Risk Factors Comparison 2024-02-06 to 2023-02-07 Form: 10-K

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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 **our other** new product candidates **, such as zanzalintinib** , is a lengthy, costly, complex and uncertain process that may **ultimately** fail ~~ultimately~~ to demonstrate **sufficiently differentiated** 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 **, such as zanzalintinib** , 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 **drug discovery,** 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 **and other** laws could have a material adverse impact on our business, financial condition and results of operations. • Data breaches ~~, cyber attacks~~ and other ~~failures in~~ **cybersecurity incidents impacting** 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 **successfully. • Our goals** and ~~expand~~ **disclosures related to environmental, social and governance matters subjects us to risks, including risks to** our ~~operations~~ **market perception and stock price** . BASIS OF PRESENTATION We have adopted a 52- or 53- week fiscal year policy that **generally** ends on the Friday closest to December 31st. Fiscal year ~~2022~~ **2021 ended December 31** , **2021;** ~~which was a 52- week~~ fiscal year ~~,~~ **2022** ended December 30, 2022 ~~,~~ **;** fiscal year ~~2021~~ **2023 ended December 29** , **2023; and** ~~which was a 52- week~~ fiscal year ~~,~~ **2024 will** ~~ended~~ -- **end** on ~~December 31, 2021 and fiscal year 2020, which was a 52- week fiscal year, ended~~ January ~~1~~ **3** , ~~2021~~ **2025** . For convenience, references in this report as of and for the fiscal years ended December 30, 2022, and ~~January 1~~ **December 29** , ~~2021~~ **2023** are indicated as being as of and for the years ended December 31, 2022 and ~~2020~~ **2023** , respectively **. In fiscal year 2024, the annual period and quarterly period ending January 3, 2025 are a 53- week fiscal year and a 14- week fiscal quarter, respectively; all other annual periods presented are 52- week fiscal years** . 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~~ **two of which are formulations of** 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 **and biotherapeutics** , **including** 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~~ **69** other countries **:** as ~~:~~ CABOMETYX ® (cabozantinib) tablets ~~approved~~ **for advanced renal cell carcinoma (RCC) (** both alone and in combination with Bristol- Myers Squibb Company' s (BMS) **nivolumab (** 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 **as** 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~~ **2023** was our ~~sixth~~ **seventh** year of annual profitability ~~, which~~ **; it** featured growth in net product revenues of approximately ~~30~~ **16** % year- over- year as a result of increased sales of our cabozantinib products in the U. S., supplemented by an approximately ~~16~~ **22** % year- over- year increase in royalties earned pursuant to collaboration agreements with our ex- U. S. partners. We plan to continue leveraging **our** ~~the resulting~~ operating cash flows to ~~support the ongoing investigation of cabozantinib in phase 3 trials for new indications and the advancement ---- advance 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~~ **as well as to support ongoing company- sponsored and externally sponsored trials evaluating cabozantinib. The product candidates** furthest along **in our pipeline** are **:** zanzalintinib ~~(formerly XL092)~~ , a **novel, potent,** next- generation oral tyrosine kinase inhibitor (TKI) ~~and XB002, an ADC~~ that targets **VEGF receptors, MET and the TAM kinases (TYRO3, AXL and MER); and XB002, a next- generation** tissue factor (TF) ~~. As we continue -~~ **targeting ADC, administered via intravenous infusion and composed of a human monoclonal antibody (mAb) against TF that is conjugated** to ~~bolster~~ **an auristatin- based microtubulin inhibitor (MTI) payload. Our internal drug discovery efforts are supplemented through in- licensing investigational oncology assets** ~~our -~~ **or obtaining** ~~pipeline, we pursue~~ options to acquire other investigational ~~drug candidates~~ **oncology assets** from third parties if **they** ~~those assets~~ demonstrate evidence of clinical success. ~~One example~~ **Examples are: XL309** ~~of this approach is CBX- 12 (alphalexTM exatecan)~~ , a clinical- stage ~~peptide~~ **and potentially best** - ~~drug conjugate (PDC) invented by Cybrexa Therapeutics (Cybrexa)~~ **in- class small molecule inhibitor of USP1, which has emerged as a synthetic lethal target in the context of BRCA- mutated tumors; and ADU- 1805, a clinical- stage and potentially best- in- class mAb** that **targets SIRPα** ~~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 **European Commission (** EC **)** for the European Union (EU) markets and the Japanese Ministry of Health, Labour and Welfare (MHLW) **for the Japanese market** , as well as by comparable regulatory authorities across other markets worldwide. ProductIndicationApproval DateRegimenMajor MarketsCABOMETYX ® (cabozantinib) Renal Cell Carcinoma (RCC) Patients with advanced RCC who have received prior anti- angiogenic therapyApril 25, 2016MonotherapyU. S. Advanced RCC in adults following prior VEGF- targeted therapySeptember 9, 2016MonotherapyEUPatients with advanced RCCDecember 19, 2017MonotherapyU. S. First- line treatment of adults with intermediate- or poor- risk advanced RCCMay 17, 2018MonotherapyEUPatients with curatively unresectable or metastatic RCCMarch 25, 2020MonotherapyJapanFirst- line treatment of patients with advanced RCCJanuary 22, 2021Combination with ~~OPDIVO ® (nivolumab~~ **nivolumabU** ~~) U~~ . S. First- line treatment for patients with advanced RCCMarch 31, 2021Combination with ~~OPDIVOEUPatients~~ **nivolumabEUPatients** with unresectable or metastatic RCCAugust 25, 2021Combination with ~~OPDIVOJapanHepatocellular~~ **nivolumabJapanHepatocellular** Carcinoma (HCC) HCC in adults who have previously been treated with sorafenibNovember 15, 2018MonotherapyEUPatients with HCC who have been previously treated with sorafenibJanuary 14, 2019MonotherapyU. S. Patients with unresectable HCC that has progressed after cancer chemotherapyNovember 27, 2020MonotherapyJapanDifferentiated 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 ineligibleSeptember 17, 2021MonotherapyU. S. Adult patients with locally advanced or metastatic DTC, refractory pr not eligible to RAI who have progressed during or after prior systemic therapyMay 3, 2022MonotherapyEUCOMETRIQ ® (cabozantinib) Medullary Thyroid Cancer (MTC) Patients with progressive, metastatic MTCNovember 29, 2012MonotherapyU. S. Adult patients with progressive, unresectable locally advanced or metastatic MTCMarch 25, 2014MonotherapyEU In **2023,** 2022 ~~,~~ **and** 2021 ~~and 2020~~ , we generated $ 1, **628. 9 million, $ 1,** 401. 2 million ~~,~~ **and** $ 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~~ **our cabozantinib products** ; 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 **2023,** 2022 ~~,~~ **and** 2021 ~~and 2020~~ , we earned $ **148. 5 million, $** 121. 4 million ~~,~~ **and** $ 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~~ **2023** , approximately 32, ~~200~~ **700** patients with advanced kidney cancer required systemic therapy in the U. S., with over ~~20~~ **21** , 000 patients receiving first- line treatment. Since CABOMETYX was first approved, we have deployed our ~~promotional and medical~~ **Medical** ~~affairs~~ **Affairs and Commercial** teams to educate physicians about

CABOMETYX. We believe that the **commercial** ~~product' s~~ success **of CABOMETYX** is attributable to the strength of the clinical data reflected in its FDA- approved labeling for advanced RCC. The **indications for the treatment of RCC in the** CABOMETYX label ~~incorporates~~ **are based on** 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~~ **To date** , **CABOMETYX remains the only single- agent therapy to have achieved these clinical results** in **previously treated advanced RCC. 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 **(the Alliance)** , 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 **CABOMETYX** ~~OPDIVO, an ICI developed by BMS,~~ in combination with ~~CABOMETYX~~ **nivolumab** versus sunitinib in patients with previously untreated, advanced or metastatic RCC. Results from CheckMate- 9ER demonstrated that the combination of CABOMETYX and ~~OPDIVO~~ **nivolumab** 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. **At four years of follow- up, the CheckMate- 9ER results continued to show superior PFS and ORR in patients treated with CABOMETYX in combination with nivolumab over sunitinib, regardless of risk classification (as determined by International Metastatic Renal Cell Carcinoma Database Consortium scores). Superior OS was also observed in patients treated with the combination.