 was stable with low levels of free payload.

- In November 2022, we announced an agreement with Cybrexa that provides us the right to acquire CBX-12, a clinical-stage PDC that utilizes Cybrexa's proprietary alphalex technology to enhance delivery of exatecan to tumor cells.
- In November 2022, we announced an exclusive option and license agreement and clinical development collaboration with Sairopa to develop ADU-1805, a mAb that targets SIRPα.
- In November 2022, we announced a new license agreement with Catalent for three target programs with lead antibody and/or ADC candidates.
- In December 2022, we announced initial dose-escalation results from QUARTZ-101, our phase 1 trial evaluating XL102 in patients with advanced solid tumors, during the Poster Session at the 2022 San Antonio Breast Cancer Symposium. The data demonstrated that XL102 was well tolerated at multiple dose levels.
- In December 2022, we announced results from the phase 3 CONTACT-01 trial evaluating cabozantinib in combination with atezolizumab in patients with previously treated NSCLC, in which the combination did not meet its primary endpoint of OS at final analysis.
- In December 2022, we announced the initiation of STELLAR-304, a global phase 3 pivotal trial evaluating zanzalintinib in combination with nivolumab in previously untreated patients with advanced non-clear cell RCC. The primary endpoints are PFS and ORR per RECIST v. 1.1, and the secondary endpoint is OS.
- In December 2022, we appointed Dana T. Aftab, Ph.D., as Executive Vice President, Discovery and Translational Research, and Chief Scientific Officer.
- In January 2023, the Delaware District Court issued a ruling in the MSN I trial, rejecting MSN's challenge to U.S. Patent No. 7,759,473, which expires August 14, 2026. The Delaware District Court also ruled that MSN's proposed ANDA product does not infringe U.S. Patent No. 8,877,776, which expires October 8, 2030, and entered judgment that the effective date of any final FDA approval of MSN's ANDA shall not be a date earlier than August 14, 2026, the expiration date of U.S. Patent No. 7,759,473. This ruling in MSN I does not address the parties' claims in the MSN II lawsuit. For a more detailed discussion of the MSN I litigation matter, see "Legal Proceedings" in Part I, Item 3 of this Annual Report on Form 10-K.
- In February 2023, we received a notice letter regarding an ANDA submitted to the FDA by Cipla, including a Paragraph IV certification with respect to our U.S. Patents No. 8,877,776 (salt and polymorphic forms), 9,724,342 (formulations), 10,039,757 (methods of treatment), 11,098,015 (methods of treatment), 11,091,439 (crystalline salt forms), 11,091,440 (pharmaceutical composition) and 11,298,349 (pharmaceutical composition). Cipla's ANDA requests approval to market a generic version of CABOMETYX tablets prior to the expiration of the aforementioned patents. We have not yet responded to this Paragraph IV certification notice letter but are evaluating it and will vigorously defend our cabozantinib intellectual property estate.
- In February 2023, cabozantinib in patients with forms of RCC will be the subject of multiple data presentations at the 2023 ASCO Genitourinary Cancers Symposium.

Financial Highlights

- Net product revenues for 2022 were $1,401.2 million, as compared to $1,077.3 million for 2021.
- Total revenues for 2022 were $1,611.1 million, as compared to $1,435.0 million for 2021.
- Research and development expenses for 2022 were $891.8 million, as compared to $693.7 million for 2021.
- Selling, general and administrative expenses for 2022 were $459.9 million, as compared to $401.7 million for 2021.
- Provision for income taxes for 2022 was $52.1 million, as compared to $63.1 million for 2021.
- Net income for 2022 was $182.3 million, or $0.57 per share, basic, and $0.56 per share, diluted, as compared to $231.1 million, or $0.73 per share, basic, and $0.72 per share, diluted, for 2021.

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

Outlook, Challenges and Risks

We will continue to face numerous challenges and risks that may impact our ability to execute on our 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, both alone and in combination with other therapies, as a treatment for the highly competitive indications for which it is approved, and possibly for other indications for which cabozantinib is currently being evaluated in potentially label-enabling clinical trials, if warranted by the data generated from these trials. However, we cannot be certain that the clinical trials we and our collaboration partners are conducting 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 the required regulatory approvals to market CABOMETYX for additional indications are achieved, 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. 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. In addition, healthcare policymakers in the U.S. are increasingly expressing concern over healthcare costs, and corresponding legislative and policy initiatives and activities have been launched aimed at increasing the healthcare cost burdens borne by pharmaceutical manufacturers, as well as expanding access to, and restricting the prices and growth in prices of, pharmaceuticals.

Achievement of our business objectives will also depend on our ability to maintain a competitive position in the shifting landscape of therapeutic strategies for the treatment of cancer, which we may not be able to do. On an ongoing basis, we assess the constantly evolving landscape of other approved and investigational cancer therapies that could be competitive, or complementary in combination, with our products, and then we adapt our development strategies for the cabozantinib franchise and our pipeline product candidates accordingly, such as by modifying our clinical trials to include evaluation of our therapies with ICIs and other targeted agents. Even if our current and future clinical trials, including those evaluating cabozantinib in combination with an ICI in mCRPC or evaluating zanzalintinib in combination with an ICI in CRC and RCC, produce positive results sufficient to obtain marketing approval by the FDA and other global regulatory authorities, it is uncertain whether physicians will choose to prescribe regimens containing our products instead of competing products and product combinations in approved indications.

In the longer term, we may eventually face competition from potential manufacturers of generic versions of our marketed products, including the proposed generic versions of CABOMETYX tablets that are the subject of ANDAs submitted to the FDA by MSN, Teva and Cipla. The approval of any of these ANDAs and subsequent launch of any generic version of CABOMETYX could significantly decrease our revenues derived from the U.S. sales of CABOMETYX and thereby materially harm our business, financial condition and results of operations.

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 drug discovery operations, especially on the global level. 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, others are common to companies in the biopharmaceutical industry with development and commercial operations, and an additional category are macroeconomic, affecting all companies. For a more detailed 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

We have adopted a 52- or 53-week fiscal year policy that ends on the Friday closest to December 31st. Fiscal year 2022, which was a 52-week fiscal year, ended December 30, 2022, fiscal year 2021, which was a 52-week fiscal year, ended December 31, 2021 and fiscal year 2020, which was a 52-week fiscal year, ended January 1, 2021. For convenience, references in this report as of and for the fiscal years ended December 30, 2022, and January 1, 2021 are indicated as being as of and for the years ended December 31, 2022 and 2020, respectively.

This discussion and analysis generally addresses 2022 and 2021 items and year-over-year comparisons between 2022 and 2021. Discussions of 2020 items and year-over-year comparisons between 2021 and 2020 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, 2021, filed with the SEC on February 18, 2022.

Revenues

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

	Year Ended December 31,		Percent Change
	2022	2021	
Net product revenues	$ 1,401,243	$ 1,077,256	30 %
License revenues	162,056	249,956	-35 %
Collaboration services revenues	47,763	107,758	-56 %
Total revenues	$ 1,611,062	$ 1,434,970	12 %

Net Product Revenues

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

	Year Ended December 31,		Percent Change
	2022	2021	
Gross product revenues	$ 1,951,169	$ 1,452,913	34 %
Discounts and allowances	(549,926)	(375,657)	46 %
Net product revenues	$ 1,401,243	$ 1,077,256	30 %

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

	Year Ended December 31,		Percent Change
	2022	2021	
CABOMETYX	$ 1,375,909	$ 1,054,050	31 %
COMETRIQ	25,334	23,206	9 %
Net product revenues	$ 1,401,243	$ 1,077,256	30 %

The increase in net product revenues for the year ended December 31, 2022, as compared to 2021, was primarily related to a 26% increase in the number of CABOMETYX units sold as a result of the FDA's approval of CABOMETYX in combination with OPDIVO as a first-line treatment of patients with advanced RCC, in part due to the longer duration of therapy for this combination and an increase in related market share, and to a lesser extent a 4% increase in the average net selling price of CABOMETYX.

We project our net product revenues will increase in fiscal year 2023, as compared to fiscal year 2022, primarily due to an increase in market share that occurred in fiscal year 2022, reflecting the continued evolution of the metastatic RCC, HCC and DTC treatment landscapes, as well as an increase in selling price.

We recognize product revenues net of discounts and allowances that are described in "Note 1. Organization and Summary of Significant Accounting Policies" to our "Notes to Consolidated Financial Statements" included in Part II, Item 8 of this Annual Report on Form 10-K. Discounts and allowances as a percentage of gross revenues have increased over time as the number of patients participating in government programs has increased and as the discounts given and rebates paid to government payers have also increased. The increase in discounts and allowances for the year ended December 31, 2022, as compared to 2021, was generally attributed to an increase in units sold and an increase in the utilization and the dollar amount of chargebacks related to the government's 340B Program, which mandates drug manufacturers offer discount drug pricing for certain eligible covered entities that meet 340B Program requirements.

We project our discounts and allowances as a percentage of gross revenues may increase during fiscal year 2023 for similar reasons noted above.

License Revenues

License revenues include: (a) 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 a milestone would be achieved and a significant reversal of revenues would not occur in future periods; (b) royalty revenues; and (c) the profit on the U.S. commercialization of COTELLIC from Genentech.

See "Note 3. Collaborations and Business Development Activities—Cabozantinib Commercial Collaborations—*Performance Obligations and Transaction Prices for our Ipsen and Takeda Collaborations*" in the "Notes to Consolidated Financial Statements" contained in Part II, Item 8 of this Annual Report on Form 10-K for a discussion on the allocation of transaction price which impacts the proportion of milestone revenues allocated to license revenues and collaboration services revenues.

Milestone revenues, which are allocated between license revenues and collaboration services revenues, were $28.9 million for the year ended December 31, 2022, as compared to $133.8 million for 2021. Milestone revenues by fiscal year included the following:

- For the year ended December 31, 2022, $25.8 million in revenues was recognized in connection with two regulatory milestones totaling $27.0 million upon the approval by the EC and Health Canada, of cabozantinib as a monotherapy for the treatment of adult patients with locally advanced or metastatic DTC, refractory or not eligible to RAI who have progressed during or after prior systemic therapy.
- For the year ended December 31, 2021, milestone revenues included: (1) $100.0 million related to a commercial sales milestone from Ipsen upon their achievement of $400.0 million of net sales of cabozantinib in the related Ipsen license territory over four consecutive quarters; (2) $11.9 million related to a $12.5 million regulatory milestone Ipsen achieved upon submission of a variation application to the EMA for CABOMETYX as a treatment for patients with previously treated, RAI-refractory DTC; and (3) $18.9 million in connection with a $20.0 million milestone achieved following Takeda's first commercial sale in Japan of CABOMETYX in combination with OPDIVO for the treatment of patients with curatively unresectable or metastatic RCC.

Due to uncertainties surrounding the timing and achievement of development, regulatory and commercial milestones, it is difficult to predict the timing of future milestones revenues; consequently, milestones may vary significantly from period to period.

Royalty revenues increased primarily as a result of an increase in Ipsen's net sales of cabozantinib outside of the U.S. and Japan. Ipsen royalty revenues were $110.1 million for the year ended December 31, 2022, as compared to $97.2 million for 2021. Ipsen's net sales of cabozantinib have continued to grow since their first commercial sale of the product in the fourth quarter of 2016, as a result of continued increased global demand of CABOMETYX, as monotherapy for the treatment of adult patients with advanced RCC following prior VEGF-targeted therapy and CABOMETYX in combination with OPDIVO as a first-line treatment of patients with advanced RCC. Royalty revenues for the year ended December 31, 2022 also included $11.3 million, as compared to $7.9 million for 2021, related to Takeda's net sales of CABOMETYX, which have continued to grow since their first commercial sale of product in Japan in 2020. Additionally, Takeda royalty revenues have increased for similar reasons noted above. As of December 31, 2022, CABOMETYX is approved and commercially available in 62 countries outside of the U.S.

Our share of profits on the U.S. commercialization of COTELLIC under our collaboration agreement with Genentech was $7.7 million for the year ended December 31, 2022, as compared to $8.1 million for 2021. We also earned royalty revenues on ex-U.S. net sales of COTELLIC by Genentech of $4.8 million for the year ended December 31, 2022, as compared to $4.1 million for 2021.

We project our license revenues may decrease in fiscal year 2023, as compared to fiscal year 2022, as a result of the anticipated achievement of fewer milestones in 2023, partially offset by an increase in royalty revenues related to an increase in product sales by Ipsen and Takeda.

Collaboration Services Revenues

Collaboration services revenues include the recognition of deferred revenues for the portion of upfront and milestone payments that have been allocated to research and development services performance obligations, development cost reimbursements earned under our collaboration agreements, and product supply revenues, which are net of product supply costs and the royalties we pay to Royalty Pharma on sales by Ipsen and Takeda of products containing cabozantinib.

Development cost reimbursements were $60.3 million for the year ended December 31, 2022, as compared to $116.8 million for 2021. The decrease in development cost reimbursements was primarily due to Ipsen's decision to opt in and co-fund COSMIC-311 development costs in the second quarter of 2021, which included a cumulative catch up for Ipsen's share of global development costs incurred since the beginning of the study. To a lesser extent, the decrease was attributable to decreases in spending on the COSMIC-312, COSMIC-021 and COSMIC-311 studies, which was partially offset by an increase in spending on the CONTACT-02 study.

Collaboration services revenues were reduced by $16.2 million and $14.3 million for the years ended December 31, 2022 and 2021, respectively, with respect to the 3% royalty we are required to pay on the net sales by Ipsen and Takeda of any product incorporating cabozantinib. As royalty generating sales of cabozantinib by Ipsen and Takeda have increased as described above, our royalty payments have also increased.

We project our collaboration services revenues may decrease in fiscal year 2023, as compared to fiscal year 2022, primarily as a result of a decrease in development cost reimbursement revenues on certain studies with our collaborators Ipsen and Takeda.

Cost of Goods Sold

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

	Year Ended December 31,		Percent Change
	2022	2021	
Cost of goods sold	$ 57,909	$ 52,873	10 %
Gross margin %	96 %	95 %	

Cost of goods sold is related to our product revenues and consists of a 3% royalty payable 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, excess and obsolete inventory, and other third-party logistics costs. The increase in cost of goods sold for the year ended December 31, 2022, as compared to 2021, was primarily the result of increases in royalty payments as a result of increased U.S. CABOMETYX sales, which was partially offset by a decrease in certain period costs. We project our gross margin in fiscal year 2023 will remain consistent with fiscal year 2022.

Research and Development Expenses

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, including in-licensed technologies, to enable the rapid discovery, optimization and extensive characterization of lead compounds and biotherapeutics 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 (dollars in thousands):

	Year Ended December 31,		Percent Change
	2022	2021	
Research and development expenses:			
Development:			
Clinical trial costs	$ 253,519	$ 225,018	13 %
Personnel expenses	137,831	112,083	23 %
Licenses and other collaboration costs[1]	49,500	38,500	29 %
Consulting and outside services	35,651	25,463	40 %
Other development costs	45,121	26,429	71 %
Total development	521,622	427,493	22 %
Drug discovery:			
License and other collaboration costs[1]	154,412	137,568	12 %
Other drug discovery[2]	95,301	49,760	92 %
Total drug discovery	249,713	187,328	33 %
Stock-based compensation	45,350	46,654	-3 %
Other research and development[3]	75,128	32,241	133 %
Total research and development expenses	$ 891,813	$ 693,716	29 %

(1) License and other collaboration costs presented in total development includes upfront license fees and development milestone payments associated with programs currently in clinical development stage while license and other collaboration costs presented in total drug discovery primarily includes upfront license fees, development milestone payments, and research funding commitments and other payments associated with our in-licensing collaboration programs in preclinical development stage.

(2) Primarily includes personnel expenses, consulting and outside services and laboratory supplies, if not separately presented.

(3) Includes the allocation of general corporate costs to research and development services, and development cost reimbursements in connection with our collaboration arrangement with Roche executed in December 2019.

The increase in research and development expenses for the year ended December 31, 2022, as compared to 2021, was primarily related to increases in license and other collaboration costs, personnel expenses, consulting and outside services costs, clinical trial costs and other research and development costs. Drug discovery-related license and other collaboration costs increased primarily due to increases in upfront license fees, including, in connection with our recent agreements with Sairopa and Catalent in the fourth quarter of 2022, and other increases in program initiation fees, development milestones, and research funding commitments related to collaboration agreements. Development-related license and other collaboration costs increased primarily due to our recent agreement with Cybrexa in the fourth quarter of 2022 for the right to acquire CBX-12, partially offset by the reversal of a development milestone in 2022, which was recorded in 2021. The milestone was reversed as the compound has not progressed as expected and therefore we are no longer able to predict when the milestone will occur. Personnel expenses increased primarily due to an increase in headcount to support our expanding discovery and development organizations. Consulting and outside services expenses increased primarily as a result of the continued growth in our discovery and research and development activities. Clinical trial costs, which include services performed by third-party contract research organizations and other vendors who support our clinical trials, increased primarily due to higher costs associated with various studies evaluating zanzalintinib and XB002, as well as the CONTACT-02 cabozantinib study, which were partially offset by decreases in costs associated with the COSMIC-312, COSMIC-313, and COSMIC-021 cabozantinib studies. Other research and development costs increased primarily related to technology costs, including our investments in digital transformation initiatives to support productivity and efficiency in our organization, and an increase in rent expenses, which were partially offset by development cost reimbursements in connection with our collaboration arrangement with Roche.

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. These factors include enrollment in clinical trials for our drug candidates, preliminary data and final results from clinical trials, the potential market indications and overall 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 continue to focus our development efforts on cabozantinib to maximize the therapeutic and commercial potential of this compound and, as a result, we project that a substantial portion of our research and development expenses will relate to the continuing late-stage clinical development program of cabozantinib. Notable ongoing company-sponsored studies resulting from this program include: COSMIC-313, for which BMS is providing nivolumab and ipilimumab free of charge; and CONTACT-02 for which Roche is sharing the development costs and providing atezolizumab free of charge.

We are expanding our oncology product pipeline through drug discovery efforts, which encompass both biotherapeutics and small molecule programs with multiple modalities and mechanisms of action, with the goal of identifying new product candidates to advance into clinical trials. We also continue to engage in business development initiatives aimed at acquiring and in-licensing promising oncology platforms and assets, with the goal of utilizing our established preclinical and clinical development infrastructure to further characterize and develop such platforms and assets.

We project our research and development expenses may increase in fiscal year 2023, as compared to fiscal year 2022, primarily driven by an increase in personnel expenses to support our expanding discovery and development organization and an increase in clinical trial costs, including our ongoing clinical evaluation of cabozantinib in late-stage trials, the initiation of new clinical trials and expansion of ongoing clinical trials evaluating other product candidates in our pipeline, including STELLAR-303 and STELLAR-304 and planned initiation of multiple additional phase 3 pivotal trials evaluating zanzalintinib, and also our current early-stage trials evaluating zanzalintinib, XB002 and XL102, as well as anticipated business development activities.

A discussion of the risks and uncertainties with respect to our research and development activities, 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,		Percent Change
	2022	2021	
Selling, general and administrative expenses [1]	$ 397,632	$ 328,549	21 %
Stock-based compensation	62,224	73,166	-15 %
Total selling, general and administrative expenses	$ 459,856	$ 401,715	14 %

[1] Excludes stock-based compensation allocated to selling, general and administrative expenses.

Selling, general and administrative expenses consist primarily of personnel expenses, stock-based compensation, marketing costs and certain other administrative costs.

The increase in selling, general and administrative expenses for the year ended December 31, 2022, as compared to 2021, was primarily related to increases in personnel expenses, technology costs, rent expenses and marketing costs. Personnel expenses increased primarily due to an increase in administrative headcount to support our commercial and research and development organizations. The increase in technology costs includes our investments in digital transformation initiatives to support productivity and efficiency in our organization. Rent expenses increased primarily related to the commencement of new leases in 2022. Marketing costs increased primarily due to increased spending to expand our brand recognition.

We project our selling, general and administrative expenses may increase in fiscal year 2023, as compared to fiscal year 2022, in support of our continued commercial investment in CABOMETYX and the growth in the broader organization.

Non-Operating Income

Non-operating income was as follows (dollars in thousands):

	Year Ended December 31,		Percent Change
	2022	2021	
Interest income	$ 33,065	$ 7,672	331 %
Other expense, net	(197)	(184)	7 %
Non-operating income	$ 32,868	$ 7,488	339 %

The increase in non-operating income for the year ended December 31, 2022, as compared to 2021, was primarily the result of an increase in interest income due to higher interest rates and higher investment balances.

Provision for Income Taxes

The provision for income taxes and the effective tax rates were as follows (dollars in thousands):

	Year Ended December 31,		Percent Change
	2022	2021	
Provision for income taxes	$ 52,070	$ 63,091	-17 %
Effective tax rate	22.2 %	21.4 %	4 %

The decrease in provision for income taxes for the year ended December 31, 2022, as compared to 2021, was primarily due to the decrease in pre-tax income. The effective tax rate for the year ended December 31, 2022 differed from the U.S. federal statutory rate of 21% primarily due to the change in valuation allowance and a non-deductible warrant purchase, offset by the generation of federal tax credits. The effective tax rate for the year ended December 31, 2021 differed from the U.S. federal statutory rate of 21% primarily due to non-deductible executive compensation, partially offset by excess tax benefits related to the exercise of certain stock options during the period and the generation of federal tax credits. We project that our effective tax rate will be between 20% and 22% in fiscal year 2023.

Liquidity and Capital Resources

As of December 31, 2022, we had $2.1 billion in cash, cash equivalents, restricted cash equivalents and investments, as compared to $1.9 billion as of December 31, 2021. We anticipate that the aggregate of our current cash and cash equivalents, short-term investments available for operations, net product revenues and collaboration revenues will enable us to maintain our operations for at least 12 months and thereafter for the foreseeable future.

Our primary cash requirements for operating activities, which we project will increase in fiscal year 2023 as compared to fiscal year 2022, are for: employee related expenditures; costs related to our development programs and discovery programs; income tax payments; cash payments for inventory; royalty payments on our net product sales; and our leased facilities.

The Tax Cuts and Jobs Act, signed into law on December 22, 2017, modified the tax treatment of research and development expenditures beginning in fiscal year 2022. Research and development expenditures are no longer currently deductible but instead must be amortized ratably over five years for domestic expenditures or 15 years for foreign expenditures. As a result, we generated a larger federal income tax liability in fiscal year 2022, which required larger estimated federal tax payments. We will realize a reduction of our federal income tax liability in future years as the capitalized research and development expenditures are amortized for tax purposes.

Our primary sources of operating cash are: cash collections from customers related to net product sales, which we project will increase in fiscal year 2023, as compared to fiscal year 2022; cash collections related to royalties earned from our commercial collaboration arrangements with Ipsen, Takeda and others and cash collections upon achievement of certain development, regulatory and commercial milestones; and cash collections for cost reimbursements under certain of our development programs. The timing of cash generated from commercial collaborations and cash payments required for in-licensing collaborations relative to upfront license fee payments, research funding commitments, cost reimbursements, exercise of options payments and other contingent payments such as development milestone payments may vary from period to period.

We also have cash requirements related to capital expenditures to support the planned growth of our business including investments in laboratory facilities and equipment. We project that we may continue to spend significant amounts of cash to fund the development and commercialization of cabozantinib and the development of other product candidates in our pipeline, including zanzalintinib. In addition, we intend to continue to expand our oncology product pipeline through our drug discovery efforts, including additional research collaborations, in-licensing arrangements and other strategic transactions that align with our oncology drug development, and regulatory and commercial 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 based on market conditions or strategic considerations.

Letters of Credit

We have obtained standby letters of credit related to our lease obligations and certain other obligations with combined credit limits of $1.5 million and $16.7 million as of December 31, 2022 and 2021, respectively.

The standby letter of credit entered in January 2021, as a guarantee of our obligation to fund our portion of the tenant improvements related to our Alameda build-to-suit lease was extinguished and the related collateral was returned in the third quarter of 2022, following the substantial completion of the building and the commencement of the lease.

Sources and Uses of Cash (dollars in thousands):

	Year Ended December 31,		Percent Change
	2022	2021	
Working capital	$ 1,294,403	$ 1,497,157	-14 %
Cash, cash equivalents, restricted cash equivalents and investments	$ 2,066,681	$ 1,854,908	11 %

Working capital: The decrease in working capital as of December 31, 2022, as compared to December 31, 2021, was primarily due to the unfavorable impacts to our net current assets resulting from purchases of long-term investments and estimated tax payments made that are classified as long-term assets and liabilities in our Consolidated Balance Sheets. In the future, our working capital may be impacted by one of these factors or other factors, the amounts and timing of which are variable.

Cash, cash equivalents, restricted cash equivalent and investments: Cash and cash equivalents primarily consist of cash deposits held at major banks, commercial paper, money market funds and other securities with original maturities 90 days or less. Restricted cash equivalents relate to our letters of credit agreements and are invested in short-term certificates of deposit as of December 31, 2022 and marketable securities as of December 31, 2021. For additional information regarding our cash, cash equivalents, restricted cash equivalents and investments, see “Note 4. Cash and Investments,” in our “Notes to Consolidated Financial Statements” contained in Part II, Item 8 of this Annual Report on Form 10-K. The increase in cash, cash equivalents, restricted cash equivalent and investments at December 31, 2022, as compared to December 31, 2021, was primarily due to cash inflows generated by our operations, including collections of amounts due from customers, and collection of a $100.0 million milestone payment from Ipsen, partially offset by operating cash payments for employee related expenditures, cash payments to support our development and discovery programs, cash payments for capital expenditures, lease payments and tax payments.

Cash flow activities were as follows (in thousands):

	Year Ended December 31,	
	2022	2021
Net cash provided by operating activities	$ 362,614	$ 400,804
Net cash used in investing activities	$ (524,414)	$ (42,884)
Net cash provided by (used in) financing activities	$ 586	$ (14,801)

Operating 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.

Net cash provided by operating activities decreased for the year ended December 31, 2022, as compared to 2021, primarily due to an increase in cash paid for certain operating expenses primarily employee related expenses, collaboration related research and development payments and tax payments, partially offset by an increase in cash received on sales of our products and from our commercial collaboration arrangements, including the collection of a $100.0 million milestone payment from Ipsen.

Investing Activities

The changes in cash flows from investing activities primarily relates to the timing of marketable securities investment activity, acquisition of acquired in-process research and development technology and capital expenditures. Our capital expenditures primarily consist of investments to expand our operations and acquire assets that further support our research and development activities.

Net cash used in investing activities increased for the year ended December 31, 2022, as compared to 2021, primarily due to a decrease in cash proceeds from maturities and sales of investments, an increase in purchases of investments, and an increase in purchases of in-process research and development technology related to certain of our in-licensing collaboration arrangements, which were partially offset by a decrease in capital expenditures. Capital expenditures primarily consisted of investments in leasehold improvements and equipment related to an expansion of laboratory facilities at our corporate campus and technology infrastructure investments to support our digital transformation initiatives.

Financing Activities

The changes in cash flows from financing activities primarily relate to proceeds from employee stock programs and taxes paid related to net share settlement of equity awards.

Net cash was provided by financing activities for the year ended December 31, 2022, as compared to net cash used in financing activities in the prior year ended December 31, 2021. The increase in cash provided by financing activities was primarily due to lower withholding taxes remitted to the government related to net share settlements of equity awards partially offset by a decrease in proceeds received from the issuance of common stock under our equity incentive and stock purchase plans.

Contractual Obligations

As of December 31, 2022, we anticipate the aggregate of our cash, cash equivalents and short-term investments and cash generated from operations to be sufficient to fund our contractual obligations, as well as cash requirements to support our ongoing operations and capital expenditures. Our contractual obligations as of December 31, 2022 primarily consist of:

Operating leases: We have certain lease agreements related to our corporate campus facilities and other short term leases, under which we are obligated to make minimum lease payments. As of December 31, 2022, we had $19.6 million of minimum lease payments due in one year and $310.4 million due over the remaining lease term. The amounts presented herein include the estimated lease commitment payments at the estimated commencement of the lease.

Purchase obligations: Purchase obligations include firm purchase commitments related to manufacturing of inventory, software services and other facilities and equipment. As of December 31, 2022, we had $55.0 million total purchase obligations due within one year and $11.0 million due after one year.

Contingent payments: We have committed to make certain contingent payments for potential future milestones, research funding commitments and royalties to certain collaboration partners, including contingent exercise fee payments if we decide to exercise certain of our options to in-license or acquire in-process research and development technology as part of our agreements with those parties. We do not expect these contingent payments to have a significant impact on our liquidity in the near term.

Notes 3 and 11 of “Notes to Consolidated Financial Statements” contained in Part II, Item 8 of this Annual Report on Form 10-K include additional information regarding our contractual obligations and contingencies.

As of December 31, 2022, 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 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; and the amounts of deferred tax assets and liabilities including the related valuation allowance. 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 revenues 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.

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. We update our estimates every quarter to reflect actual claims and other current information. Actual rebates and chargebacks claimed for prior periods have varied from our estimates by less than 1% of the amount deducted from gross product revenues for the years ended December 31, 2022 and 2021. Our current estimates may differ significantly from actual results.

Collaboration Revenues

We enter into collaboration arrangements with third parties, under which we license certain rights to our intellectual property, and account for the arrangements as either license revenue or collaboration services revenue when the counterparty is a customer. 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. For arrangements that may include sales-based royalties, including milestone payments based on the level of sales, and the license is deemed to be the predominant item to which the royalties relate, we recognize revenue at the later of (i) when the related sale occurs or (ii) when the performance obligation to which some or all of the royalty has been allocated has been satisfied (or partially satisfied). Development milestone adjustments are recorded on a cumulative catch-up basis, which would affect collaboration services revenues in the period of adjustment. In addition, in recording revenues for our research and development services performance obligations, we use projected development cost estimates to determine the amount of revenue to record as we satisfy this performance obligation.

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 and Collaboration 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 performed for each patient, the number of active clinical sites and the duration for which the patients will be enrolled in the trial. Certain of our in-licensing collaboration arrangements include contingent payments in the form of development, regulatory and commercial milestones. We recognize expense for contingent payments when they are deemed probable of achievement which requires judgment as to the probability and timing of the achievement of the underlying milestones. To the extent actual results, or updated probability estimates, differ from current estimates, such amounts are recorded as an adjustment in the period estimates are revised. We monitor patient enrollment levels and assess the related research and development activities progress, including the probability of achieving milestones payments associated to the respective terms and conditions of our in-licensing and collaboration arrangements to the extent possible through internal reviews and estimates of the operational progress of our discovery and early-stage clinical development programs, 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, performance-based restricted stock units (PSUs) and PSUs subject to market conditions, and the estimated the number of shares subject to PSUs that will ultimately vest. To determine the fair value, we use models that require a number of complex and subjective assumptions including our stock price volatility, employee exercise patterns and risk-free interest rates. 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 volatility as well as our historical volatility 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. Monte Carlo simulation models are used to determine grant date fair value of awards with market conditions. The assumptions used in calculating the fair value of stock options and PSUs 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 expense 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 and as such, can materially affect our stock-based compensation expense in the current period and in the future.

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.

We recognize the tax benefit from an uncertain tax position only if it is more likely than not that the tax position will be sustained upon examination by tax authorities based on the technical merits of the position. The tax benefit recognized in the Consolidated Financial Statements for a particular tax position is based on the largest benefit that is more likely than not to be realized. The amount of unrecognized tax benefits is adjusted as appropriate for changes in facts and circumstances, such as significant amendments to existing tax law, new regulations or interpretations by tax authorities, new information obtained during a tax examination or resolution of an examination. We have elected to record interest and penalties in the accompanying Consolidated Statements of Income as a component of income taxes.