** ~~The~~ **These updated results, including data showing health- related quality- of- life benefits of the combination compared with sunitinib, were featured in an oral presentation at the American Society of Clinical Oncology (ASCO) 2024 Genitourinary Cancers Symposium in January 2024. In addition, 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~~ **nivolumab** in its Clinical Practice Guidelines for Kidney Cancer as a Category 1 **preferred** option for the first- line treatment of patients with clear cell RCC **across all risk groups, and as a Category 2A other recommended option for first- line non- clear cell RCC** . The NCCN also lists single- agent CABOMETYX as a **recommended** ~~category 1 preferred~~ regimen ~~in subsequent treatments~~ for patients with **previously treated advanced** ~~clear cell RCC, and as a preferred systemic therapy regimen for non-~~ clear cell RCC, supporting CABOMETYX' s position in the RCC treatment landscape **across lines of therapy** . In ~~2022~~ **2023** , 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~~ **nivolumab** , as well as in preparation for submission of applications for **potential additional** 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~~ **nivolumab** for RCC indications in ~~62~~ **69** countries outside of the U. S., including the Member States of the EU, Japan, the U. K., Canada, Brazil, Taiwan, South Korea ~~and~~ **,** Australia **and Hong Kong** , 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 **and 800, 000 deaths** each year. In the U. S., the incidence of liver cancer **has** ~~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~~ **600** cases of liver cancer estimated to be diagnosed in the U. S. during ~~2023~~ **2024** , 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~~ **However, during recent years, biopharmaceutical companies have developed** new and demonstrably more effective therapies **for previously untreated patients** , 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~~ **These** new treatment options **have** ~~are expected to improve~~ **improved** longer- term outcomes **for HCC patients** , thereby resulting in a greater number of ~~patients~~ **them** receiving multiple lines of therapy. **Thus, the second- and later- line market for HCC therapies appears to have grown and become increasingly competitive, and we believe this trend may continue over the coming years,** ~~With~~ **with monotherapy** ~~the approval of~~ CABOMETYX **maintaining an important place** in **the** ~~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 **the** ~~CABOMETYX' s~~ HCC indication **for CABOMETYX in January 2019** 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~~ **Hepatocellular Carcinoma** as a Category 1 option for the treatment of patients with HCC (Child- Pugh Class A only) ~~who have been previously treated with sorafenib~~ **as a subsequent- line systemic therapy if disease progression occurs** , 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~~ **2024** . 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 **receiving** up to two prior VEGF receptor- targeted therapies, met **one of** its **two** ~~co-~~ primary ~~endpoint~~ **endpoints** ~~of~~ **,** demonstrating **a statistically** 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. **Since our** ~~We commenced the~~ commercial launch of CABOMETYX in this patient group upon the FDA' s approval, ~~and~~ we have ~~seen~~ **established** a strong **market position** ~~uptake in prescriptions~~ for CABOMETYX ~~in~~ **amongst these** previously treated DTC **patients** ~~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~~ **960** MTC cases diagnosed in the U. S. in ~~2023~~ **2024** , 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~~ **with** 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. **Beyond the established clinical benefits of cabozantinib in its approved indications,** ~~Objective~~ **objective** ~~tumor~~ responses have been observed in patients treated with cabozantinib in ~~multiple~~ **additional** individual tumor types investigated in **early-** ~~phase 1, 2~~ and ~~3~~ **late- stage** 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~~ **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~~ **facilitating label expansion for the cabozantinib franchise, including potential regulatory submissions for cabozantinib to treat neuroendocrine tumors (NET) based on the positive results from the phase 3 CABINET study, data sets from these externally sponsored clinical** trials ~~with us~~ **may also prove valuable by informing our development plans for zanzalintinib. Moreover** , our collaboration partners Ipsen and Takeda have conducted trials in their respective territories through ~~similar~~ independently- sponsored programs **, as well as co- funding select cabozantinib trials with us** . 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~~ **nivolumab** on January 22, 2021 as a first- line treatment of patients with advanced RCC. We continue to evaluate ~~these~~ -- **the triplet** ~~combinations~~ - **combination of cabozantinib with nivolumab and ipilimumab** 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 **[HR]** : 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~~ **two** prespecified interim ~~analysis~~ **analyses** for the secondary endpoint of OS, **conducted most recently during** the ~~triplet combination~~ **third quarter of 2023, the data** did not ~~demonstrate a~~ **meet the threshold for statistical** ~~significant~~ **significance ;** ~~benefit, and~~ therefore, the trial ~~will continue~~ **continues** to the next **planned OS** analysis ~~of OS~~, ~~expected~~ **anticipated** in ~~2023~~ **2024** . 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. **We** ~~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 **, provided such results are supportive** . We are sponsoring COSMIC- 313, and BMS is providing nivolumab and ipilimumab for the study free of charge. Combination Studies with Roche We have **also** 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~~ **in combination with** atezolizumab ~~combination~~ in patients with **a wide variety of** 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~~ **completed enrollment in January 2022** . Enrollment in the expansion phase of this study ~~includes~~ **included** 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~~ **the parties co- funded and undertook three pivotal phase 3 studies** evaluating the **combination of** cabozantinib and atezolizumab **. Two of these** ~~combination in two late- stage clinical~~ trials **(each sponsored by Roche) did not meet their respective primary endpoints** : CONTACT- ~~03~~ **01** , which **evaluated** ~~focuses on patients with inoperable, locally advanced or metastatic RCC who have progressed during or following treatment with an ICI as~~ the **combination versus docetaxel in** ~~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 **; and CONTACT- 03** , ~~did not meet its primary endpoint of OS~~ **which evaluated the combination versus monotherapy cabozantinib in patients with inoperable, locally advanced or metastatic RCC who previously received an ICI as their immediate preceding therapy. Detailed findings from CONTACT- 01 and CONTACT- 03 were presented** at ~~final analysis~~ **the European Lung Cancer Congress in March 2023 and the ASCO Annual Meeting in June 2023, respectively. The third trial, CONTACT- 02, is sponsored by us and continues to evaluate the combination in patients with mCRPC as described below** . 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~~ - **02** ~~, in July~~ **- mCRPC. In June** 2020, we and Roche initiated CONTACT- ~~03~~ **02** , a global, multicenter, randomized, open- label phase 3 pivotal trial evaluating cabozantinib in combination with atezolizumab versus ~~cabozantinib alone~~ **a second novel hormonal therapy (NHT) (either abiraterone and prednisone or enzalutamide)** in patients with ~~inoperable, locally advanced or metastatic RCC~~ **mCRPC and measurable extra- pelvic soft- tissue disease** who **have** progressed **after** ~~during or following~~ treatment with **one prior NHT. CONTACT- 02 is Informed by positive early- stage results from** an ~~ICI~~ **mCRPC cohort of COSMIC- 021,** as ~~the immediate preceding~~ **well as by COMET- 1, our earlier phase 3 trial that evaluated** ~~therapy~~ **monotherapy cabozantinib in mCRPC. The CONTACT- 02 trial enrolled 575 patients at 275 sites globally, and enrollment was completed in the second half of 2023** . Patients ~~are~~ **were** randomized 1: 1 to the experimental arm of cabozantinib in combination with atezolizumab or to the control arm of ~~cabozantinib alone~~ **a second NHT** . The two primary efficacy endpoints for CONTACT- ~~03~~ **02** are **BIRC- assessed** PFS per Response Evaluation Criteria in Solid Tumors (RECIST) v. 1. 1 ~~as assessed by BIRC~~ and OS ~~, and~~ **; key** secondary **and other** efficacy endpoints include ~~PFS,~~ ORR **, prostate- specific antigen response rate** and duration of response (DOR) ~~as assessed by the investigators~~ . ~~CONTACT- 03 is sponsored by Roche and co- funded by us. In addition, both~~ **Both** Ipsen and Takeda have ~~the right to opt~~ **opted** ~~in~~ **into** and **are** co- ~~fund~~ **funding** the trial ~~and if doing so~~ , ~~they~~ **and each** will have access to the results to support potential future regulatory submissions in their respective territories outside of the U. S. In ~~January~~ **August** ~~2022~~ **2023** , we announced ~~the completion of enrollment of 523 patients~~ **positive top- line results from CONTACT- 02, and detailed findings were presented** at ~~168 sites globally~~ **the ASCO Genitourinary Cancers Symposium in January 2024** . **At** ~~Based on current event rates, we anticipate announcing results of~~ the primary PFS analysis **, conducted** in the first ~~half of 2023. We~~ **400 randomized patients in the** ~~intend~~ **intent - to- treat population and per protocol, the trial met one of** ~~to~~ **two** ~~use~~ **primary endpoints, demonstrating a statistically significant improvement in PFS for the combination regimen, reducing the risk of disease**

progression or death by 35 % (HR: 0. 65; 95 % CI: 0. 50- 0. 84; p = 0. 0007). At a median follow- up of 14. 3 months, median PFS was 6. 3 months for cabozantinib in combination with atezolizumab versus 4. 2 months for the control arm. A statistically significant improvement in BIRC- assessed PFS was also observed both in the intent- to- treat population (n = 507) and according to the Prostate Cancer Clinical Trials Working Group 3 evaluation criteria (PCWG3). At a prespecified interim analysis for the primary endpoint of OS, a trend toward improvement of OS was observed; however, the data **were immature and did not meet** ~~from CONTACT- 03 to further study~~ the **threshold for statistical significance. Therefore** ~~therapeutic potential of cabozantinib in this patient population~~ , ~~both~~ **the trial continues to the next planned OS analysis, anticipated in 2024. The safety profile observed in the trial** ~~as~~ **was** ~~a~~ **reflective of the known safety profiles for each** single agent ~~and in~~ **, as well as the** combination **regimen used in this study. We are discussing a potential regulatory submission** with **the FDA** ~~ICIs. CONTACT- 02- mCRPC~~ . According to the American Cancer Society, in ~~2023~~ **2024** , approximately ~~288~~ **299** , 000 new cases of prostate cancer will be diagnosed in the U. S., and ~~34~~ **35** , 000 people will die from the disease **in 2024** . 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. **Men** ~~Researchers estimate that in the U. S. in 2020, 43, 000 men were~~ diagnosed with mCRPC **often have a poor prognosis** , which has ~~a median~~ **an estimated** survival of less than **one to** two years. ~~In~~ **We believe that cabozantinib in combination with atezolizumab, if ultimately approved by the FDA for an mCRPC indication, may be a compelling chemotherapy- free treatment option to** ~~response~~ **respond** to this significant unmet need **. Trials Conducted through our CRADA with NCI- CTEP** and ~~based~~ **our IST Program Clinical trials conducted with support from external partners have enabled further expansion of the cabozantinib development program with less burden** on ~~positive early~~ **our internal development resources. In October 2011, we entered into a CRADA with NCI** - ~~stage~~ **CTEP for the clinical development of cabozantinib and have extended its term through October 2026. The CRADA reflects a commitment by NCI- CTEP to provide funding for the broad exploration of cabozantinib' s potential in a wide variety of cancers, each representing a substantial unmet medical need. Investigational New Drug (IND) applications for trials under the CRADA are held by NCI- CTEP. NCI- CTEP also retains rights to any inventions made in whole or in part by NCI- CTEP investigators. However, for inventions that claim the use and / or the composition of cabozantinib, we have an automatic option to elect a worldwide, non- exclusive license to cabozantinib inventions for commercial purposes, with the right to sublicense to affiliates or collaborators working on our behalf, as well as an additional, separate option to negotiate an exclusive license to cabozantinib inventions. Further, before any trial proposed under the CRADA may commence, the protocol is subject to our review and approval. As reflected by the** results from **completed trials and ongoing clinical trials** ~~Cohort 6 of COSMIC- 021, in June 2020~~ , we ~~and Roche initiated CONTACT~~ **believe our CRADA with NCI** - ~~02,~~ **CTEP has facilitated and may continue to facilitate the expansion of the cabozantinib franchise in** a **cost** ~~global, multicenter, randomized, open-~~ ~~label~~ **efficient manner. CABINET- NET. The Alliance led the CABINET** phase 3 pivotal ~~trial evaluating~~ **study under the CRADA that evaluated** cabozantinib **versus placebo** ~~in combination with atezolizumab~~ in patients ~~with mCRPC~~ who ~~have been previously treated with~~ **experienced progression after prior systemic therapy in two independently powered cohorts:** one ~~NHT. The trial aims to~~ **for advanced pancreatic neuroendocrine tumors (pNET) that** ~~enroll~~ **enrolled 93** ~~approximately 580~~ patients **;** ~~at approximately 280 sites globally,~~ and ~~we expect~~ **another for extra- pancreatic neuroendocrine tumors (epNET, historically referred** to ~~complete~~ **as carcinoid tumors) that** ~~enrollment~~ - **enrolled 193 patients** ~~in the second half of 2023~~ . Patients ~~are being~~ **in both studies were** randomized ~~1~~ **2** : 1 to **either** the experimental arm of **60 mg** cabozantinib **daily** ~~in combination with atezolizumab~~ or **placebo, respectively** ~~to the control arm of a second NHT (either abiraterone and prednisone or enzalutamide)~~ . The ~~two~~ primary ~~efficacy endpoints~~ - **endpoint** for **both studies was** ~~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~~ **August 2023** , **enrollment into the study was stopped, patients were unblinded and those on placebo were offered treatment with cabozantinib due to dramatic improvements in PFS observed at interim analyses and based upon local investigator assessment. The data from CABINET demonstrated that cabozantinib substantially prolonged the time to disease progression or death in** both **pNET (HR** ~~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~~ : **0** ~~1 to the experimental arm of cabozantinib in combination with atezolizumab and the control arm of docetaxel~~ . ~~In December 2022~~ **27; 95 % CI: 0. 14- 0. 49; P < 0. 0001) and epNET (HR: 0. 45; 95 % CI: 0. 30- 0. 66; P < 0. 0001) cohorts** , **and** ~~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~~ **observed in the trial** was consistent with ~~the~~ **its** known safety ~~profiles~~ - **profile. The median PFS for patients who received cabozantinib was 11. 4 months for pNET and 8. 3 months for epNET versus 3. 0 months and 3. 2 months, respectively, for patients who received placebo. In addition, the BIRC assessment also determined that cabozantinib substantially prolonged the time to disease progression** ~~for~~ - **or** ~~each single agent,~~ **death in both pNET (HR: 0. 25; 95 % CI: 0. 12- 0. 54; P < 0. 0001)** and ~~no new safety signals were identified~~ **epNET (HR: 0. 50; 95 % CI: 0. 32- 0. 79; P < 0. 0001) cohorts** . Detailed findings from ~~CONTACT- 01 will be submitted for presentation~~ **CABINET were presented during a Proffered Paper Session** at ~~a future medical meeting~~ **the ESMO Congress in October 2023** . ~~A complete~~ **We are discussing these results with the FDA to support a potential regulatory submission in 2024. In the U. S., more than 12, 000 people are diagnosed with NET each year, and approximately 171, 000 people are** ~~listing~~ **living with the disease. The number** of ~~all ongoing cabozantinib trials~~ **people**