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, Takeda 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 or Japanese Yen. 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 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 December 30, 2022 and December 31, 2021, the related consolidated statements of income, comprehensive income, stockholders' equity and cash flows for each of the three years in the period ended December 30, 2022, and the related notes (collectively referred to as the "consolidated financial statements"). In our opinion, the consolidated financial statements present fairly, in all material respects, the financial position of the Company at December 30, 2022 and December 31, 2021, and the results of its operations and its cash flows for each of the three years in the period ended December 30, 2022, in conformity with U.S. generally accepted accounting principles.

We also have audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States) (PCAOB), the Company's internal control over financial reporting as of December 30, 2022, 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 7, 2023 expressed an unqualified opinion thereon.

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 and accounts receivable
Description of the Matter	During the year ended December 30, 2022, the Company's gross product revenues were $1,951.2 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 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. 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 tested credit memos issued during the year and after year-end. 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.

San Mateo, California
February 7, 2023

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

	December 31,	
	2022	**2021**
ASSETS		
Current assets:		
Cash and cash equivalents	$ 501,195	$ 647,169
Short-term investments	807,273	819,905
Trade receivables, net	214,784	282,650
Inventory	33,299	27,493
Prepaid expenses and other current assets	62,211	57,530
Total current assets	1,618,762	1,834,747
Long-term investments	756,731	371,112
Property and equipment, net	110,624	104,031
Deferred tax assets, net	231,110	111,663
Goodwill	63,684	63,684
Right-of-use assets and other	290,578	131,002
Total assets	$ 3,071,489	$ 2,616,239
LIABILITIES AND STOCKHOLDERS' EQUITY		
Current liabilities:		
Accounts payable	$ 32,667	$ 24,258
Accrued compensation and benefits	77,158	61,969
Accrued clinical trial liabilities	65,072	77,544
Rebates and fees due to customers	50,350	33,700
Accrued collaboration liabilities	20,188	86,753
Other current liabilities	78,924	53,366
Total current liabilities	324,359	337,590
Long-term portion of deferred revenue	6,582	8,739
Long-term portion of operating lease liabilities	190,170	51,272
Other long-term liabilities	61,951	8,023
Total liabilities	583,062	405,624
Commitments and contingencies (Note 11)		
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: 323,951 and 318,842 at December 31, 2022 and 2021, respectively	324	319
Additional paid-in capital	2,536,849	2,427,561
Accumulated other comprehensive loss	(14,521)	(758)
Accumulated deficit	(34,225)	(216,507)
Total stockholders' equity	2,488,427	2,210,615
Total liabilities and stockholders' equity	$ 3,071,489	$ 2,616,239

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,		
	2022	**2021**	**2020**
Revenues:			
Net product revenues	$ 1,401,243	$ 1,077,256	$ 741,550
License revenues	162,056	249,956	167,295
Collaboration services revenues	47,763	107,758	78,693
Total revenues	1,611,062	1,434,970	987,538
Operating expenses:			
Cost of goods sold	57,909	52,873	36,272
Research and development	891,813	693,716	547,851
Selling, general and administrative	459,856	401,715	293,355
Total operating expenses	1,409,578	1,148,304	877,478
Income from operations	201,484	286,666	110,060
Interest income	33,065	7,672	19,865
Other income (expense), net	(197)	(184)	912
Income before income taxes	234,352	294,154	130,837
Provision for income taxes	52,070	63,091	19,056
Net income	$ 182,282	$ 231,063	$ 111,781
Net income per share:			
Basic	$ 0.57	$ 0.73	$ 0.36
Diluted	$ 0.56	$ 0.72	$ 0.35
Weighted-average common shares outstanding:			
Basic	321,526	314,884	308,271
Diluted	324,556	322,359	318,001

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,		
	2022	**2021**	**2020**
Net income	$ 182,282	$ 231,063	$ 111,781
Other comprehensive income (loss):			
Net unrealized gains (losses) on available-for-sale debt securities, net of tax impact of $3,886, $1,481, and $(394), respectively	(13,763)	(5,234)	1,407
Comprehensive income	$ 168,519	$ 225,829	$ 113,188

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, 2019	304,831	$ 305	$ 2,241,947	$ 3,069	$ (559,351)	$ 1,685,970
Net income	—	—	—	—	111,781	111,781
Other comprehensive income	—	—	—	1,407	—	1,407
Issuance of common stock under equity incentive and stock purchase plans	6,796	7	24,896	—	—	24,903
Stock transactions associated with taxes withheld on equity awards	—	—	(50,018)	—	—	(50,018)
Stock-based compensation	—	—	105,070	—	—	105,070
Balance at December 31, 2020	311,627	312	2,321,895	4,476	(447,570)	1,879,113
Net income	—	—	—	—	231,063	231,063
Other comprehensive loss	—	—	—	(5,234)	—	(5,234)
Issuance of common stock under equity incentive and stock purchase plans	7,215	7	24,360	—	—	24,367
Stock transactions associated with taxes withheld on equity awards	—	—	(39,142)	—	—	(39,142)
Stock-based compensation	—	—	120,448	—	—	120,448
Balance at December 31, 2021	318,842	319	2,427,561	(758)	(216,507)	2,210,615
Net income	—	—	—	—	182,282	182,282
Other comprehensive loss	—	—	—	(13,763)	—	(13,763)
Issuance of common stock under equity incentive and stock purchase plans	5,109	5	23,976	—	—	23,981
Stock transactions associated with taxes withheld on equity awards	—	—	(23,344)	—	—	(23,344)
Stock-based compensation	—	—	108,656	—	—	108,656
Balance at December 31, 2022	323,951	$ 324	$ 2,536,849	$ (14,521)	$ (34,225)	$ 2,488,427

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,		
	2022	2021	2020
Net income	$ 182,282	$ 231,063	$ 111,781
Adjustments to reconcile net income to net cash provided by operating activities:			
Depreciation	20,875	13,630	9,141
Stock-based compensation	107,574	119,820	105,070
Non-cash lease expense	18,315	5,332	4,830
Deferred taxes	(60,358)	46,529	15,265
Acquired in-process research and development technology	107,250	14,000	—
Other, net	(525)	9,443	3,035
Changes in operating assets and liabilities:			
Trade receivables, net	66,849	(122,324)	(42,470)
Inventory	(11,683)	(13,209)	(21,897)
Prepaid expenses and other assets	(28,259)	(39,875)	(25,831)
Deferred revenue	(2,483)	11,008	(1,051)
Accrued collaboration liabilities	(63,065)	70,297	600
Accounts payable and other liabilities	25,842	55,090	50,509
Net cash provided by operating activities	362,614	400,804	208,982
Cash flows from investing activities:			
Purchases of property, equipment and other	(27,706)	(54,225)	(30,345)
Acquired in-process research and development technology	(110,750)	(10,000)	—
Purchases of investments	(1,450,716)	(1,357,168)	(1,070,269)
Proceeds from maturities and sales of investments	1,064,758	1,378,509	969,399
Net cash used in investing activities	(524,414)	(42,884)	(131,215)
Cash flows from financing activities:			
Proceeds from issuance of common stock under equity incentive and stock purchase plans	23,886	24,307	24,886
Taxes paid related to net share settlement of equity awards	(23,300)	(39,108)	(50,018)
Net cash provided by (used in) financing activities	586	(14,801)	(25,132)
Net (decrease) increase in cash, cash equivalents and restricted cash equivalents	(161,214)	343,119	52,635
Cash, cash equivalents and restricted cash equivalents at beginning of period	663,891	320,772	268,137
Cash, cash equivalents and restricted cash equivalents at end of period	$ 502,677	$ 663,891	$ 320,772
Supplemental cash flow disclosures:			
Cash paid for taxes	$ 127,870	$ 12,960	$ 4,115
Non-cash operating activities:			
Right-of-use assets obtained in exchange for lease obligations	$ 155,935	$ 4,893	$ 4,017
Non-cash investing activities:			
Accounts receivable for unsettled investment sales	$ —	$ —	$ 6,180

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 company innovating next-generation medicines and combination regimens at the forefront of cancer care. Through the commitment of our drug discovery, development and commercialization resources, we have produced four marketed pharmaceutical products, including our flagship molecule, cabozantinib. We continue to evolve our product portfolio, leveraging our investments, expertise and strategic partnerships, to target an expanding range of tumor types and indications with our clinically differentiated pipeline of small molecules, antibody-drug conjugates (ADCs) and other biotherapeutics.

Sales related to cabozantinib account for the majority of our revenues. Cabozantinib is an inhibitor of multiple tyrosine kinases including MET, AXL, VEGF receptors and RET and has been approved by the U.S. Food and Drug Administration (FDA) and in 62 other countries as: CABOMETYX® (cabozantinib) tablets approved both alone and in combination with Bristol-Myers Squibb Company's (BMS) OPDIVO® (nivolumab) for advanced renal cell carcinoma (RCC), for previously treated hepatocellular carcinoma (HCC) and, currently by the FDA and European Commission (EC), for previously treated, radioactive iodine (RAI)-refractory differentiated thyroid cancer (DTC); and COMETRIQ® (cabozantinib) capsules approved for progressive, metastatic medullary thyroid cancer. For physicians treating these types of cancer, cabozantinib has become or is becoming an important medicine in their selection of effective therapies.

The other two products resulting from our discovery efforts are: COTELLIC® (cobimetinib), an inhibitor of MEK approved as part of multiple combination regimens to treat specific forms of 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 approved for the treatment of hypertension in Japan and licensed to Daiichi Sankyo Company, Limited (Daiichi Sankyo). See "—Collaborations and Business Development Activities—Other Collaborations."

We plan to continue leveraging our operating cash flows to support the ongoing investigation of cabozantinib in phase 3 trials for new indications and the advancement of a broad array of diverse biotherapeutics and small molecule programs for the treatment of cancer exploring multiple modalities and mechanisms of action.

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 adopted a 52- or 53-week fiscal year policy that ends on the Friday closest to December 31st. Fiscal year 2022, which was a 52-week fiscal year, ended December 30, 2022, fiscal year 2021, which was a 52-week fiscal year, ended on December 31, 2021 and fiscal year 2020, which was a 52-week fiscal year, ended January 1, 2021. For convenience, references in this report as of and for the fiscal years ended December 30, 2022 and January 1, 2021 are indicated as being as of and for the years ended December 31, 2022 and 2020, respectively.

We have made reclassifications to our prior years' Consolidated Financial Statements to conform to the current year's presentation. These reclassifications did not impact previously reported total revenues, income from operations, net income, total assets, total liabilities, total operating, investing or financing cash flows or total stockholders' equity.

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

There were no new accounting pronouncements adopted by us since our filing of the Annual Report on Form 10-K for the year ended December 31, 2021, which could have a significant effect on our Consolidated Financial Statements.

Cash, Cash Equivalents, Restricted Cash Equivalents 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. 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, 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.

Investment Impairment

Quarterly, we assess each of our investments in available-for-sale debt securities whose fair value is below its cost basis to determine if the investment's impairment is due to credit-related factors or noncredit-related factors. Factors considered in determining whether an impairment is credit-related include the extent to which the investment's fair value is less than its cost basis, declines in published credit ratings, issuer default on interest or principal payments, and declines in the financial condition and near-term prospects of the issuer. If we determine a credit-related impairment exists, we will measure the credit loss based on a discounted cash flows model. Credit-related impairments on available-for-sale debt securities are recognized as an allowance for credit losses with a corresponding adjustment to other income, net in the accompanying Consolidated Statements of Income. The portion of the impairment that is not credit-related is recorded as a reduction of other comprehensive income (loss), net of applicable taxes.

We have elected to exclude accrued interest from both the fair value and the amortized cost basis of the available-for-sale debt securities for the purposes of identifying and measuring an impairment. We write-off accrued interest as a reduction of interest income when an issuer has defaulted on interest payments due on a security.

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.

Foreign Currency 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, net in the accompanying Consolidated Statements of Income. Net foreign currency gains or losses were immaterial for the years ended December 31, 2022, 2021 and 2020, respectively.

Accounts Receivable

Trade receivables, net, contain amounts billed to our customers for product sales, and amounts billed to our collaboration partners for development, regulatory and sales-based milestone payments, royalties on the sale of licensed products, profit-sharing arrangements, development cost reimbursements, and payments for product supply services. Our customers are primarily pharmaceutical and biotechnology companies that are located in the U.S., and collaboration partners that are located in Europe and Japan. We record trade receivables net of allowances for credit losses and chargebacks, and cash discounts for prompt payment. We apply an aging method to estimate credit losses and consider our historical loss information, adjusted to account for current economic conditions, and reasonable and supportable forecasts of future economic conditions affecting our customers. We write off trade receivables and related allowances for credit losses when it becomes probable we will not collect the amount receivable. Write-offs for the years ended December 31, 2022 and December 31, 2021 were immaterial.

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 services 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 any material impairment charges in any of the periods presented.

Goodwill

We recorded goodwill amounts as the excess of purchase price over identifiable net assets acquired based on their estimated fair value. We review the carrying amount of goodwill for impairment annually and whenever events or changes in circumstance indicate that the carrying value may not be recoverable. We perform our annual assessment of the recoverability of our goodwill as of the first day of our fourth quarter. 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 for the amount by which the carrying amount of a reporting unit exceeds its fair value, limited to the goodwill balance. We operate in one business 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.

Long-Lived Assets

The carrying value of our long-lived assets, which includes property and equipment, right-of-use assets and leasehold improvements, is reviewed for impairment whenever events or changes in circumstances indicate that the

carrying value of the asset may not be recoverable. Should there be an indication of impairment, we test for recoverability by comparing the estimated undiscounted future cash flows expected to result from the use of the asset to the carrying amount of the asset or asset group. If the asset or asset group is determined to be impaired, any excess of the carrying value of the asset or asset group over its estimated fair value is recognized as an impairment loss.

Revenue

We account for revenues under the guidance of ASU Topic 606, *Revenues from Contracts with Customers* (Topic 606). 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 primarily 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 2020, the Medicare Part D prescription drug benefit mandated participating manufacturers to fund 70% of the Medicare Part D insurance coverage gap for prescription drugs sold to eligible patients. Our estimates for expected Medicare Part D coverage gap amounts are based on Customer and payer data received from specialty pharmacies and distributors and historical utilization rates. Funding of the coverage gap is invoiced and paid in arrears so that the accrual balance consists of an estimate of the amount expected to be incurred for the current quarter's shipments to Customer, plus an accrual balance for known prior quarters' unpaid claims. If actual future funding varies from estimates, we may need to adjust our accruals, which would affect net product revenues in the period of adjustment.

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

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

Collaboration Revenues

We assess whether our collaboration agreements are subject to ASC Topic 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 apply by analogy the unit of account guidance under Topic 606 to identify distinct performance obligations, and then determine whether a customer relationship exists for each distinct performance obligation. If we determine a performance obligation within the arrangement is with a customer, we apply the guidance in Topic 606. If a portion of a distinct bundle of goods or services within an arrangement is not with a customer, then the unit of account is not within the scope of Topic 606, and the recognition and measurement of that unit of account shall be based on analogy to authoritative accounting literature or, if there is no appropriate analogy, a reasonable, rational, and consistently applied accounting policy election.

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 payments to us for one or more of the following: nonrefundable 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. 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, which generally occurs at or near the inception of the contract. 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 revenues from nonrefundable up-front fees. We evaluate the measure of progress at the end of 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 variable consideration 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 the 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 revenues for these services as the performance obligations are satisfied over time based on measure of progress. However, if we conclude that our collaboration partner is not a customer for those collaborative research and development activities, we present such payments as a reduction of research and development expenses.