diagnosed with NET each year has been increasing. Most NET take years to develop and grow slowly, but some grow quickly. NET can develop in any part of the body as epNET, but most commonly start in the gastrointestinal (GI) tract or in the lungs. The five- year survival rates for advanced GI- NET and lung epNET are 68 % and 55 %, respectively. NET can also start in the pancreas as pNET. While less common, pNET can be ~~found at www~~ **more aggressive and the five- year survival rate for advanced pNET is only 23 %** . ~~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~~ **molecules that are clinically differentiated with the potential** to ~~treating~~ **improve the standard of care for** cancer **patients** . 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. **Below are** ~~The following table summarizes~~ - **summaries of** our current and planned clinical development activities outside of the cabozantinib franchise **.** ~~: CLINICAL DEVELOPMENT PROGRAM FOR PIPELINEProduct CandidateMechanism of ActionSettingStatus UpdateZanzalintinibNext- generation tyrosine kinase inhibitor (TKI) targeting MET / VEGFR / AXL / MERAdvanced or metastatic solid tumorsPhase 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) XB002Next- generation tissue factor (TF)- targeting antibody- drug conjugate (ADC) Advanced solid tumorsPhase 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 therapiesXL102Potent, selective, orally bioavailable cyclin- dependent kinase 7 (CDK7) inhibitorAdvanced or metastatic solid tumorsPhase 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 regimensCBX- 12Peptide- drug conjugate (PDC) enhancing delivery of exatecan, a highly potent, second- generation topoisomerase I inhibitor, to tumor cellsAdvanced or metastatic refractory solid tumorsPhase 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~~ **Zanzalintinib** ~~,~~ **is** a **novel, potent,** next- generation oral TKI that targets VEGF receptors, MET **and the TAM kinases (TYRO3** , AXL ~~,~~ **and** MER **)** ~~and other kinases~~ implicated in cancer' s growth and spread **, and is our first in- house compound to enter the clinic following our re- initiation of drug discovery activities in 2017** . ~~In designing~~ **Zanzalintinib has a pharmacokinetic half- life of approximately one day, supporting once- daily dosing, which could translate into a favorable safety profile compared with other VEGF- receptor TKIs. Taken together with the promising anti- tumor activity, we believe** zanzalintinib **is positioned to be a best- in- class VEGF- receptor TKI in a wide range of solid tumors when used as a monotherapy, as well as in combination regimens. Accordingly** , we ~~sought to~~ **are evaluating zanzalintinib in a growing development program that** ~~build~~ **builds** ~~upon~~ **on** our **prior** experience with cabozantinib, ~~retaining a similar target profile while~~ **which we believe reduces program risk. We have also established collaborations and will continue to explore additional opportunities for novel combinations with zanzalintinib with the goal of** improving **standards of** ~~key characteristics, including the pharmacokinetic half- life. We are~~ **care** ~~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 ~~,~~ **is** a multicenter phase 1b **/ 2** clinical trial evaluating the pharmacokinetics, safety, tolerability and preliminary anti- tumor activity of zanzalintinib. STELLAR- 001 **was initiated in 2019 and** is divided into dose- escalation and expansion phases **designed to evaluate** ~~. In October 2020, we presented data at the 32nd EORTC- NCI- AACR Symposium (the 2020 ENA Symposium) that suggest~~ zanzalintinib **both** ~~has~~ **as** a **monotherapy** ~~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~~ **a variety of solid tumors. We previously presented data from STELLAR- 001 during poster sessions at the** ~~2021~~ **2022 ESMO Congress, which demonstrated preliminary clinical activity, similar** to ~~include~~ **that observed with cabozantinib, across a range of solid tumors and** dose **levels,** ~~- 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 **manageable safety profile. The phase 2** recommended dose ~~of 100 mg~~ for both **monotherapy** ~~single- agent~~ zanzalintinib and zanzalintinib in combination with atezolizumab ~~, and we have begun enrolling~~ **was determined to be 100 mg once daily. Enrollment into the STELLAR- 001** 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~~ **is complete, and we recently presented initial results evaluating monotherapy** zanzalintinib in ~~combination~~ **patients** with ~~avelumab is ongoing, with expansion cohorts planned initially in urothelial carcinoma~~ **previously treated clear cell RCC during the Oral Abstracts session at the International Kidney Cancer Symposium** (~~UC~~ **IKCS**) ~~. We presented data from STELLAR- 001 during poster sessions at the most recent ESMO Congress~~ in ~~September~~ **November** ~~2022~~ **2023 . At a median follow- up time of 8. 3 months** , **the findings** ~~which showed zanzalintinib has~~ demonstrated ~~preliminary, clinical activity similar to that observed with cabozantinib in phase 1 across a range of solid tumors and~~ - **an** ~~dose levels, with a manageable safety profile. The primary efficacy endpoints for the expansion phase may include~~ ORR **of 38 %** per RECIST v. 1. 1 **for the entire non- clear cell RCC cohort of 32 patients, including** ~~and~~ - **an** ~~PFS per RECIST v~~ **ORR of 57 % among the 14 patients who were not previously treated with**

cabozantinib; the disease control rate was 88 % . ~~1. 1~~ **The ORR for the 26 patients who had received prior VEGF receptor- TKIs was 35 %** , **including responses** in ~~each case~~ **four of the 17 patients (24 %) who had received prior cabozantinib. Follow- up continues in this cohort** as ~~assessed~~ **well as the other completed cohorts, and we continue to be encouraged** by ~~the investigator~~ **zanzalintinib' s emerging safety and efficacy profile, both as a monotherapy and in combination with ICIs** . STELLAR- 002- Advanced Solid Tumors. In December 2021, we initiated STELLAR- 002, a multicenter phase ~~1~~ **1b / 2** clinical trial evaluating the safety, tolerability and efficacy of zanzalintinib in combination with either nivolumab, nivolumab and ipilimumab, or a fixed ~~-~~ dose **combination** of nivolumab and relatlimab, a lymphocyte activation gene- 3- blocking **(LAG- 3)** 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~~ **doses** of ~~100 mg for~~ zanzalintinib ~~in~~ **for these** combination **regimens** ~~with nivolumab,~~ and ~~we have begun enrolling~~ **are exploring them in a diverse array of solid tumor** expansion cohorts **, including** ~~for patients with~~ clear cell RCC **, non** ~~. The dose - escalation stage for zanzalintinib in~~ **clear cell RCC, HCC, mCRPC and CRC; patient enrollment into** ~~the~~ **these expansion cohorts** ~~other combination regimens~~ is ongoing **. The primary efficacy endpoints for the expansion phase are investigator- assessed ORR per RECIST v. 1. 1 and OS, and we are also evaluating additional outcomes relevant for particular tumor types in the study. Monotherapy zanzalintinib may also be evaluated to support regulatory requirements for dosing and contribution of components. STELLAR- 009- Advanced Clear Cell RCC and Other Solid Tumors. In December 2023, we initiated STELLAR- 009,** ~~and -~~ **an** ~~is continuing to enroll~~ **open- label phase 1b / 2 trial evaluating the safety, tolerability and pharmacokinetics of zanzalintinib in combination with AB521, an inhibitor of the transcription factor HIF- 2 α developed by Arcus Biosciences, Inc. (Arcus), in** patients with advanced solid tumors ~~. Depending on the dose- escalation results~~ , **including** ~~STELLAR- 002 may enroll additional expansion cohorts for patients with clear cell and non-~~ clear cell RCC **. STELLAR- 009 is divided into dose- escalation and expansion phases** , ~~mCRPC~~ **and patient enrollment into dose- escalation cohorts is ongoing. Efficacy endpoints for the expansion phase will include investigator- assessed ORR** , ~~UC~~ **DOR and PFS per RECIST v. 1. 1** , ~~HCC, NSCLC,~~ **as well as OS. STELLAR- 303-** CRC ~~and squamous cell cancers of~~ **. 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** ~~head and neck (SCCHN)~~ . The **trial aims to enroll approximately 874 patients at approximately 135 sites globally, regardless of RAS status, with approximately 350 of these patients showing no evidence of liver metastases. Patients are being randomized 1: 1 to the experimental arm of zanzalintinib in combination with atezolizumab or to the control arm of regorafenib. Under the amended trial protocol, the** primary efficacy endpoint ~~of~~ **for STELLAR- 303 is OS in** ~~the~~ **those** ~~expansion phase will be ORR, except for the cohort of~~ patients ~~with mCRPC~~ **without liver metastases** , **and** ~~for which~~ the ~~primary~~ **key secondary** efficacy endpoint ~~will be duration of radiographic~~ **is OS in the full intent- to- treat population. Additional secondary endpoints include investigator- assessed** PFS ~~. To better understand the individual contribution of the therapies~~ , **ORR and DOR per RECIST v** ~~treatment arms in the expansion cohorts may include zanzalintinib as a single agent in addition to the ICI combination regimens~~ . ~~STELLAR- 303- CRC~~ **1. 1 in each population** . 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~~ **53** , 000 people will die from the disease in ~~2023~~ **2024** . **CRC** ~~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 **CRC** ~~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~~ **40** - ~~45~~ **52** % of metastatic **CRC** ~~colorectal cancer~~ cases exhibit a RAS mutation. **STELLAR- 304- Non- Clear Cell RCC.** In ~~June~~ **December** 2022, we initiated STELLAR- ~~303~~ **304** , 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~~ **173** 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 **, respectively** . The primary efficacy endpoints ~~of~~ **for** STELLAR- 304 are **BIRC- assessed** PFS and ORR per RECIST v 1. 1 ~~., in each case as assessed by BIRC~~ . The secondary efficacy endpoint is OS. **Non- clear cell RCC represents about 25 % of RCC cases, with fewer treatment options available and poorer outcomes compared with clear cell RCC. STELLAR- 305- Squamous Cell Cancers of the Head and Neck (SCCHN). In December 2023, we initiated STELLAR- 305, a global, multicenter, randomized, double- blinded phase 2 / 3 pivotal trial evaluating zanzalintinib in combination with pembrolizumab, an ICI developed by Merck & Co., Inc. (Merck & Co.), versus monotherapy pembrolizumab in patients with previously untreated PD- L1- positive recurrent or metastatic SCCHN. The trial aims to enroll approximately 500 patients at approximately 215 sites globally. Patients will be randomized 1: 1 to receive zanzalintinib in combination with pembrolizumab or placebo in combination with pembrolizumab. The primary efficacy endpoints for STELLAR- 305 are**

BIRC- assessed PFS per RECIST v. 1. 1 and OS. Secondary endpoints include investigator- assessed PFS per RECIST v. 1. 1 and ORR and DOR per RECIST v. 1. 1 as assessed by both BIRC and the investigator. SCCHN comprises head and neck cancers that begin in the squamous cells that line the mucosal surfaces of the head and neck. Accounting for about 90 % of all head and neck cancers, SCCHN is classified by its location: it can occur in the oral cavity, oropharynx, nasal cavity and paranasal sinuses, nasopharynx, larynx or hypopharynx. Approximately 50, 000 new cases of SCCHN are diagnosed in the U. S. every year, and SCCHN is more common among men and people over the age of 50. Depending on the site of the cancer and the level of metastases, the five- year survival rate for metastatic SCCHN ranges from 4- 35 %. Beyond STELLAR- 303 ~~and~~ **,** STELLAR- 304 **and STELLAR- 305** , we intend to **initiate additional** ~~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~~ **a next-generation** ADC composed of a human ~~monoclonal antibody (~~ mAb ~~)~~ against TF that is conjugated to ~~a cytotoxic agent~~ **an MTI payload** . 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~~ **MTI payload** 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 **and assumed** ~~, 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 **is** ~~aims to enroll~~ **enrolling** ~~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~~ **. JEWEL- 001 had previously included additional dose- escalation cohorts evaluating the combination of XB002 and** bevacizumab, a mAb developed by Roche **, but those cohorts have since been discontinued** . 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 (**the** 2022 ENA Symposium). The data demonstrated that XB002 was well- tolerated at multiple dose levels, and **a** pharmacokinetic ~~analyses~~ **analysis** ~~showed~~ **confirmed** that XB002 ~~remains~~ **was** stable ~~after infusion~~ with low levels of free payload ~~in circulation~~ . ~~The planned~~ **We have initiated the** cohort- expansion phase **of JEWEL- 101 for monotherapy XB002** , which ~~we expect to initiate during 2023,~~ is designed to further explore **two** ~~the selected dose~~ **doses** of XB002 ~~, both as a single agent and in combination with either nivolumab or bevacizumab,~~ in individual tumor cohorts, ~~which may include~~ **including** ~~forms of~~ NSCLC **, SCCHN** , cervical cancer ~~,~~ **and** ovarian cancer ~~, UC, SCCHN~~ **. Additional cohorts being evaluated with monotherapy XB002 include endometrial cancer** , pancreatic cancer, esophageal cancer, mCRPC, triple negative breast cancer and hormone- receptor positive breast cancer, ~~and~~ **as** ~~will~~ **well** ~~evaluate~~ **as a TF- expressing tumor- agnostic cohort. The primary efficacy endpoint for the expansion phase is investigator- assessed** ORR per RECIST v. 1. 1 ~~as a primary endpoint as well as XB002' s safety, tolerability and pharmacokinetic profile~~ . We ~~also intend~~ **are continuing** to ~~initiate additional~~ **enroll patients in combination** dose- escalation **cohorts with nivolumab** and **will explore the combination potential with zanzalintinib. Additional** expansion cohorts **are planned for evaluating these various combinations as part of our goal to advance XB002 into full development. We intend** to evaluate the potential of XB002 **as monotherapy and** 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~~ **targeting** therapies. **XL309 Development Program In September 2023, we entered into an exclusive global license agreement with Insilico Medicine US, Inc. and its affiliate, Insilico Medicine Hong Kong Limited, along with their parent company and certain other affiliated entities (individually and collectively referred to as Insilico). The agreement with Insilico grants us global rights to develop and commercialize XL309 (formerly ISM3091), a potentially best- in- class small molecule inhibitor of USP1, which has emerged as a synthetic lethal target in the context of BRCA- mutated tumors. The FDA cleared the initial IND for XL309 for the treatment of patients with solid tumors in April 2023. XL309 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 solid tumors, and enrollment is ongoing. Our priorities for XL309 include accelerating its development as a potential therapy for tumors that have become refractory to PARP inhibitors (PARPi), including forms of ovarian, breast and prostate cancers, pursuing potential PARPi combination regimens, and potentially moving beyond the PARPi market into new patient populations. For more information on the Insilico license agreement, see " — Collaborations and Business Development Activities — Research Collaborations and In- licensing Arrangements — Insilico. " ADU- 1805 Development Program In November 2022, we executed an exclusive option and license agreement and clinical development collaboration with Sairopa B. V. (Sairopa) providing us with the right to exclusively in- license ADU- 1805, a clinical- stage and potentially best- in- class mAb developed by Sairopa that targets SIRPα. In February 2023, the FDA cleared the initial IND for ADU- 1805 to evaluate the safety and pharmacokinetics of ADU- 1805 in adults with advanced solid tumors. ADU- 1805 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 solid tumors. The ADU- 1805 study includes future plans to investigate the compound' s potential in combination with approved ICIs. For more information on the Sairopa option arrangement, see " — Collaborations and Business Development Activities — Research Collaborations and In- licensing Arrangements — Sairopa. " XL102 Development Program **and QUARTZ- 101 (Advanced Solid Tumors)** 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 **) discovered by Aurigene Oncology, Ltd** . ~~Based on encouraging preclinical data for~~ **(Aurigene). We exercised our exclusive option to license** XL102 ~~, which we presented, along~~ **in December 2020 pursuant to our collaboration** 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~~ **Based on initial findings from QUARTZ- 101 and research** into **potential formulations** ~~dose- escalation and cohort- expansion phases and aims to enroll approximately 298 patients with advanced solid tumors, with the primary objective~~ of **XL102, we have discontinued development** ~~determining the maximum tolerated dose or recommended dose levels for daily oral administration~~ of XL102 as **of November** ~~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~~ **2023** ~~, we announced initial dose- escalation results from QUARTZ- 101 during the Poster Session at the 2022 San Antonio Breast Cancer Symposium~~ . **CBX** ~~The data demonstrated that XL102 was well~~ - **12** ~~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 **Program** ~~of CBX- 12~~ In November 2022, we executed an exclusive collaboration agreement with Cybrexa **Therapeutics, LLC (Cybrexa)** providing us with the right to acquire CBX- 12 **(alphalexTM exatecan)** , a clinical- stage, first- in- class ~~PDC~~ **peptide- drug conjugate** that utilizes Cybrexa' s proprietary alphalex technology to enhance delivery of exatecan **, a highly potent, second- generation topoisomerase I inhibitor,** 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 **at various doses and schedules** 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 **elected** ~~exercised our exclusive option~~ to **terminate** ~~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 **Cybrexa in January** ~~Aurigene, see " — Collaborations and Business Development Activities — Research Collaborations and In- licensing Arrangements — Aurigene. " In April 2022~~ **2024** ~~we initiated a first- in- human, phase 1 clinical trial evaluating the safety, tolerability, pharmacokinetics~~ and **subsequently relinquished all rights** ~~preliminary anti- tumor activity of XL114 as a monotherapy in patients~~ with ~~non~~ **respect to CBX** - **12** ~~Hodgkin' s lymphoma (NHL)~~ . **A complete listing of all ongoing** ~~Based on initial findings in this phase 1 trial~~ **trials can be found at www. ClinicalTrials. gov** ~~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~~ **the number of** novel anti- cancer agents **in our pipeline** is essential to our ~~pipeline~~ **overall** 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 **and continue to include** research collaborations, in- licensing arrangements and other strategic transactions that **collectively incorporate** ~~increase our discovery bandwidth and allow us to access~~ a wide range of technology platforms ~~. In November 2022, we executed an~~ **and assets** ~~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. TTM. 