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 the commercialization of cobimetinib. We account for this arrangement in accordance with Topic 606. We have determined that we are an agent under the agreement and therefore revenues are recorded net of costs incurred. We record revenues for the variable consideration associated with the profits and losses under the collaboration agreement when it is probable that a significant reversal in the amount of cumulative revenues recognized will not occur.

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 revenues 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 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 are not capitalized as inventory but are expensed as research and development costs.

Research and Development Expenses

Research and development expenses consist of (1) direct and indirect internal costs for drug discovery; (2) upfront license and project initiation fees, license option fees and option exercise fees, funded research and milestone payments incurred or probable to be incurred for our in-licensing arrangements with our collaboration partners for research programs in development and prior to regulatory approval; 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.

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 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 *ASU 2016-02*, *Leases* (Topic 842) for short-term leases.

Advertising

Advertising expenses were $41.6 million, $31.8 million and $25.1 million for the years ended December 31, 2022, 2021 and 2020, respectively. We expense the costs of advertising, including promotional expenses, as incurred. Advertising expenses are recorded in selling, general and administrative expenses.

Stock-Based Compensation

We account for stock-based payments to employees, including grants of service-based restricted stock units (RSUs), performance-based restricted stock units (PSUs), service-based stock options 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 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 certain PSUs and RSUs with market vesting conditions and a Black-Scholes Merton option pricing model for stock options. Both 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 volatility 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 related 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. Compensation expense related to RSUs with market vesting conditions is recognized regardless of the outcome of the market conditions.

Variable Interest Entities

We continually assess our ownership, contractual and other interests in entities that are not wholly-owned whether we are the primary beneficiary of a variable interest entity (VIE) and therefore we must consolidate the entity. We apply a qualitative approach that determines whether we have both (1) the power to direct the activities that most significantly impact the economic performance of the entity and (2) the obligation to absorb losses of, or the right to receive benefits from, the entity that could potentially be significant to that entity. We perform this assessment, as changes to existing relationships or future transactions may result in consolidation or deconsolidation of a VIE.

Provision for Income Taxes

Our provision for income taxes is computed under the asset and liability method. Significant estimates are required in determining our provision for income taxes. 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 provision for income taxes in the period of such reversal. Based on our evaluation of various factors, including our achievement of a cumulative three-year income position as of December 31, 2022 and forecasts of future operating results, we do not have a valuation allowance against our deferred tax assets as described in "Note 9. Provision For Income Taxes", below. We continue to maintain a valuation allowance against our California state deferred tax assets.

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

Recent Accounting Pronouncements Not Yet Adopted

There were no new accounting pronouncements issued since our filing of the Annual Report on Form 10-K for the year ended December 31, 2021, which could have a significant effect on our Consolidated Financial Statements.

NOTE 2. REVENUES

Revenues consisted of the following (in thousands):

	Year Ended December 31,		
	2022	2021	2020
Product revenues:			
Gross product revenues	$ 1,951,169	$ 1,452,913	$ 962,591
Discounts and allowances	(549,926)	(375,657)	(221,041)
Net product revenues	1,401,243	1,077,256	741,550
Collaboration revenues:			
License revenues	162,056	249,956	167,295
Collaboration services revenues	47,763	107,758	78,693
Total collaboration revenues	209,819	357,714	245,988
Total revenues	$ 1,611,062	$ 1,434,970	$ 987,538

Net product revenues and license revenues are recorded in accordance with Topic 606. 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 current period that the milestone would be achieved and a significant reversal of revenues would not occur, as well as royalty revenues and our share of profits under our collaboration agreement with Genentech. Collaboration services revenues were recorded in accordance with Topic 808. Collaboration services revenues include the recognition of deferred revenues for the portion of upfront and milestone payments allocated to our research and development services performance obligations, development cost reimbursements earned under our collaboration agreements, product supply revenues, net of product supply costs, and the royalties we paid on sales of products containing cabozantinib by our collaboration partners.

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

	Year Ended December 31,		
	2022	2021	2020
CABOMETYX	$ 1,375,909	$ 1,054,050	$ 718,687
COMETRIQ	25,334	23,206	22,863
Net product revenues	$ 1,401,243	$ 1,077,256	$ 741,550

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,		
	2022	2021	2020
Affiliates of AmerisourceBergen Corporation	18 %	14 %	11 %
Affiliates of McKesson Corporation	17 %	14 %	12 %
Affiliates of CVS Health Corporation	17 %	14 %	14 %
Ipsen Pharma SAS	10 %	21 %	15 %
Accredo Health, Incorporated	10 %	9 %	9 %
Affiliates of Optum Specialty Pharmacy	10 %	8 %	11 %

As of December 31, 2022 and 2021, the percentage of trade receivables by customer who individually accounted for 10% or more of our trade receivables were as follows:

	December 31,	
	2022	2021
Affiliates of McKesson Corporation	22 %	10 %
Ipsen Pharma SAS	20 %	50 %
Affiliates of AmerisourceBergen Corporation	18 %	11 %
Affiliates of CVS Health Corporation	18 %	9 %
Cardinal Health, Inc.	11 %	6 %

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

	Year Ended December 31,		
	2022	2021	2020
U.S.	$ 1,413,743	$ 1,089,396	$ 752,890
Europe	168,592	302,073	151,631
Japan	28,727	43,501	83,017
Total revenues	$ 1,611,062	$ 1,434,970	$ 987,538

Total revenues include net product revenues attributed to geographic regions based on ship-to location and license and collaboration services revenues 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, Discounts for Prompt Payment and Other	Other Customer Credits/Fees and Co-pay Assistance	Rebates	Total
Balance at December 31, 2020	$ 9,853	$ 3,279	$ 17,404	$ 30,536
Provision related to sales made in:				
Current period	243,119	30,728	100,361	374,208
Prior periods	(64)	(111)	1,624	1,449
Payments and customer credits issued	(238,283)	(25,021)	(94,564)	(357,868)
Balance at December 31, 2021	14,625	8,875	24,825	48,325
Provision related to sales made in:				
Current period	355,865	50,312	143,516	549,693
Prior periods	611	(169)	(209)	233
Payments and customer credits issued	(344,220)	(44,094)	(132,706)	(521,020)
Balance at December 31, 2022	$ 26,881	$ 14,924	$ 35,426	$ 77,231

The allowance for chargebacks, discounts for prompt payment and other 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. 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. For those contracts that have multiple performance obligations, contract assets and liabilities are reported on a net basis at the contract level. As of December 31, 2022 and 2021, respectively, contract assets are primarily related to contract assets from Ipsen Pharma SAS (Ipsen) and contract liabilities are primarily related to deferred revenues from Takeda Pharmaceutical Company Limited (Takeda).

Contract assets and liabilities were as follows (in thousands):

	December 31,	
	2022	2021
Contract assets[1]	$ 1,659	$ 1,665
Contract liabilities:		
Current portion[2]	$ 7,488	$ 7,814
Long-term portion[3]	6,582	8,739
Total contract liabilities	$ 14,070	$ 16,553

(1) Presented in other long-term assets in the accompanying Consolidated Balance Sheets.
(2) Presented in other current liabilities in the accompanying Consolidated Balance Sheets.
(3) Presented in the long-term portion of deferred revenues in the accompanying Consolidated Balance Sheets.

During the years ended December 31, 2022, 2021 and 2020, we recognized $8.1 million, $8.5 million and $9.2 million, respectively, in revenues that were included in the beginning deferred revenues balance for those years.

During the years ended December 31, 2022, 2021 and 2020, we recognized $161.6 million, $148.7 million and $169.7 million, respectively, in revenues for performance obligations satisfied in previous periods. Such revenues were primarily related to milestone and royalty payments allocated to our license performance obligations for our collaborations with Ipsen, Takeda, Daiichi Sankyo and Genentech.

As of December 31, 2022, $73.0 million of the combined transaction prices for our Ipsen and Takeda collaborations were allocated to performance obligations that had not yet been satisfied. See "Note 3. Collaboration Agreements— Cabozantinib Collaborations —*Performance Obligations and Transaction Prices for our Ipsen and Takeda Collaborations"* for additional information about the expected timing to satisfy these performance obligations.

NOTE 3. COLLABORATION AGREEMENTS AND BUSINESS DEVELOPMENT ACTIVITIES

We have established multiple collaborations with leading biopharmaceutical companies for the commercialization and further development of our cabozantinib franchise. Additionally, we have made considerable progress under our existing research collaboration and in-licensing arrangements to further enhance our early-stage pipeline and expand our ability to discover, develop and commercialize novel therapies with the goal of providing new treatment options for cancer patients and their physicians. Historically, we also entered into other collaborations with leading biopharmaceutical companies pursuant to which we out-licensed other compounds and programs in our portfolio.

Under these collaborations, we are generally entitled to receive milestone and royalty payments, and for certain collaborations, to receive payments for product supply services, development cost reimbursements, and/or profit-sharing payments. See "Note 2. Revenues" for additional information on revenues recognized under our collaboration agreements during the years ended December 31, 2022, 2021 and 2020.

Cabozantinib Commercial Collaborations

Ipsen Collaboration

Description of the Collaboration

In February 2016, we entered into a collaboration and license agreement with Ipsen, which was subsequently amended, for the commercialization and further development of cabozantinib. Under the collaboration agreement, as amended, Ipsen received exclusive commercialization rights for current and potential future cabozantinib indications outside of the U.S. and Japan. 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.

During the second quarter of 2021, Ipsen opted into and is now co-funding the development costs for COSMIC-311, our 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. Under the collaboration agreement, Ipsen is obligated to reimburse us for their share of COSMIC-311 global development costs, as well as an additional payment calculated as a percentage of such costs, triggered by the timing of the exercise of its option. We determined that the decision to opt in and co-fund the development costs for COSMIC-311 represented a contract modification for additional distinct services at their standalone selling price and therefore was treated as a separate contract under Topic 606. Accordingly, collaboration services revenues for the year ended December 31, 2021, includes a cumulative catch-up of $43.2 million for Ipsen's share of global development costs incurred since the beginning of the study and through the opt-in date.

Unless earlier terminated, 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 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, 2022, we have achieved aggregate milestones of $489.5 million related to regulatory, development and sales-based threshold by Ipsen since the inception of the collaboration agreement, including $27.0 million, $112.5 million, and $20.0 million in milestones achieved during the years ended December 31, 2022, 2021 and 2020, respectively.

As of December 31, 2022, we are eligible to receive additional regulatory and development milestone payments from Ipsen totaling an aggregate of $19.5 million, as well as sales-based milestones, including milestone payments earned for the first commercial sale of a product, of up to $350.0 million and CAD$26.5 million. We excluded these milestones from the transaction price as of December 31, 2022 because we determined such payments to be fully constrained under Topic 606 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. We will adjust the constraint applied to the variable consideration at each reporting period as uncertain events are resolved or other changes in circumstances occur. See *"—Performance Obligations and Transaction Prices for our Ipsen and Takeda Collaborations"*, below, for additional information related to the revenue recognition for this collaboration.

We also receive royalty revenues on the net sales of cabozantinib by Ipsen outside of the U.S. and Japan. During the year ended December 31, 2022 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.

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 are required to pay a 3% royalty 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 certain clinical trials, including: CheckMate-9ER, COSMIC-021, COSMIC-311, COSMIC-312, CONTACT-01 and CONTACT-02.

We remain responsible for manufacturing and supply of cabozantinib for all development and commercialization activities under the collaboration agreement. Relatedly, 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 as well as a quality agreement that provides respective quality responsibilities for the aforementioned supply. The product is supplied at our cost, as defined in the agreement. 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 territories outside of U.S. and Japan from sources other than our sponsored global clinical development trials, we rely on data collected and reported to us by Japan.

Revenues from the Collaboration

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

	Year Ended December 31,		
	2022	2021	2020
License revenues	$ 133,732	$ 207,982	$ 93,495
Collaboration services revenues	34,860	94,091	58,136
Total	$ 168,592	$ 302,073	$ 151,631

During the year ended December 31, 2022, we recognized $25.8 million in revenues in connection with two regulatory milestones totaling $27.0 million upon approval by the EC and Health Canada, of cabozantinib a monotherapy for the treatment of adult patients with locally advanced or metastatic DTC, refractory or not eligible to RAI who have progressed during or after prior systemic therapy.

As of December 31, 2022, $35.4 million of the transaction price was allocated to our research and development services performance obligation that has not yet been satisfied.

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, May 2019 and September 2020, 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, as well as modify certain cost-sharing obligations related to the Japan-specific development costs associated with CONTACT-01 and CONTACT-02.

Takeda is responsible for a portion 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, certain cohorts of COSMIC-021, CONTACT-01 and CONTACT-02. Under the collaboration agreement, as amended, 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. We may terminate the agreement if Takeda challenges or opposes any patent covered by the collaboration agreement. 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, 2022, we have also achieved regulatory and development milestones in the aggregate of $127.0 million since the inception of the collaboration agreement, including $0, $35.0 million and $66.0 million in milestones achieved during the years ended December 31, 2022, 2021 and 2020, respectively.

Under the collaboration agreement, as amended in 2020, we are eligible to receive additional regulatory and development milestone payments, without contractual 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 $119.0 million. We excluded these milestones from the transaction price as of December 31, 2022 because we determined such payments to be fully constrained under Topic 606 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. We will adjust the constraint applied to the variable consideration at each reporting period as uncertain events are resolved or other changes in circumstances occur.

We also receive royalty revenues 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. 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 are required to pay a 3% royalty on all net sales of any product incorporating cabozantinib, including net sales by Takeda.

Under the collaboration agreement, we are responsible for the manufacturing and supply of cabozantinib for all development and commercialization activities under the collaboration agreement. Relatedly, 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 services revenues under the collaboration agreement with Takeda were as follows (in thousands):

	Year Ended December 31,		
	2022	2021	2020
License revenues	$ 11,335	$ 26,058	$ 61,115
Collaboration services revenues	12,903	13,667	20,557
Total collaboration revenues	$ 24,238	$ 39,725	$ 81,672

As of December 31, 2022, $37.6 million of the transaction price was allocated to our research and development services performance obligations that have not yet been satisfied.

Performance Obligations and Transaction Prices for our Ipsen and Takeda Collaborations

There is one remaining performance obligation for the Ipsen collaboration agreement: the 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). As part of the original contract, we also had a performance obligation associated with exclusive license for the commercialization and further development of cabozantinib, which was transferred in 2016.

There are two remaining performance obligations for the Takeda collaboration agreement: (1) the 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) and (2) the research and development services associated with CONTACT-01, CONTACT-02, and certain cohorts of COSMIC-021 studies. As part of the original contract, we had a performance obligation associated with the exclusive license for the commercialization and further development of cabozantinib, which was transferred in 2017.

We have allocated the transaction price for each of these collaborations to the originally 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.

We adjust the constraint applied to the variable consideration 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, 2022, 2021 and 2020, the transaction price of the Ipsen and Takeda collaboration agreements increased as a result of the achievement of various milestones, and the reimbursements of research and development services related to committed and opt-in studies. 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, 2022, variable consideration related to the remaining unearned regulatory and development milestones for both agreements remained constrained due to the fact that it was not probable that a significant reversal of cumulative revenue would not occur.

Cabozantinib Development Collaborations

BMS

In February 2017, we entered into a clinical trial collaboration agreement with BMS for the purpose of exploring the therapeutic potential of cabozantinib in combination with BMS's immune checkpoint inhibitors (ICIs), nivolumab and/or ipilimumab, to treat a variety of types of cancer. As part of the collaboration, we are evaluating the triplet combination of cabozantinib, nivolumab and ipilimumab as a treatment option for RCC in the COSMIC-313 trial. Under the collaboration agreement with BMS, we may also evaluate these combinations in other phase 3 pivotal trials in various other tumor types.

Under the collaboration agreement with BMS, as amended, 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 is conducted under a combination Investigational New Drug application, unless otherwise required by a regulatory authority. Each party is 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.

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. Under 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 the phase 3 pivotal clinical trials in advanced non-small cell lung cancer (CONTACT-01), metastatic castration-resistant prostate cancer (CONTACT-02) and RCC (CONTACT-03). If a party to the joint clinical research agreement proposes any additional combined therapy trials beyond these 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.

In July 2020, a supplement to the joint clinical research agreement was signed amongst us, Roche and Takeda due to Takeda opting into fund the combined therapy trial of CONTACT-01 sponsored by Roche. Chugai was added as an affiliate of Roche. All parties including Chugai conduct combined therapy trials in Japan upon the terms of the joint clinical research agreement.

Under 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 of their drug 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 and Royalty Pharma

In October 2002, we established a product development and commercialization collaboration agreement with GlaxoSmithKline (GSK), that required us to pay a 3% royalty to GSK on the total worldwide net sales of any product incorporating cabozantinib by us and our collaboration partners. Effective January 1, 2021, Royalty Pharma plc (Royalty Pharma) acquired from GSK all rights, title and interest in royalties on total net sales of any product containing cabozantinib for non-U.S. markets for the full term of the royalty and for U.S. market through September 2026, after which time U.S. royalties will revert back to GSK. Royalty fees earned by GSK and Royalty Pharma in connection with our sales of cabozantinib are included in cost of goods sold and as a reduction of collaboration services revenues for sales by our collaboration partners. Such royalty fees earned by GSK and Royalty Pharma were $58.2 million, $46.6 million and $32.7 million during the years ended December 31, 2022, 2021 and 2020, respectively.

Other Collaborations

Genentech Collaboration

We have out-licensed to Genentech under a worldwide collaboration agreement, the development and commercialization of cobimetinib, under the brand name COTELLIC. The terms of the collaboration agreement require that we share in the profits and losses received or incurred in connection with the commercialization of COTELLIC in the U.S. In

addition to our profit share in the U.S., we are entitled to low double-digit royalties on net sales of COTELLIC outside the U.S.

During the years ended December 31, 2022, 2021 and 2020, we recognized $12.5 million, $12.1 million, and $11.3 million, in revenues from profits and losses on U.S commercialization and royalties on ex-U.S. sales under the collaboration agreement with Genentech and are included within license revenues on our Consolidated Statements of Income.

Research Collaborations, In-Licensing Arrangements and Other Business Development Activities

We entered into collaborative arrangements with other pharmaceutical or biotechnology companies to develop and commercialize drug candidates or intellectual property. Our research collaborations and in-licensing arrangements are intended to enhance our early-stage pipeline and expand our ability to discover, develop and commercialize novel therapies with the goal of providing new treatment options for cancer patients and their physicians. Our research collaborations, in-licensing arrangements and other strategic transactions include upfront payments, development, regulatory, commercial milestone payments and royalty payments, contingent upon the occurrence of certain future events linked to the success of the asset in development. Certain of our research collaborations provide us exclusive options that give us the right to license programs or acquire the intellectual property developed under the research collaborations for further discovery and development. When we decide to exercise the options, we are required to pay an exercise fee and then assume the responsibilities for all subsequent clinical development, manufacturing and commercialization.

In June 2022, we entered into an exclusive option and license agreement with BioInvent International AB (BioInvent), upon which we paid an upfront payment of $25.0 million. If we decide to exercise the option, we will pay BioInvent an option exercise fee, and BioInvent would be eligible for additional payments from us for future development and commercial milestones, as well as royalties on future net sales of products.

In November 2022, we entered into an agreement with Cybrexa Therapeutics, LLC (Cybrexa), which provides us the right to acquire CBX-12 (alphalex™ exatecan), a clinical-stage peptide-drug conjugate that utilizes Cybrexa's proprietary alphalex technology to enhance delivery of exatecan to tumor cells. Under the terms of the agreement, we made an upfront payment of $60.0 million for a warrant entitling us to the right to acquire the Cybrexa affiliate that controls CBX-12 and related assets, and to fund certain development and manufacturing expenses incurred by Cybrexa to advance CBX-12 during the warrant period. Cybrexa will continue the development of CBX-12 according to an agreed development plan, including phase 1 studies, and may be eligible to receive up to $65.0 million in additional development milestone payments, during the warrant period. We may exercise the warrant for up to $300.0 million based upon our evaluation of a pre-specified clinical data package to be delivered by Cybrexa. Following exercise of the warrant, Cybrexa would be eligible to receive up to $277.5 million in additional payments upon achievement of further regulatory and commercial milestones.

We have determined our arrangement with Cybrexa constitutes a variable interest in the Cybrexa affiliate that controls CBX-12 and related assets, and that the Cybrexa affiliate is a VIE; however, we are not the primary beneficiary of the Cybrexa affiliate as we do not control the activities that are most significant to the Cybrexa affiliate.

We have accounted for our arrangement with Cybrexa as an acquisition of in-process research and development technology that does not have an alternative future use, and accordingly, recognized the upfront payment of $60.0 million in research and development expenses during the year-ended December 31, 2022.

In November 2022, we entered into an exclusive option and license agreement with Sairopa, B.V. (Sairopa). Under the terms of the agreement, we made an upfront payment of $40.0 million for an option to obtain an exclusive, worldwide license to develop and commercialize ADU-1805 and other anti-SIRPα antibodies. Sairopa is eligible to receive additional development milestone payments during the option period totaling up to $97.5 million. Following the completion of the clinical studies, we may exercise the option for $225.0 million based upon our evaluation of a pre-specified clinical data package to be delivered by Sairopa. Following the exercise of the option, Sairopa would be eligible to receive up to $465.0 million in additional payments upon achievement of further development and commercial milestones, as well as royalties on future net sales of products.

In November 2022, we entered into a new license agreement with Catalent, Inc.'s wholly owned subsidiaries Redwood Bioscience, Inc., R.P. Scherer Technologies, LLC and Catalent Pharma Solutions, Inc., (individually and collectively referred to as Catalent). Under the terms of the agreement, we made an upfront payment of $30.0 million in exchange for rights to three biologics programs. We will also contribute research funding to Catalent for discovery and preclinical

development work. Catalent would be eligible to receive potential future development, regulatory and commercial milestone payments, as well as royalties on future net sales of products.

During the years ended December 31, 2022, 2021 and 2020, we recognized $203.9 million, $176.1 million and $96.4 million, respectively, relating to upfront license payments, research and development funding, development milestones, option fees and other fees within research and development expenses on the Consolidated Statements of Income. During the year ended December 31, 2022, we reversed $12.5 million of previously recorded research and development expenses associated with a development milestone. The impact of the change in estimate on our basic and diluted earnings per share for the fiscal year ended December 31, 2022 was an increase of $0.04 per share. The milestone was reversed as the compound has not progressed as expected and therefore we are no longer able to predict when the milestone will occur.

As of December 31, 2022, in conjunction with these collaborative in-licensing arrangements we are subject to potential future development milestones of up to $652.0 million, regulatory milestones of up to $634.3 million and commercial milestones of up to $3,153.0 million, each in the aggregate per product or target, as well as royalties on future net sales of products.

NOTE 4. CASH AND INVESTMENTS

Cash, Cash Equivalents and Restricted Cash Equivalents

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

	December 31,	
	2022	**2021**
Cash and cash equivalents	$ 501,195	$ 647,169
Restricted cash equivalents included in other long-term assets	1,482	16,722
Cash, cash equivalents and restricted cash equivalents as reported within the accompanying Consolidated Statements of Cash Flows	$ 502,677	$ 663,891

Restricted cash equivalents are used to collateralize letters of credit agreements and are invested in short-term certificates of deposit with original maturity of 90 days or less as of December 31, 2022 and money market fund securities as of December 31, 2021. The restricted cash equivalents are classified as other long-term assets. The standby letter of credit entered into in January 2021, as a guarantee of our obligation to fund our portion of the tenant improvements related to our Alameda build-to-suit lease was extinguished and the related collateral was returned in the third quarter of 2022, following the substantial completion of the building and the commencement of the lease.

Cash, Cash Equivalents, Restricted Cash Equivalents and Investments

Cash, cash equivalents, restricted cash equivalents and investments consisted of the following (in thousands):

	December 31, 2022			
	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Fair Value
Debt securities available-for-sale:				
Commercial paper	$ 722,018	$ —	$ —	$ 722,018
Corporate bonds	810,439	541	(13,132)	797,848
U.S. Treasury and government-sponsored enterprises	338,218	48	(5,679)	332,587
Municipal bonds	16,385	—	(223)	16,162
Total debt securities available-for-sale	1,887,060	589	(19,034)	1,868,615
Cash	41	—	—	41
Money market funds	94,344	—	—	94,344
Certificates of deposit	103,681	—	—	103,681
Total cash, cash equivalents, restricted cash equivalents and investments	$ 2,085,126	$ 589	$ (19,034)	$ 2,066,681

	December 31, 2021			
	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Fair Value
Debt securities available-for-sale:				
Commercial paper	$ 945,801	$ 42	$ (2)	$ 945,841
Corporate bonds	541,774	876	(1,672)	540,978
U.S. Treasury and government-sponsored enterprises	33,965	1	(21)	33,945
Municipal bonds	12,924	15	(35)	12,904
Total debt securities available-for-sale	1,534,464	934	(1,730)	1,533,668
Cash	135,653	—	—	135,653
Money market funds	66,531	—	—	66,531
Certificates of deposit	119,056	—	—	119,056
Total cash, cash equivalents, restricted cash equivalents and investments	$ 1,855,704	$ 934	$ (1,730)	$ 1,854,908

Interest receivable was $7.3 million and $2.9 million as of December 31, 2022 and 2021, respectively, and is included in prepaid and other current assets in the accompanying Consolidated Balance Sheets.

Realized gains and losses on the sales of investments were insignificant during the years ended December 31, 2022, 2021 and 2020.

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 debt securities available-for-sale in an unrealized loss position were as follows (in thousands):

	December 31, 2022	
	Fair Value	Gross Unrealized Losses
Corporate bonds	$ 706,711	$ (13,132)
U.S. Treasury and government-sponsored enterprises	308,307	(5,679)
Municipal bonds	15,792	(223)
Total	$ 1,030,810	$ (19,034)

	December 31, 2021	
	Fair Value	Gross Unrealized Losses
Corporate bonds	$ 385,053	$ (1,672)
Commercial paper	43,290	(2)
U.S. Treasury and government-sponsored enterprises	18,962	(21)
Municipal bonds	7,475	(35)
Total	$ 454,780	$ (1,730)

There were 285 and 133 debt securities available-for-sale in an unrealized loss position as of December 31, 2022 and 2021, respectively. All securities presented above have been in an unrealized loss position for less than twelve months except for 76 corporate bond securities, 4 municipal bond securities and 1 U.S. Treasury and government-sponsored enterprises security with an aggregate fair value of $237.6 million and an aggregate $6.1 million unrealized losses as of December 31, 2022. During the years ended December 31, 2022 and 2021, we did not record an allowance for credit losses or other impairment charges on our investment 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 and market liquidity. 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 debt securities available-for-sale by contractual maturity was as follows (in thousands):

	December 31,	
	2022	2021
Maturing in one year or less	$ 1,114,884	$ 1,168,256
Maturing after one year through five years	753,731	365,412
Total debt securities available-for-sale	$ 1,868,615	$ 1,533,668

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; and

- 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, 2022		
	Level 1	Level 2	Total
Commercial paper	$ —	$ 722,018	$ 722,018
Corporate bonds	—	797,848	797,848
U.S. Treasury and government-sponsored enterprises	—	332,587	332,587
Municipal bonds	—	16,162	16,162
Total debt securities available-for-sale	—	1,868,615	1,868,615
Money market funds	94,344	—	94,344
Certificates of deposit	—	103,681	103,681
Total financial assets carried at fair value	$ 94,344	$ 1,972,296	$ 2,066,640

	December 31, 2021		
	Level 1	Level 2	Total
Commercial paper	$ —	$ 945,841	$ 945,841
Corporate bonds	—	540,978	540,978
U.S. Treasury and government-sponsored enterprises	—	33,945	33,945
Municipal bonds	—	12,904	12,904
Total debt securities available-for-sale	—	1,533,668	1,533,668
Money market funds	66,531	—	66,531
Certificates of deposit	—	119,056	119,056
Total financial assets carried at fair value	$ 66,531	$ 1,652,724	$ 1,719,255

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, receivables and payables, approximate their fair values due to their short-term nature.

Forward Foreign Currency Contracts

In January 2021, we initiated an operational hedging program and entered into forward contracts to hedge certain operational exposures for the changes in foreign currency exchange rates associated with assets or liabilities denominated in foreign currencies, primarily the Euro.

As of December 31, 2022, we had one forward contract outstanding to sell €3.6 million. The forward contract with a maturity of three months is recorded at fair value and is included in prepaid expenses and other current assets in the Consolidated Balance Sheets. The unrealized loss on the forward contract is not material as of December 31, 2022. The forward contract is considered a Level 2 in the fair value hierarchy of our fair value measurements. For the years ended December 31, 2022 and 2021 we recognized $1.2 million and $0.8 million of net gains on the maturity of forward contracts, which were included in other income (expense), net on our Consolidated Statements of Income.

NOTE 6. INVENTORY

Inventory consisted of the following (in thousands):

	December 31,	
	2022	2021
Raw materials	$ 8,077	$ 8,867
Work in process	43,564	27,717
Finished goods	10,635	12,927
Total	$ 62,276	$ 49,511
Balance Sheet classification:		
Current portion included in inventory	$ 33,299	$ 27,493
Long-term portion included in other long-term assets	28,977	22,018
Total	$ 62,276	$ 49,511

NOTE 7. PROPERTY AND EQUIPMENT

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

		December 31,	
	Estimated Useful Lives	2022	2021
Leasehold improvements	up to 15 years	$ 83,334	$ 73,589
Computer equipment and software	up to 3 years	19,569	14,877
Furniture and fixtures	7 years	24,054	15,780
Laboratory equipment	5 years	39,606	23,744
Construction in progress		4,933	16,872
Total property and equipment		171,496	144,862
Less: accumulated depreciation		(60,872)	(40,831)
Total property and equipment, net		$ 110,624	$ 104,031

Depreciation expense was $20.9 million, $13.6 million and $9.1 million during the years ended December 31, 2022, 2021 and 2020, 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,		
	2022	2021	2020
Research and development	$ 45,350	$ 46,654	$ 37,198
Selling, general and administrative	62,224	73,166	67,872
Total stock-based compensation expense	$ 107,574	$ 119,820	$ 105,070

	Year Ended December 31,		
	2022	2021	2020
Stock options	$ 12,790	$ 19,048	$ 19,863
Restricted stock units	69,775	53,629	35,675
Performance stock units	21,616	43,428	47,106
ESPP	3,393	3,715	2,426
Total stock-based compensation expense	$ 107,574	$ 119,820	$ 105,070

We have several equity incentive plans under which we granted stock options and RSUs, including PSUs, to employees and directors. On May 25, 2022, at the 2022 Annual Meeting of Stockholders, our stockholders approved the amendment and restatement of Exelixis, Inc. 2017 Equity Incentive Plan (as amended and restated, the 2017 Plan). The amendment and restatement increased the share reserve under the 2017 Plan by 28,500,000 shares. As of December 31, 2022, 31,971,047 shares were available for grant under the 2017 Plan. The share reserve is reduced by 1 share for each share issued pursuant to a stock option and 2 shares for full value awards, including RSUs.

The Board of Directors delegated responsibility for administration of our equity incentive plans to the Compensation Committee of our Board of Directors, 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. RSUs granted to our employees and directors generally have a four-year vesting term and a one-year vesting term, respectively. PSUs granted pursuant to our equity incentive plans vest upon specified service conditions and the achievement of a performance target or market condition.