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~~ -- **probability** of **success** ~~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~~ **two** ~~five~~ new development candidates into preclinical development during ~~2023~~ **2024** . **We** ~~In addition, we~~ will continue to engage in ~~business development~~ **pipeline expansion** initiatives with the goal of acquiring and in- licensing promising **investigational** oncology ~~platforms and~~ assets and then further characterize and develop them utilizing our established preclinical and clinical development infrastructure. Biotherapeutics Programs **We are** ~~Much of our drug discovery activities focuses on discovering and~~ advancing ~~various~~ **a variety of** biotherapeutics that have the potential to become anti- cancer therapies, **including** ~~such as~~ bispecific antibodies ~~,~~ **and** ADCs ~~and other innovative treatments~~ . ADCs in particular present a unique opportunity for new cancer treatments, given their capabilities to deliver anti- cancer **drug** ~~payload~~ **payloads** ~~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~~ **our various biotherapeutics** programs, we have established multiple research collaborations and in- licensing arrangements and entered into other strategic transactions **, aimed at conserving capital and managing risks,** that provide us with access to antibodies ~~and ,~~ binders **, payloads and conjugation technologies** , which are the **components** ~~starting point for use with additional technology platforms that we employ~~ **employed** to generate next- generation ADCs or multispecific antibodies. In addition to the option ~~deals~~ **deal** 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 SAFEbodyTM 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; **and** • 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~~ **2024** 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 **JEWEL- 101 and our development plans for** 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~~ **five** biotherapeutics development candidates **toward potential IND filings in 2024, 2025, and 2026** : XB010, ~~XB014 and~~ XB628 **, XB371, XB064, and XB033** . XB010, our first ADC advanced internally, targets the tumor antigen 5T4 ~~,~~**and** incorporates an antibody sourced from Invenra and was constructed using Catalent' s SMARTag site- specific bioconjugation platform. ~~XB014 and~~ XB628 ~~are~~ **is a** bispecific ~~antibodies~~ **antibody that** ~~; 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 **key regulators of natural killer cell activity, and was discovered, in part, in collaboration with Invenra. XB371 is a next- generation TF- targeting ADC that is differentiated from XB002 by its topoisomerase inhibitor payload, and was discovered, in part, in collaboration with Catalent. XB064 is a high- affinity mAb that targets immunoglobin- like transcript 2 (ILT2), which is associated with resistance to PD- 1 pathway inhibitors, with potential to combine broadly with our internal pipeline and approved immunotherapy agents, and was discovered, in part, in collaboration with Invenra. XB033 is** an ~~emerging immune~~ **ADC targeting the tumor antigen IL13Ra2, and was discovered, in part, in collaboration with Invenra and Catalent. In December 2023, we announced that we had discontinued our preclinical development program for XB014, a bispecific antibody combining a PD- L1 targeting arm with a CD47 targeting arm to block a macrophage** checkpoint **,** ~~that may mediate resistance to classical checkpoint inhibition. Both XB014~~ and ~~XB628 were developed through our~~ **was discovered, in part, in** 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 **over** 25 compounds to the IND- stage, either independently or with collaboration partners, and today we deploy our drug discovery expertise to advance small molecule **programs** ~~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. **The furthest along of our internally- discovered small molecule product candidates is zanzalintinib, which is now being evaluated in phase 3 clinical trials.** We **are also advancing a small molecule development candidate, XL495, toward a potential IND filing in 2024. XL495 is an inhibitor of protein kinase membrane associated tyrosine / threonine 1 (PKMYT1) with best- in- class potential to treat solid tumors due to its improved selectivity and pharmacokinetics. In addition, we** augment our small molecule discovery activities through research collaborations and in- licensing arrangements with other companies engaged in small molecule discovery **. Most recently** , ~~including: • STORM Therapeutics LTD (STORM)~~ **in September 2023, we entered into an exclusive global license agreement with Insilico, granting us global rights to develop and commercialize XL309, a potentially best- in- class small molecule inhibitor of USP1** , which **has emerged** ~~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 **a synthetic lethal target in** ~~therapies for cancer; and • StemSynergy Therapeutics, Inc. (StemSynergy), which is focused on~~ the **context** ~~discovery and development~~ of **BRCA- mutated** ~~novel oncology compounds aimed to inhibit tumor~~ **tumors . In April 2023,** ~~growth by targeting Casein Kinase 1 alpha (CK1α) and~~ the ~~Notch pathway~~ **FDA cleared the initial IND for XL309 for the treatment of patients with solid tumors** . For additional information on ~~these research collaborations and in- licensing arrangements related to~~ our ~~small molecule programs~~ **development plans for XL309** , 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 ~~.~~ **— XL309 Development Program** " **in Part I, Item 1 of this Annual Report on Form 10- K, and for additional information on our research collaborations and in- licensing arrangements related to our small molecule programs, see " — Collaborations and Business Development Activities — Research Collaborations and** In ~~addition, we~~ **- licensing Arrangements. " We also** 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~~ **2024 and beyond** . 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. 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~~ **has been** subsequently amended on ~~four~~ **multiple** 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~~ **2023** , 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~~ **2023** , we have earned royalties of $ ~~382~~ **517** . ~~1~~ **9** 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~~ **containing** 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 **European Medicines Agency (** 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~~ **as** 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~~ **2023** , we have also achieved ~~regulatory and development milestones in the~~ aggregate **milestone payments** of $ ~~127~~ **138** . 0 million related to regulatory and commercial progress by Takeda since the inception of the collaboration agreement **, including one commercial milestone payment during 2023 for $ 11. 0 million upon Takeda' s achievement of $ 150. 0 million of cumulative net sales of cabozantinib in Japan** . 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~~ **108** . 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~~ **2023** , we have earned royalties of $ ~~21~~ **34** . ~~5~~ **2** 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~~ **containing** 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 **certain clinical trials, including:** 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. 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~~ **nivolumab** 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. 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 **any** ~~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 **To** ~~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 **, and Arcus' AB521** . 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. " 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 **incorporate** ~~serve to increase our discovery bandwidth and allow us to access~~ a wide range of technology platforms **and assets and increase our probability of success** . More recently, we have focused our business development activities on late preclinical and early- stage clinical assets that align with our oncology **drug** development **, regulatory and commercial** expertise **,** and **that** 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~~ **to explore the applicability of** 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. **• Insilico.