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. As of December 31, 2022, we had 2,561,567 shares available for issuance under our ESPP. Pursuant to the ESPP, we issued 606,787, 536,226 and 534,419 shares of common stock at an average price per share of $16.63, $17.76 and $14.55 during the years ended December 31, 2022, 2021 and 2020, respectively. Cash received from purchases under the ESPP for the years ended December 31, 2022, 2021 and 2020 was $10.1 million, $9.5 million and $7.8 million, respectively.

We used a Black-Scholes Merton option pricing model to value 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,		
	2022	2021	2020
Stock options	$ 8.36	$ 9.04	$ 9.44
ESPP	$ 5.80	$ 6.12	$ 6.12

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

	Year Ended December 31,		
	2022	2021	2020
Stock options:			
Risk-free interest rate	2.35 %	0.74 %	0.30 %
Dividend yield	— %	— %	— %
Volatility	48 %	51 %	54 %
Expected life	4.6 years	4.6 years	4.4 years
ESPP:			
Risk-free interest rate	1.49 %	0.08 %	0.79 %
Dividend yield	— %	— %	— %
Volatility	45 %	47 %	52 %
Expected life	6 months	6 months	6 months

We considered both implied and historical volatility 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 PSUs, was based on the closing price of the underlying common stock on the date of grant.

Activity for stock options during the year ended December 31, 2022 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, 2021	13,671	$ 16.79		
Granted	589	$ 19.99		
Exercised	(2,743)	$ 5.74		
Cancelled	(635)	$ 21.29		
Stock options outstanding at December 31, 2022	10,882	$ 19.49	3.0 years	$ 9,377
Stock options exercisable at December 31, 2022	8,743	$ 19.17	2.4 years	$ 9,373

As of December 31, 2022, there was $16.6 million of unrecognized compensation expense related to our unvested stock options. The compensation expense for the unvested stock options will be recognized over a weighted-average period of 2.2 years.

The aggregate intrinsic value in the table above represents the total intrinsic value (the difference between our closing stock price on the last trading day of fiscal year 2022 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, 2022. The total intrinsic value of stock options exercised during the years ended December 31, 2022, 2021 and 2020 was $36.5 million, $76.0 million and $106.5 million, respectively. Cash received from stock option exercises during the years ended December 31, 2022, 2021 and 2020 was $13.9 million, $14.8 million and $26.9 million, respectively.

Activity for RSUs during the year ended December 31, 2022 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, 2021	6,828	$ 21.58		
Awarded	7,933	$ 21.84		
Vested and released	(2,164)	$ 21.31		
Forfeited	(1,303)	$ 21.43		
RSUs outstanding at December 31, 2022	11,294	$ 21.83	1.8 years	$ 181,156

As of December 31, 2022, there was $183.6 million of unrecognized compensation expense related to our unvested RSUs which will be recognized over a weighted-average period of 2.9 years.

Activity for PSUs, during the year ended December 31, 2022 was as follows (in thousands**,** except per share amounts):

	Shares	Weighted Average Grant Date Fair Value	Weighted Average Remaining Contractual Term	Aggregate Intrinsic Value
PSUs outstanding at December 31, 2021	6,310	$ 23.00		
Awarded	—	$ —		
Vested and released	(942)	$ 21.32		
Forfeited	(404)	$ 24.56		
PSUs outstanding at December 31, 2022	4,964	$ 23.26	2.3 years	$ 79,628

In March 2022, in connection with our long-term incentive compensation program, we awarded to certain employees an aggregate of 1,003,482 (the 2022 target amount) RSUs that are subject to a total shareholder return (TSR) market condition (the 2022 TSR-based RSUs). The TSR market condition for the 2022 TSR-based RSUs is based on our relative TSR percentile rank compared to companies in the NASDAQ Biotechnology Index during the performance period, which is January 1, 2022 through January 3, 2025. Depending on the results relative to the TSR market condition, the holders of the 2022 TSR-based RSUs may earn up to 175% of the 2022 target amount of shares. 50% of the shares earned pursuant to the 2022 TSR-based RSU awards will vest at the end of the performance period, and the remainder will vest approximately one year later, subject to employee's continuous service. These TSR-based RSUs will be forfeited if the market condition at or above a threshold level is not achieved at the end of the performance period on January 3, 2025.

We used a Monte Carlo simulation model and the following assumptions to determine the grant date fair value of $33.17 per share for the 2022 TSR-based RSUs:

Fair value of Exelixis common stock on grant date	$	20.70
Expected volatility		46.85 %
Risk-free interest rate		1.59 %
Dividend yield		— %

The Monte Carlo simulation model also assumed correlations of returns of the stock prices of Exelixis common stock and the common stock of a peer group of companies and historical stock price volatility of the peer group of companies. The valuation model also used terms based on the length of the performance period and compound annual growth rate goals for total stockholder return based on the provisions of the award.

In March 2021, in connection with our long-term incentive compensation program, we awarded certain employees 1,027,650 (the 2021 target amount) PSUs, subject to a performance and a market condition (the 2021 PSUs). Pursuant to the terms of 2021 PSUs, the holders of the awards may earn up to 200% of the 2021 target amount, or up to 2,055,300 total shares, depending on the level of achievement of the performance condition related to certain net product revenues and a TSR market condition. The TSR market condition for the 2021 PSUs is based on our relative TSR percentile rank compared to companies in the Nasdaq Biotechnology Index during the performance period, which is January 2, 2021 through December 29, 2023. 50% percent of the shares earned subject to the performance and market conditions will vest at the end of the performance period and the remainder will vest approximately one year later subject to an employee's continuous service. The 2021 PSUs will be forfeited if the performance condition at or above a threshold level is not achieved by December 29, 2023. The performance condition for target achievement of net product revenues relative to the 2021 PSUs was deemed probable of achievement in the fourth quarter of 2022 representing 100% of the 2021 PSUs target amount.

A Monte Carlo simulation model was used to determine the grant date fair value of $24.54 for the 2021 PSUs based on the following assumptions:

Fair value of Exelixis common stock on grant date	$	21.31
Expected volatility		49.21 %
Risk-free interest rate		0.29 %
Dividend yield		— %

During the year ended December 31, 2020, in connection with our long-term incentive compensation program, we awarded 2,327,840 PSUs (the 2020 target amount) that will vest upon the achievement of performance targets related to (i) clinical trial positive top-line results and (ii) product approvals by the FDA (the 2020 PSUs). Pursuant to the terms of the 2020 PSUs, employees may earn up to 200% of the 2020 target amount, or 4,655,680 total shares, depending on the volume and timing of achievement of the performance targets. The 2020 PSUs will be forfeited if the performance targets are not met by December 31, 2024. The performance condition for threshold achievement of a product approval by the FDA relative to the 2020 PSUs occurred in the third quarter of 2021, representing 25% of the 2020 target amount. The performance condition for threshold achievement of positive top-line results by the FDA relative to the 2020 PSUs occurred in the third quarter of 2022, representing 25% of the 2020 target amount.

Expense recognition for PSUs commences when it is determined that attainment of the performance target is probable. Of the outstanding PSUs as of December 31, 2022, 869,502 relate to awards for which we achieved the performance target. As of December 31, 2022, the remaining unrecognized compensation expense for the PSUs achieved or deemed probable of achievement related to the PSUs was $11.0 million, which will be recognized over a weighted-average period of 2.3 years. The total unrecognized compensation expense for the PSUs for which we have not yet determined that attainment of the performance target is probable was $79.5 million as of December 31, 2022.

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

We sponsor the 401(k) Plan under which we make matching cash contributions to our employees' 401(k) accounts. We recorded compensation expense of $11.7 million, $9.5 million and $6.7 million for the years ended December 31, 2022, 2021 and 2020, respectively, for matching contributions.

NOTE 9. PROVISION FOR INCOME TAXES

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

	Year Ended December 31,		
	2022	2021	2020
Current:			
Federal	$ 100,525	$ 11,338	$ —
State	11,903	5,224	3,791
Total current tax expense	$ 112,428	$ 16,562	$ 3,791
Deferred:			
Federal	$ (54,223)	$ 46,416	$ 14,886
State	(6,135)	113	379
Total deferred tax expense	(60,358)	46,529	15,265
Provision for income taxes	$ 52,070	$ 63,091	$ 19,056

The provision for income taxes for the years ended December 31, 2022, 2021, and 2020 primarily relates to the utilization of federal tax attributes and state taxes in jurisdictions outside of California, for which we do not have net operating loss carryforwards due to a limited operating history. Our historical net operating losses were sufficient to fully offset any federal taxable income for the year ended December 31, 2020 but were not sufficient to fully offset federal taxable income for the years ended December 31, 2022 and 2021.

The reconciliation of the U.S. federal income tax provision at the statutory federal income tax rate of 21% for each of the years ended December 31, 2022, 2021 and 2020, respectively, to our provision for income taxes was as follows (in thousands):

	Year Ended December 31,		
	2022	2021	2020
U.S. federal income tax provision at statutory rate	$ 49,213	$ 61,772	$ 27,476
State tax (benefit) expense	(2,632)	1,336	(2,232)
Change in valuation allowance	7,162	2,883	5,525
Research credits	(14,130)	(6,263)	(11,356)
Stock-based compensation	(2,864)	(11,831)	(20,399)
Non-deductible executive compensation	4,549	11,182	18,067
Branded prescription drug fee	3,855	2,897	2,537
Non-deductible warrant purchase	6,300	—	—
Other	617	1,115	(562)
Provision for income taxes	$ 52,070	$ 63,091	$ 19,056

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,	
	2022	2021
Deferred tax assets:		
Net operating loss carryforwards	$ 33,635	$ 17,993
Tax credit carryforwards	40,217	101,460
Depreciation and amortization	176,208	7,764
Stock-based compensation	27,531	23,162
Lease liabilities	46,759	12,385
Accruals and reserves not currently deductible	22,418	19,531
Deferred revenue	7,656	8,040
Other assets	6,746	1,303
Total deferred tax assets	361,170	191,638
Valuation allowance	(77,230)	(70,068)
Net deferred tax assets	283,940	121,570
Deferred tax liabilities:		
Lease right-of-use assets	(52,830)	(9,907)
Net deferred taxes	$ 231,110	$ 111,663

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, 2022, 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, 2022 and forecasts of future operating results, as well as considering the utilization of net operating losses and tax credits prior to their expiration, management has continued to determine 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, 2022 and 2021, we continue to carry a valuation allowance of $77.2 million and $70.1 million, respectively, against our California state deferred tax assets. The valuation allowance increased by $7.2 million and $2.9 million during the years ended December 31, 2022 and 2021, respectively.

At December 31, 2022, we had state net operating loss carryforwards of approximately $414 million, which expire in the years 2023 through 2036, California research and development tax credits of approximately $52 million, which do not expire, and California Competes Tax Credits of approximately $1 million, which begin to expire in 2028.

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, 2022, 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,		
	2022	2021	2020
Beginning balance	$ 83,583	$ 80,941	$ 79,078
Change relating to prior year provision	715	728	591
Change relating to current year provision	4,129	2,215	3,305
Reductions based on the lapse of the applicable statutes of limitations	(721)	(301)	(2,033)
Ending balance	$ 87,706	$ 83,583	$ 80,941

We classify unrecognized tax benefits as a reduction of deferred tax assets or as other long-term liabilities in the accompanying consolidated balance sheets. We do not anticipate that the amount of unrecognized tax benefits existing as of December 31, 2022 will significantly change over the next 12 months. As of December 31, 2022, we had $87.7 million in unrecognized tax benefits, of which $55.4 million would reduce our income tax provision and 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 2001 through 2022 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,		
	2022	2021	2020
Numerator:			
Net income	$ 182,282	$ 231,063	$ 111,781
Denominator:			
Weighted-average common shares outstanding - basic	321,526	314,884	308,271
Dilutive securities	3,030	7,475	9,730
Weighted-average common shares outstanding - diluted	324,556	322,359	318,001
Net income per share - basic	$ 0.57	$ 0.73	$ 0.36
Net income per share - diluted	$ 0.56	$ 0.72	$ 0.35

Dilutive securities included outstanding stock options, unvested RSUs, unvested RSUs with market conditions, PSUs 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 were related to shares from PSUs that were contingently issuable and the contingency had not been satisfied at the end of the reporting period. See “Note 8. Employee Benefit Plans” for a further description of our equity awards. The weighted-average potential common shares excluded from our calculation were as follows (in thousands):

	Year Ended December 31,		
	2022	2021	2020
Anti-dilutive securities and contingently issuable shares excluded	17,063	14,305	10,959

NOTE 11. COMMITMENTS AND CONTINGENCIES

Leases

We have noncancellable operating leases of corporate headquarters, office and laboratory space in California and Pennsylvania totaling 673,978 square feet with lease terms ending in 2024 through 2037. Certain of our leases include options to renew the lease or to early terminate the lease. As of December 31, 2022, it is not probable we will exercise our options to renew these leases, nor is it probable that we will not exercise our option to terminate certain of our leases before the end of the lease term.

As of December 31, 2022, we have lease agreements for laboratory spaces located in Pennsylvania totaling 28,228 square feet for which the leases of the premises have not commenced. We expect these leases to commence upon substantial completion of leasehold improvements by the lessor and upon receiving access to those premises.

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

	December 31,	
	2022	2021
Assets:		
Right-of-use assets included in other long-term assets	$ 234,811	$ 45,122
Liabilities:		
Current portion included in other current liabilities	$ 17,659	$ 5,137
Long-term portion of operating lease liabilities	190,170	51,272
Total operating lease liabilities	$ 207,829	$ 56,409

The components of operating lease costs were as follows (in thousands):

	Year Ended December 31,		
	2022	2021	2019
Operating lease cost	$ 18,315	$ 5,332	$ 4,825
Variable lease cost	3,098	2,685	2,830
Total operating lease costs	$ 21,413	$ 8,017	$ 7,655

Cash paid for amounts included in the measurement of lease liabilities for the years ended December 31, 2022, 2021 and 2020 was $11.4 million, $5.0 million and $4.6 million, respectively, and was included in net cash provided by operating activities in our Consolidated Statements of Cash Flows.

As of December 31, 2022, the maturities of our operating lease liabilities were as follows (in thousands):

Year Ended December 31,	Amount
2023	$ 18,057
2024	23,682
2025	23,111
2026	23,608
2027	24,313
Thereafter	206,605
Total lease payments	319,376
Less:	
Imputed interest	(88,310)
Future tenant improvement reimbursements	(23,237)
Operating lease liabilities	$ 207,829

As of December 31, 2022, the weighted average discount rate used to determine the operating lease liability was 5.3% and the weighted average remaining lease term was 12.7 years.

Lease cost for leases with initial terms less than 1 year for the year ended December 31, 2022 was $0.4 million, and immaterial for the years ended December 31, 2021 and 2020.