** In ~~addition~~ **September 2023** , we ~~are~~ **entered into an exclusive global license agreement with Insilico. Under the agreement, Insilico granted us global rights to develop and commercialize XL309, a clinical- stage and potentially best- in- class small molecule inhibitor of USP1, which has emerged as a synthetic lethal target in the context of BRCA- mutated tumors, and other USP1- targeting compounds, in exchange for an upfront payment to Insilico of $ 80 million. Insilico is also eligible to receive future development, commercial, and sales- based milestone payments, as well as tiered royalties on net sales. In the fourth quarter of 2023, we completed the transfer of stewardship of the ongoing phase 1 clinical trial evaluating XL309 from Insilico to us. We** ~~continuing~~ **continue** 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~~ **toward** 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 **- targeting** 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 -~~ **XB002** , 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- BodyTM 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~~ **up to 20** 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. **In order to prioritize the advancement of our deep pipeline of clinical and near- clinical programs, we are rebalancing our investment priorities and research and development resources toward our product development activities. Accordingly, we elected to terminate certain of our research collaborations, in- licensing and other arrangements in January 2024:** • **Aurigene** ~~StemSynergy. In January 2018 -~~ , **which was focused on** ~~we entered into an exclusive collaboration and license agreement with StemSynergy for~~ the discovery and development of novel ~~oncology compounds~~ **small molecules as therapies for cancer, and included our discontinued programs for XL102 and XL114; •**

BioInvent International AB (BioInvent), which was intended to expand our portfolio of antibody- based therapies and utilizes 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 ~~targeting --- **target** CK1α **and antibody discovery; • Cybrexa** , ~~a component of~~ **which was focused on** the **development of CBX- 12 (** ~~Wnt signaling pathway implicated in key oncogenic processes,~~ including **our right to acquire CBX** ~~in colorectal cancers. One such compound, EXEL - 4329~~ **12); • NBE- Therapeutics AG (NBE)** , ~~reached~~ **which was focused on the discovery and** development **of multiple ADCs by leveraging NBE' s unique expertise** ~~candidate status in 2021. In May 2021, we amended the agreement to provide for an~~ **and proprietary** ~~additional research platform~~ **platforms** ~~to explore~~ **in ADC discovery, including NBE' s SMAC- Technology ™ (a site-specific conjugation technology) and novel payloads; and • STORM Therapeutics LTD, which was focused on the discovery and development of** inhibitors of **novel RNA modifying enzymes, including ADAR1. The terminations for** ~~the~~ **these** ~~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~~ **agreements** ~~, 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 **effective in April 2024** ~~solely responsible for the commercialization of products that arise from the collaboration~~ . Prior to the commercialization of our first product, COMETRIQ, our primary business strategy was focused on the development and out- ~~license~~ **licensing** of **innovative drug candidate** compounds to pharmaceutical and biotechnology companies under collaboration agreements that allowed us to retain economic participation in ~~compounds~~ **the asset** 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 **operate our** own ~~or operate~~ **current Good Manufacturing Practice (GMP)** 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 **mostly** 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 **are** ~~continue to expand~~ **expanding internal CMC development laboratories to augment** our **external network focusing on our product candidates. We expect this to enable us to maximize application of our internal expertise and scientific know- how and advance our product candidates more efficiently and with greater technical precision, speed, agility and quality, while working in close collaboration with our expanding external manufacturing and** 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~~ **. This external network consists of** well- established and reputable global third- party **GMP** 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 **legal and** regulatory requirements, including the FDA' s ~~Current~~ **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. **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.** We **continually** 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~~ **Where appropriate, 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~~ **forecasts of global** market demand, production lead times, potential supply interruptions and shelf life for our drug substance and drug products. **We** ~~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~~ **hostilities in Eastern Europe and the Middle East or other global events** . 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~~ **, including** 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 **underinsured** ~~under- insured~~ patients who meet certain clinical and financial criteria. In addition, EASE provides comprehensive reimbursement support services, such as prior authorization ~~support~~ **assistance** , 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, **including** ~~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. **To** ~~In an effort to~~ maintain a safe environment for all staff, we **have established a Lab Safety Committee to oversee the working conditions in our laboratory and office environments and conduct regular safety inspections, with reports provided to our Ethics Committee on a regular basis. 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~~ **to maintain a safe working environment. We also** 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~~ **help keep our employees** 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 **product** ~~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~~ **a supplemental New Drug Application (** 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 **required post- marketing clinical** 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~~ **allows** 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 **. Moreover, in September 2023, the U. S. Federal Trade Commission (FTC) issued a policy statement, supported by the FDA, warning brand pharmaceutical companies that they could face legal action under the FTC Act if they improperly list patents in the Orange Book, and in November 2023, the FTC subsequently initiated challenges against patents held by brand pharmaceutical companies and listed in the Orange Book under the FDA' s patent listing dispute process** . 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 **based** 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~~ **Decentralized** 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 **became** ~~will be~~ enforceable in **certain** ~~most key~~ respects **in** ~~beginning on~~ July ~~1,~~ 2023 **, with the CPRA' s implementing regulations currently subject to a stay of enforcement until one year from their issuance** . 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~~ **Pricing** Program (the 340B Program)). CMS continues to issue guidance and rulemaking governing our participation in the Medicaid Drug Rebate Program **(MDRP)** , 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~~ **and sub- regulatory guidance that may impact pricing for pharmaceutical products. These initiatives include** , among ~~other~~ **others** ~~things~~ : **• efforts to reevaluate,** reduce or limit the prices ~~of drugs and make them more affordable for~~ patients **pay (including,** for **pharmaceutical products** ~~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~~ **implementation of** additional data collection and transparency reporting regarding drug pricing, rebates, fees and other remuneration provided by drug manufacturers; **• revisions** ~~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; **• changes to the MDRP, including through a recent CMS- proposed rulemaking for this program, that could significantly increase manufacturer** ~~create~~ **rebate** ~~new AKS~~ **liability; and • reevaluation of** 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 **AKS** ~~Medicaid Drug Rebate Program~~ . For instance, in August 2022, President Biden signed the Inflation Reduction Act **of 2022 (Inflation Reduction Act)** , which among other things: allows ~~for~~ CMS to ~~impose~~ **establish the** ~~price~~ **prices of** ~~controls for~~ certain single- source drugs and biotherapeutics reimbursed under Medicare Part B and Part D **(the Medicare Drug Price Negotiation Program)** ; subjects drug manufacturers to **potential** civil monetary penalties and a ~~potential~~ **significant "** 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~~ **certain Part B and Part D drugs where relevant pricing metrics associated with the products** ~~increases~~ **increase faster**