Legal Proceedings

MSN I ANDA Litigation

In September 2019, we received a notice letter regarding an Abbreviated New Drug Application (ANDA) submitted to the FDA by MSN Pharmaceuticals, Inc. (individually and collectively with certain of its affiliates, including MSN Laboratories Private Limited, referred to as MSN), requesting approval to market a generic version of CABOMETYX tablets. MSN's initial notice letter included a Paragraph IV certification with respect to our U.S. Patents No. 8,877,776 (salt and polymorphic forms), 9,724,342 (formulations), 10,034,873 (methods of treatment) and 10,039,757 (methods of treatment), which are listed in the Approved Drug Products with Therapeutic Equivalence Evaluations, also referred to as the Orange Book, for CABOMETYX. MSN's initial notice letter did not provide a Paragraph IV certification against U.S. Patents No. 7,579,473 (composition of matter) or 8,497,284 (methods of treatment), each of which is listed in the Orange Book. On October 29, 2019, we filed a complaint in the United States District Court for the District of Delaware (the Delaware District Court) for patent infringement against MSN asserting infringement of U.S. Patent No. 8,877,776 arising from MSN's ANDA filing with the FDA. On November 20, 2019, MSN filed its response to the complaint, alleging that the asserted claims of U.S. Patent No. 8,877,776 are invalid and not infringed. On May 5, 2020, we received notice from MSN that it had amended its ANDA to include additional Paragraph IV certifications. In particular, the May 5, 2020 amended ANDA requested approval to market a generic version of CABOMETYX tablets prior to expiration of two previously unasserted CABOMETYX patents: U.S. Patents No. 7,579,473 and 8,497,284. On May 11, 2020, we filed a complaint in the Delaware District Court for patent infringement against MSN asserting infringement of U.S. Patents No. 7,579,473 and 8,497,284 arising from MSN's amended ANDA filing with the FDA. Neither of our complaints have alleged infringement of U.S. Patents No. 9,724,342, 10,034,873 and 10,039,757. On May 22, 2020, MSN filed its response to the complaint, alleging that the asserted claims of U.S. Patents No. 7,579,473 and 8,497,284 are invalid and not infringed. On March 23, 2021, MSN filed its First Amended Answer and Counterclaims (amending its prior filing from May 22, 2020), seeking, among other things, a declaratory judgment that U.S. Patent No. 9,809,549 (salt and polymorphic forms) is invalid and would not be infringed by MSN if its generic version of CABOMETYX tablets were approved by the FDA. U.S. Patent No. 9,809,549 is not listed in the Orange Book. On April 7, 2021, we filed our response to MSN's First Amended Answer and Counterclaims, denying, among other things, that U.S. Patent No. 9,809,549 is invalid or would not be infringed. The two lawsuits comprising this litigation (collectively referred to as MSN I), numbered Civil Action Nos. 19-02017 and 20-00633, were consolidated in April 2021.
On October 1, 2021, pursuant to a stipulation between us and MSN, the Delaware District Court entered an order that (i) MSN's submission of its ANDA constitutes infringement of certain claims relating to U.S. Patents No. 7,579,473 and 8,497,284, if those claims are not found to be invalid, and (ii) upon approval, MSN's commercial manufacture, use, sale or offer for sale within the U.S., and importation into the U.S., of MSN's ANDA product prior to the expiration of U.S. Patents No. 7,579,473 and 8,497,284 would also infringe certain claims of each patent, if those claims are not found to be invalid. Then, on October 12, 2021, pursuant to a separate stipulation between us and MSN, the Delaware District Court entered an order dismissing MSN's counterclaims with respect to U.S. Patent No. 9,809,549. In our MSN I complaints, we sought, among other relief, an order that the effective date of any FDA approval of MSN's ANDA be a date no earlier than the expiration of all of U.S. Patents No. 7,579,473, 8,497,284 and 8,877,776, the latest of which expires on October 8, 2030, and equitable relief enjoining MSN from infringing these patents. In an effort to streamline the case, the parties narrowed their assertions. On April 8, 2022, MSN withdrew its validity challenge to U.S. Patent No. 8,877,776. On April 14, 2022, we agreed not to assert U.S. Patent No. 8,497,284 at trial and MSN, correspondingly, agreed to withdraw its validity challenges to U.S. Patent No. 8,497,284, as well as claims 1-4 and 6-7 of U.S. Patent No. 7,579,473. As a result of this narrowing, the trial addressed two issues: (1) infringement of claim 1 of the U.S. Patent No. 8,877,776; and (2) validity of claim 5 of the U.S. Patent No. 7,579,473. A bench trial for MSN I occurred in May 2022, and on January 19, 2023, the Delaware District Court issued a ruling rejecting MSN's invalidity challenge to U.S. Patent No. 7,759,473. The Delaware District Court also ruled that MSN's proposed ANDA product does not infringe U.S. Patent No. 8,877,776 and entered judgment that the effective date of any final FDA approval of MSN's ANDA shall not be a date earlier than August 14, 2026, the expiration date of U.S. Patent No. 7,759,473. This ruling in MSN I does not impact our separate and ongoing MSN II lawsuit.

MSN II ANDA Litigation

On January 11, 2022, we received notice from MSN that it had further amended its ANDA to assert additional Paragraph IV certifications. In particular, the January 11, 2022 amended ANDA requested approval to market a generic

version of CABOMETYX tablets prior to expiration of three previously-unasserted CABOMETYX patents that are now listed in the Orange Book: U.S. Patents No. 11,091,439 (crystalline salt forms), 11,091,440 (pharmaceutical composition) and 11,098,015 (methods of treatment). On February 23, 2022, we filed a complaint in the Delaware District Court for patent infringement against MSN asserting infringement of U.S. Patents No. 11,091,439, 11,091,440 and 11,098,015 arising from MSN's further amendment of its ANDA filing with the FDA. On February 25, 2022, MSN filed its response to the complaint, alleging that the asserted claims of U.S. Patents No. 11,091,439, 11,091,440 and 11,098,015 are invalid and not infringed. On June 7, 2022, we received notice from MSN that it had further amended its ANDA to assert an additional Paragraph IV certification. As currently amended, MSN's ANDA now requests approval to market a generic version of CABOMETYX tablets prior to expiration of a previously-unasserted CABOMETYX patent that is now listed in the Orange Book: U.S. Patent No. 11,298,349 (pharmaceutical composition). On July 18, 2022, we filed a complaint in the Delaware District Court for patent infringement against MSN asserting infringement of U.S. Patent No. 11,298,349 arising from MSN's further amendment of its ANDA filing with the FDA. On August 9, 2022, MSN filed its response to the complaint, alleging that the asserted claims of U.S. Patent No. 11,298,349 are invalid and not infringed and amended its challenges to U.S. Patents No. 11,091,439, 11,091,440 and 11,098,015 to allege that these patents are not enforceable based on equitable grounds. The two lawsuits comprising this litigation (collectively referred to as MSN II), numbered Civil Action Nos. 22-00228 and 22-00945, were consolidated in October 2022 and involve Exelixis patents that are different from those asserted in the MSN I litigation described above.

On June 21, 2022, pursuant to a stipulation between us and MSN, the Delaware District Court entered an order that (i) MSN's submission of its ANDA constitutes infringement of certain claims relating to U.S. Patents No. 11,091,439, 11,091,440 and 11,098,015, if those claims are not found to be invalid, and (ii) upon approval, MSN's commercial manufacture, use, sale or offer for sale within the U.S., and importation into the U.S., of MSN's ANDA product prior to the expiration of U.S. Patents No. 11,091,439, 11,091,440 and 11,098,015 would also infringe certain claims of each patent, if those claims are not found to be invalid. In our MSN II complaints, we are seeking, among other remedies, equitable relief enjoining MSN from infringing the asserted patents, as well as an order that the effective date of any FDA approval of MSN's ANDA would be a date no earlier than the expiration of all of U.S. Patents No. 11,091,439, 11,091,440, 11,098,015 and 11,298,349, the latest of which expires on February 10, 2032. A bench trial for MSN II has been scheduled for October 2023.

Teva ANDA Litigation

In May 2021, we received notice letters from Teva Pharmaceutical Industries Limited, Teva Pharmaceuticals Development, Inc. and Teva Pharmaceuticals USA, Inc. (individually and collectively referred to as Teva) regarding an ANDA Teva submitted to the FDA, requesting approval to market a generic version of CABOMETYX tablets. Teva's notice letters included a Paragraph IV certification with respect to our U.S. Patents No. 9,724,342 (formulations), 10,034,873 (methods of treatment) and 10,039,757 (methods of treatment), which are listed in the Orange Book. Teva's notice letters did not provide a Paragraph IV certification against any additional CABOMETYX patents. On June 17, 2021, we filed a complaint in the Delaware District Court for patent infringement against Teva asserting infringement of U.S. Patents No. 9,724,342, 10,034,873 and 10,039,757 arising from Teva's ANDA filing with the FDA. On August 27, 2021, Teva filed its answer and counterclaims to the complaint, alleging that the asserted claims of U.S. Patents No. 9,724,342, 10,034,873 and 10,039,757 are invalid and not infringed. On September 17, 2021, we filed an answer to Teva's counterclaims. On July 29, 2022, we received notice from Teva that it had amended its ANDA to assert an additional Paragraph IV certification. As amended, Teva's ANDA now requests approval to market a generic version of CABOMETYX tablets prior to expiration of a previously-unasserted CABOMETYX patent that is now listed in the Orange Book: U.S. Patent No. 11,298,349 (pharmaceutical composition). On September 2, 2022, we filed a complaint in the Delaware District Court for patent infringement against Teva, asserting infringement of U.S. Patent No. 11,298,349 arising from Teva's amended ANDA filing with the FDA. We are seeking, among other relief, an order that the effective date of any FDA approval of Teva's ANDA be a date no earlier than the expiration of all of U.S. Patents No. 9,724,342, 10,034,873, 10,039,757 and 11,298,349, the latest of which expires on July 9, 2033, and equitable relief enjoining Teva from infringing these patents. On September 30, 2022, the parties filed a stipulation to consolidate the two lawsuits, numbered Civil Action Nos. 21-00871 and 22-01168, and to stay all proceedings, which was granted by the Delaware District Court on October 3, 2022. Following a similar order granted by the Delaware District Court on February 9, 2022 to stay all proceedings with respect to Civil Action No. 21-00871, this case remained administratively closed, and Civil Action No. 22-01168 was administratively closed on October 3, 2022.

Other

On February 6, 2023, we received a notice letter regarding an ANDA submitted to the FDA by Cipla Limited (Cipla), including a Paragraph IV certification with respect to our U.S. Patents No. 8,877,776 (salt and polymorphic forms),

9,724,342 (formulations), 10,039,757 (methods of treatment), 11,098,015 (methods of treatment), 11,091,439 (crystalline salt forms), 11,091,440 (pharmaceutical composition) and 11,298,349 (pharmaceutical composition). Cipla's ANDA requests approval to market a generic version of CABOMETYX tablets prior to the expiration of the aforementioned patents. We have not yet responded to this Paragraph IV certification notice letter but are evaluating it.

The sale of any generic version of CABOMETYX earlier than its patent expiration could significantly decrease our revenues derived from the U.S. sales of CABOMETYX and thereby materially harm our business, financial condition and results of operations. It is not possible at this time to determine the likelihood of an unfavorable outcome or estimate of the amount or range of any potential loss.

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 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 2022 fiscal year, management conducted an assessment of the effectiveness of our internal control over financial reporting based on the framework established in the original *Internal Control – Integrated Framework* issued by the Committee of Sponsoring Organizations of the Treadway Commission (2013 framework) (COSO). Based on this assessment, management has determined that our internal control over financial reporting as of December 31, 2022 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 December 30, 2022, based on criteria established in Internal Control-Integrated Framework issued by the Committee of Sponsoring Organizations of the Treadway Commission (2013 framework) (the COSO criteria). In our opinion, Exelixis, Inc. (the Company) maintained, in all material respects, effective internal control over financial reporting as of December 30, 2022, based on the COSO criteria.

We also have audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States) (PCAOB), the consolidated balance sheets of the Company as of December 30, 2022 and December 31, 2021, the related consolidated statements of income, comprehensive income, stockholders' equity and cash flows for each of the three fiscal years in the period ended December 30, 2022, and the related notes and our report dated February 7, 2023 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

San Mateo, California
February 7, 2023

Item 9B. Other Information

Not applicable.

Item 9C. Disclosure Regarding Foreign Jurisdictions that Prevent Inspections

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 2023 Annual Meeting of Stockholders to be filed with the SEC within 120 days after December 30, 2022, which we refer to as our 2023 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 2023 Proxy Statement. The information, if any, 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 "Delinquent Section 16(a) Reports" appearing in our 2023 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 and information."

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 2023 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 2023 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, 2022, which consists of our 2000 Employee Stock Purchase Plan (the ESPP), 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]	27,000,905	$ 7.75 [2]	34,532,614
Equity compensation plans not approved by stockholders [3]	140,000	$ 19.86	—
Total	27,140,905	$ 7.81	34,532,614

(1) Equity plans approved by our shareholders include the 2014 Plan, the 2017 Plan and the ESPP. As of December 31, 2022, a total of 2,561,567 shares of our common stock remained available for issuance under the ESPP, and up to a maximum of 1,221,398 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 and the weighted-average exercise price of such rights as of December 31, 2022, as those numbers are not known.

(2) The weighted-average exercise price takes into account the shares subject to outstanding restricted stock units (RSUs), including such awards with performance conditions, which have no exercise price. The weighted-average exercise price, excluding such outstanding RSUs, is $19.48.

(3) Represents shares of our common stock issuable pursuant to the 2016 Plan. As of December 31, 2022, no shares of our common stock remained available for additional grants under the 2016 Plan. In November 2016, the Board of Directors 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 non-statutory stock options, stock appreciation rights, RSUs, or any other stock award.

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 2023 Proxy Statement.

Item 14. Principal Accountant 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 2023 Proxy Statement.

PART IV

Item 15. Exhibits and 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	Restated Certificate of Incorporation of Exelixis, Inc.	10-Q	000-30235	3.1	8/5/2021	
3.2	Amended and Restated Bylaws of Exelixis, Inc.	8-K	000-30235	3.1	3/3/2021	
4.1	Specimen Common Stock Certificate.	10-Q	000-30235	4.1	8/5/2021	
4.2	Description of the Common Stock of Exelixis, Inc. Registered Pursuant to Section 12 of the Securities Exchange Act of 1934, as amended	10-K	000-30235	4.2	2/18/2022	
10.1†	Form of Indemnification Agreement	10-K	000-30235	10.1	2/18/2022	
10.2†	Exelixis, Inc. 2000 Employee Stock Purchase Plan	Schedule 14A	000-30235	A	4/13/2016	
10.3†	Exelixis, Inc. 2014 Equity Incentive Plan	10-Q	000-30235	10.1	8/6/2020	
10.4†	Form of Stock Option Agreement under the Exelixis, Inc. 2014 Equity Incentive Plan	10-Q	000-30235	10.2	7/31/2014	
10.5†	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	
10.6†	Form of Restricted Stock Unit Agreement under the Exelixis, Inc. 2014 Equity Incentive Plan	10-Q	000-30235	10.5	7/31/2014	
10.7†	Exelixis, Inc. 2016 Inducement Award Plan	10-Q	000-30235	10.2	8/6/2020	
10.8†	Form of Stock Option Agreement under the 2016 Inducement Award Plan	8-K	000-30235	10.2	11/22/2016	
10.9†	Form of Restricted Stock Unit Agreement under the 2016 Inducement Award Plan	8-K	000-30235	10.2	11/22/2016	

Exhibit Number	Exhibit Description	Incorporation by Reference				Filed Herewith
		Form	File Number	Exhibit/ Appendix Reference	Filing Date	
10.10†	Exelixis, Inc. 2017 Equity Incentive Plan	10-Q	000-30235	10.1	8/9/2022	
10.11†	Form of Stock Option Agreement under the Exelixis, Inc. 2017 Equity Incentive Plan	10-K	000-30235	10.11	2/11/2021	
10.12†	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	
10.13†	Form of Restricted Stock Unit Agreement under the Exelixis, Inc. 2017 Equity Incentive Plan	10-Q	000-30235	10.5	8/6/2020	
10.14†	Form of Restricted Stock Unit Agreement (Non-Employee Director) under the Exelixis, Inc. 2017 Equity Incentive Plan	10-Q	000-30235	10.6	8/6/2020	
10.15†	Non-Employee Director Equity Compensation Policy	10-Q	000-30235	10.4	5/5/2020	
10.16†	Offer Letter Agreement, dated February 3, 2000, between Exelixis, Inc. and Michael Morrissey, Ph.D.	10-Q	000-30235	10.43	8/5/2004	
10.17†	Offer Letter Agreement, dated June 30, 2015, between Exelixis, Inc. and Christopher Senner	10-Q	000-30235	10.5	11/10/2015	
10.18†	Offer Letter Agreement, dated December 2, 2021, between Exelixis, Inc. and Vicki L. Goodman, M.D.	10-K	000-30235	10.18	2/18/2022	
10.19†	Offer Letter Agreement, dated February 10, 2014, between Exelixis, Inc. and Jeffrey J. Hessekiel.	10-Q	000-30235	10.4	5/1/2014	
10.20†	Terms of Employment Offer, dated December 15, 2022, for Dana T. Aftab, Ph.D.					X
10.21†	Offer Letter Agreement, dated August 19, 2010, between Exelixis, Inc. and Patrick J. Haley	10-K	000-30235	10.26	2/27/2017	
10.22†	Annual Cash Bonus Compensation Plan for Executives	8-K	000-30235	10.1	2/16/2018	
10.23†	Cash Compensation Information for Non-Employee Directors.	10-Q	000-30235	10.1	11/1/2022	
10.24†	Exelixis, Inc. Change in Control and Severance Benefit Plan, as amended and restated.	10-Q	000-30235	10.5	5/2/2018	
10.25†	Policy for Recoupment of Variable Compensation	10-Q	000-30235	10.4	5/1/2019	
10.26	Lease Agreement dated May 2, 2017, between Ascentris 105, LLC and Exelixis, Inc.	10-Q	000-30235	10.1	8/2/2017	
10.27	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	
10.28	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	

Exhibit Number	Exhibit Description	Incorporation by Reference				Filed Herewith
		Form	File Number	Exhibit/ Appendix Reference	Filing Date	
10.29	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	
10.30	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	
10.31	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.	10-K	000-30235	10.37	2/25/2020	
10.32	Sixth Amendment dated December 11, 2020, to Lease Agreement dated May 2, 2017, between SCG Harbor Bay Parkway Phase I, LLC (as successor in interest to Waterfront EDP, LLC) and Exelixis, Inc.	10-K	000-30235	10.32	2/10/2021	
10.33	Seventh Amendment dated May 16, 2022, to Lease Agreement dated May 2, 2017, between SCG Harbor Bay Parkway Phase I, LLC and Exelixis, Inc.	10-Q	000-30235	10.3	8/9/2022	
10.34	Lease Agreement dated October 25, 2019, between Ernst Development Partners, Inc. and Exelixis, Inc.	10-Q	000-30235	10.2	10/30/2019	
10.35	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.	10-K	000-30235	10.39	2/25/2020	
10.36**	Collaboration and License Agreement dated February 29, 2016, by and between Exelixis, Inc. and Ipsen Pharma SAS	10-Q	000-30235	10.1	5/6/2021	
10.37**	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-Q	000-30235	10.2	5/6/2021	
10.38**	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	10.3	5/6/2021	
10.39**	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-Q	000-30235	10.4	5/6/2021	

Exhibit Number	Exhibit Description	Incorporation by Reference				Filed Herewith
		Form	File Number	Exhibit/ Appendix Reference	Filing Date	
10.40**	Fourth Amendment dated October 11, 2022, to the Collaboration and License Agreement dated February 29, 2016, by and between Exelixis, Inc. and Ipsen Pharma SAS					X
10.41**	Supply Agreement dated February 29, 2016, by and between Exelixis, Inc. and Ipsen Pharma SAS	10-Q	000-30235	10.5	5/6/2021	
10.42**	First Amendment dated October 26, 2017, to the Supply Agreement dated February 29, 2016, by and between Exelixis, Inc. and Ipsen Pharma SAS	10-Q	000-30235	10.6	5/6/2021	
10.43**	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	
10.44**	Third Amendment dated December 10, 2021, to the Supply Agreement dated February 29, 2016, by and between Exelixis, Inc. and Ipsen Pharma SAS	10-K	000-30235	10.42	2/18/2022	
10.45**	Collaboration and License Agreement dated January 30, 2017, by and between Exelixis, Inc. and Takeda Pharmaceutical Company Limited	10-Q	000-30235	10.1	5/10/2022	
10.46**	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	
10.47**	Second Amendment dated May 7, 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	10.2	5/10/2022	
10.48**	Third Amendment dated September 3, 2020, 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	11/5/2020	
10.49**	Joint Clinical Research Agreement dated December 18, 2019, by and between Exelixis, Inc. and F. Hoffmann-La Roche Ltd	10-K	000-30235	10.62	2/25/2020	
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

Exhibit Number	Exhibit Description	Incorporation by Reference				Filed Herewith
		Form	File Number	Exhibit/ Appendix Reference	Filing Date	
32.1‡	Certifications of Principal Executive Officer and Principal Financial Officer Pursuant to 18 U.S.C. Section 1350					X
101.INS	XBRL Instance Document	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 7, 2023
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 7, 2023
/s/ CHRISTOPHER J. SENNER **Christopher J. Senner**	Executive Vice President and Chief Financial Officer (Principal Financial and Accounting Officer)	February 7, 2023
/s/ STELIOS PAPADOPOULOS **Stelios Papadopoulos, Ph.D.**	Chairman of the Board	February 7, 2023
/s/ CARL B. FELDBAUM **Carl B. Feldbaum, Esq.**	Director	February 7, 2023
/s/ MARIA C. FREIRE **Maria C. Freire, Ph.D.**	Director	February 7, 2023

Signatures	Title	Date
/s/ ALAN M. GARBER **Alan M. Garber, M.D., Ph.D.**	Director	February 7, 2023
/s/ VINCENT T. MARCHESI **Vincent T. Marchesi, M.D., Ph.D.**	Director	February 7, 2023
/s/ GEORGE POSTE **George Poste, DVM, Ph.D., FRS**	Director	February 7, 2023
/s/ JULIE A. SMITH **Julie A. Smith**	Director	February 7, 2023
/s/ LANCE WILLSEY **Lance Willsey, M.D.**	Director	February 7, 2023
/s/ JACQUELINE WRIGHT **Jacqueline Wright**	Director	February 7, 2023
/s/ JACK L. WYSZOMIERSKI **Jack L. Wyszomierski**	Director	February 7, 2023

Exhibit 10.20

TERMS OF EMPLOYMENT – DANA T. AFTAB

(as of December 15, 2022)

TITLE: Executive Vice President, Discovery and Translational Research, and Chief Scientific Officer

ANNUAL BASE SALARY: $560,000.22 annually

BONUS TARGET: 50% of Annual Base salary

INITIAL RESTRICTED STOCK UNIT (RSU) AWARD: 100,000 shares of Exelixis, Inc. common stock pursuant to the Exelixis, Inc. 2017 Equity Incentive Plan. The vesting schedule for this RSU award is 1/4th on the first established RSU vesting date following the one year anniversary of the grant date (the "Initial RSU Vesting Date") and 1/4th of the original number of shares subject to the RSU award on each succeeding annual anniversary of the Initial RSU Vesting Date until fully-vested, provided that vesting ceases upon termination of "continuous service" with Exelixis, Inc., as such term is defined in the Exelixis, Inc. 2017 Equity Incentive Plan.

Exhibit 10.40

FOURTH AMENDMENT TO COLLABORATION AND LICENSE AGREEMENT

This **Fourth Amendment to the Collaboration and License Agreement** (the "**Fourth Amendment**") is entered into as of October 11, 2022 (the "**Fourth Amendment Effective Date**") by and between **Exelixis, Inc.**, a Delaware company having an address at 1851 Harbor Bay Parkway, Alameda, CA 94502, USA ("**Exelixis**") and **Ipsen Pharma SAS**, a French corporation having an address at 65 Quai Georges Gorse, 92100 Boulogne-Billancourt, France ("**Licensee**"). Exelixis and Licensee may be referred to herein individually as a "**Party**" or collectively as the "**Parties**."

Recitals

Whereas, Exelixis and Licensee are parties to that certain Collaboration and License Agreement dated February 29, 2016, as amended by First Amendment dated effective December 20, 2016, Second Amendment dated effective September 14, 2017, and Third Amendment dated effective October 26, 2017 (together, the "**License Agreement**"), under which the Parties have been collaborating on the development and commercialization of cabozantinib; and

Whereas, the Parties desire to enter into this Fourth Amendment to update certain definitions and payment terms related to the PV Costs under the License Agreement, all on the terms and conditions set forth below.

Now, Therefore, in consideration of the foregoing premises and the mutual covenants contained herein and other good and valuable consideration, the receipt and sufficiency of which are hereby acknowledged, the Parties agree as follows:

1. Definitions

1.1 All capitalized terms used herein but not defined shall have their respective meanings set forth in the License Agreement.

1.2 Section 5.5 of the License Agreement is hereby deleted in its entirety and replaced with the following:

5.5 Adverse Event Reporting; Pharmacovigilance Agreement. Within sixty (60) days after the Effective Date, but in any case prior to transfer of the marketing authorization, the Parties shall enter into a pharmacovigilance agreement setting forth the worldwide pharmacovigilance procedures for the Parties with respect to the Products, such as Safety Data sharing, adverse events reporting and safety signal and risk management (the "**Pharmacovigilance Agreement**"), which agreement shall be amended by the Parties [*] to comply with any changes in Applicable Laws or any guidance received from Regulatory Authorities. Such procedures shall be in accordance with, and enable the Parties to fulfill, local and national regulatory reporting obligations under Applicable Laws (including to the extent applicable, those obligations contained in ICH guidelines, E2A, E2B, E2C, E2D and E2F) to monitor the patients' safety. Exelixis has established and shall continue to hold at its costs and expenses the global safety database for the Products, and shall maintain such global safety database for so long as such Product is under Development and/or Commercialization by the Parties. The Parties will collaboratively agree on data cut points for periodic aggregate safety reports and

Exelixis will author such reports; the Parties will jointly review and approve such reports before submission to worldwide Regulatory Authorities as required.

(a) Parties' Respective Contributions to PV Costs.

(i) From the Effective Date through [*], Exelixis shall bear one hundred percent (100%) of the cost and expense for establishing and maintaining such global database and the preparation of periodic aggregate safety reports ("**PV Costs**").

(ii) For the [*] commencing on [*], Licensee shall pay Exelixis, as a contribution towards the PV Costs, an amount equal to [*] (the "**PV Contribution Fee**"), in the manner set forth in clauses (A) and (B) immediately below, which amount shall not be subject in any respect to audit or renegotiation.

(A) Within [*] of the Fourth Amendment Effective Date, Licensee shall pay Exelixis the previously invoiced and outstanding PV Costs for the Calendar Quarters ending [*], which aggregate amount shall equal [*].

(B) Licensee shall pay Exelixis an amount equal to [*] within [*] of receipt of the invoice for such amount.

(iii) For each Calendar Quarter commencing on [*] through the end of the Calendar Quarter in which the First LOE Event (as defined below) occurs, Licensee shall pay Exelixis an amount equal to [*] within [*] of the end of such quarter, which amount shall be invoiced and shall not be subject in any respect to audit or renegotiation. For purposes of this Fourth Amendment, LOE Event, U.S. LOE Event, EU LOE Event, First LOE Event and Second LOE Event shall be defined as follows:

(A) Loss of exclusivity ("**LOE**") occurs at the earliest of (i) the latest of expiration of the last-to-expire Valid Claim of the Exelixis Patents or Licensee Patents covering the Product in either the US or the EU, as applicable, [*] and (ii) the first time there is a Generic Entry with respect to such Product in either the US or any country of the Top 5 EU. For purposes of this definition, "Generic Entry" means, with respect to a particular Product, that one or more Generic Products to such Product [*].

(B) There are two separate LOE Events based on the following Territories: the U.S. ("**U.S. LOE Event**"), and the EU ("**EU LOE Event**").

(C) The earliest to occur of either the U.S. LOE Event or the EU LOE Event is the "**First LOE Event**." The

latest to occur of either the U.S. LOE Event or the EU LOE Event is the "**Second LOE Event**."

(iv) For each Calendar Quarter following the First LOE Event through the end of the Calendar Quarter in which the Second LOE Event occurs, Licensee shall pay Exelixis an amount equal to [*] within [*] of the end of such quarter, which amount shall be [*] at the end of [*] Calendar Quarters, which shall be invoiced and shall not be subject in any respect to audit or renegotiation. For the sake of clarity, by way of example, after the occurrence of the First LOE Event, Licensee pays Exelixis [*] for [*] Calendar Quarters, then [*] for [*] Calendar Quarters, and so on until the end of the Calendar Quarter in which the Second LOE Event occurs.

(v) Further, for the sake of clarity, Licensee shall have no obligation to pay Exelixis [*] under this Section 5.5(a) for any Calendar Quarter from, and after, the end of the Calendar Quarter in which the Second LOE Event occurs.

(b) Exelixis will ensure that each Party and any Future Exelixis Licensee are able to access the data, if necessary indirectly, from the global safety database in order to meet legal and regulatory obligations. The Parties agree that Exelixis shall not transfer the responsibility or holding of the global safety database to any CRO, sublicensee, Future Exelixis Licensee or any Third Party without Licensee's prior written consent and approval, which shall not be unreasonably withheld, conditioned or delayed if such transferee (and its Affiliates) is a pharmaceutical company of comparable size as Licensee and agrees to grant Licensee access and other rights to the global safety database substantially equivalent to those granted by Exelixis under the Pharmacovigilance Agreement. The use by Exelixis of a CRO, sublicensee, Future Exelixis Licensee shall be at Exelixis' sole cost and expenses.

(c) The JDC shall establish a joint safety subcommittee which shall have the role and responsibility of reviewing and maintaining up to date the Pharmacovigilance Agreement. As per the applicable Pharmacovigilance Agreement each Party shall be primarily responsible for reporting quality complaints, adverse events and Safety Data related to the Products to any Regulatory Authorities and responding to safety issues and to all requests of Regulatory Authorities related to the Products under any MAA or Regulatory Approval for the Product held by such Party and filed with such Regulatory Authorities, in each case at its own cost. Each Party agrees to comply with its respective obligations under the Pharmacovigilance Agreement and to cause its Affiliates, licensees and sublicensees to comply with such obligations.

1.3 Section 9.2(e) (PV Costs) of the License Agreement is hereby deleted in its entirety.

2. General Provisions

2.1 Effect of Amendment. Except as expressly modified herein, all terms and conditions set forth in the License Agreement, as in effect on the Fourth Amendment Effective Date, shall remain in full force and effect.

2.2 Entire Agreement. The License Agreement as modified by this Fourth Amendment is both a final expression of the Parties' agreement and a complete and exclusive statement with respect to its subject matter. This Fourth Amendment supersedes all prior and contemporaneous agreements and communications, whether written or oral, of the Parties regarding this subject matter.

2.3 Severability. If, for any reason, any part of this Fourth Amendment is adjudicated invalid, unenforceable, or illegal by a court of competent jurisdiction, such adjudication shall not, to the extent feasible, affect or impair, in whole or in part, the validity, enforceability, or legality of any remaining portions of this Fourth Amendment. All remaining portions shall remain in full force and effect as if the original Fourth Amendment had been executed without the invalidated, unenforceable, or illegal part.

2.4 Counterparts; Electronic or Facsimile Signatures. This Fourth Amendment may be executed in any number of counterparts, each of which shall be an original, but all of which together shall constitute one instrument. This Fourth Amendment may be executed and delivered electronically or by facsimile and upon such delivery such electronic or facsimile signature will be deemed to have the same effect as if the original signature had been delivered to the other Party.

In Witness Whereof, the Parties hereto have caused this Fourth Amendment to be executed and entered into by their duly authorized representatives as of the Fourth Amendment Effective Date.

EXELIXIS, INC.	IPSEN PHARMA S.A.S
By: /s/ Jeffrey J. Hessekiel	By: /s/ Francois Garnier
Name: Jeffrey J. Hessekiel	Name: Francois Garnier
Title: EVP & General Counsel	Title: EVP General 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 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. 333-266707, 333-241667, 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 7, 2023, 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 December 30, 2022.

/s/ Ernst & Young LLP

Redwood City, California

February 7, 2023

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 7, 2023

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 7, 2023

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 December 30, 2022, 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 7th day of February 2023.

/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)