~~that~~ **than** ~~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~~ **certain provisions currently are** subject to various legal challenges. As of the date of this Annual Report on Form 10- K, **for example,** CMS has **begun to implement** ~~commenced public rulemaking and issued guidance addressing certain~~ aspects of the Inflation Reduction Act ~~,~~ and ~~overtime~~ **has released revised guidance addressing the Medicare Part B and Medicare Part D inflation rebate provisions of the Inflation Reduction Act. These provisions generally require manufacturers of Medicare Part B and Part D rebatable drugs to pay inflation rebates to the Medicare program if pricing metrics associated with their products increase faster than the rate of inflation. In addition, in June 2023, CMS released revised guidance setting forth the requirements and procedures for implementing the Medicare Drug Price Negotiation Program for the first round of drug pricing evaluations, which will occur in 2023 and 2024 and result in prices effective in 2026. In July and August 2023, CMS also issued draft guidance on the Medicare Prescription Payment Plan, under which Medicare Part D beneficiaries may opt to make their cost- sharing payments in capped monthly installments; CMS expects that this program will most likely benefit those beneficiaries with high cost- sharing early in their respective plan years. Over time,** the Inflation Reduction Act could reduce the revenues we are able to collect from sales of our products **or present challenges for payor negotiations** and **formulary access for our products, as well as** 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 **and regulatory agencies** 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 **, advance notices of price increases** , 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 **MDRP** ~~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~~ **effect** in **January** 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. 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 **compete** successfully ~~compete~~ **with cabozantinib in the therapeutic markets where it is or may be approved** 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, **substantially** 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 **additional** 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; **and Novartis' everolimus. Additionally,** ~~the~~ **there** ~~combination~~ **are a variety** of **therapies being developed for advanced RCC, including:** Merck & Co.' s ~~pembrolizumab, Eisai' s lenvatinib and Peloton Therapeutics'~~ belzutifan; the combination of Merck & Co.' s **belzutifan** ~~pembrolizumab and quavonlimab~~ and Eisai' s lenvatinib; ~~and Peloton Therapeutics~~ **the combination of Merck & Co.** ' **s pembrolizumab and** belzutifan **and Eisai' s lenvatinib; the combination of Merck & Co.' s pembrolizumab and quavonlimab and Eisai' s lenvatinib; and BMS' nivolumab (administered subcutaneously)** . 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~~ **2024** 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~~ **. This has** ~~lead~~ **led** to ~~an~~ **increased competition due to the** increase in prescribing and sequencing of TKIs in subsequent **lines of therapy as more patients overall receive multiple** lines of therapy. It is difficult to predict how these changes will affect sales of CABOMETYX during ~~2023~~ **2024** 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 generic versions of sorafenib** ; and Eisai' s lenvatinib. In addition, we believe there is also competition for CABOMETYX from **mutation- targeted** therapies approved **or in development** 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), **or patients with BRAF V600E mutations,** including: Blueprint Medicine' s and Roche' s pralsetinib; ~~and Loxo Oncology' s (a wholly owned subsidiary of~~ Eli Lilly ~~)~~ **' s** selpercatinib **; and the combination of Novartis' dabrafenib and trametinib** . 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~~ **Eli Lilly** ' 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~~ **2024** . 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 **and measurable extra- pelvic soft- tissue disease** who have ~~been previously~~ **progressed after** ~~treated~~ **treatment** with one **prior** NHT. Should the combination of cabozantinib and atezolizumab be approved for the treatment of these mCRPC patients, we believe its principal competition may include **the following approved therapies or therapies in late- stage development** : 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; **the combination of Clovis Oncology' s rucaparib and Pfizer' s enzalutamide; the combination of Clovis Oncology' s rucaparib and BMS' s nivolumab; the combination of Janssen Biotech' s abiraterone and prednisone, with or without Eli Lily' s ademaciclib; and Hinova Pharmaceuticals' HC- 1119;** 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' **lutetium Lu177 vipivotide tetraxetan (formerly** 177Lu- PSMA- 617 **)** ; POINT Biopharma' s **(a wholly owned subsidiary of Eli Lilly) PNT2002 (formerly** 177Lu- PNT2002 **)** ; Telix International' s 177Lu- DOTA- rosopatamab; and Curium US LLC' s 177Lu- PSMA- I & T. **Cabozantinib** ~~Competition for Zanzalintinib Zanzalintinib in combination with ICI - CRC~~ **pNET / epNET** : **CABINET** ~~STELLAR- 303~~ is a phase 3 pivotal trial ~~evaluating the combination of zanzalintinib~~ **, which evaluated cabozantinib versus placebo in patients who experienced progression after prior systemic therapy in two independently powered cohorts: pNET** and ~~atezolizumab~~ **epNET. Should cabozantinib be approved for treatment** in patients with **pNET** ~~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~~ **or epNET** ~~the treatment of these CRC patients~~ , we believe its principal competition may include **the following approved therapies or therapies in late- stage development: Novartis' lutetium Lu177 dotatate; Novartis' s everolimus; Pfizer' s sunitinib; the combination of Roche' s capecitabine and Merck & Co.' s temozolomide; and RayzeBio' s Actinium- 225 dotatate. Competition for Zanzalintinib While we have not yet submitted an NDA to the FDA for zanzalintinib, we believe that the factors that will impact our ability to compete in indications where zanzalintinib may be approved would be similar to those for the cabozantinib franchise, as described above. Below is a summary of the principal competition for zanzalintinib in the indications for which it 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 zanzalintinib or a combination therapy regimen that includes zanzalintinib. Competition in Potential Zanzalintinib Indications 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 the following approved therapies or therapies in late- stage development** : 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 **; the combination of Taiho Oncoloy' s trifluridine / tipiracil** and Roche' s bevacizumab **; Hutchison MediPharma' s fruquintinib; and the combination of Agenus' botensilimab and balstilimab** . 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 **approved** therapies **or therapies in late- stage development** that compete with cabozantinib or combination regimens containing cabozantinib in ~~their~~ various ~~approved~~ RCC indications **. Zanzalintinib in combination with ICI- SCCHN: STELLAR- 305 is a phase 2 / 3 pivotal trial evaluating zanzalintinib in combination with Merck & Co.' s ICI, pembrolizumab, versus pembrolizumab alone in patients with previously untreated PD- L1- positive recurrent or metastatic SCCHN. Should the combination of zanzalintinib and pembrolizumab be approved for the treatment of these SCCHN patients, we believe its principal competition may include the following approved therapies or therapies in late- stage development: the combination of Eli Lily' s cetuximab, platinum chemotherapy and 5- fluoruracil; Merck & Co.' s pembrolizumab; and the combination of Merck & Co.' s pembrolizumab, platinum chemotherapy and 5- fluorouracil** . 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~~ **product** 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~~ **product** 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~~ **product** candidates, as further described below. 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~~ **U. S.** 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. ProductPatent No. General Subject MatterPatent ExpirationCABOMETYX 7, 579, 473Composition of matter20268, 497, 284Methods of treatment20248, 877, 776Salt and polymorphic forms of cabozantinib 20309, 724, 342Formulations of cabozantinib203310, 034, ~~873 Methods~~ **873Methods** of treatment203110, 039, 757Methods of treatment203111, 091, ~~439 Crystalline~~ **439Crystalline** salt forms of cabozantinib203011, 091, ~~440 Pharmaceutical~~ **440Pharmaceutical** composition 203011, 098, ~~015 Methods~~ **015Methods** of treatment203011, 298, ~~349 Pharmaceutical~~ **349Pharmaceutical** composition2032COMETRIQ 7, 579, 473Composition of matter20268, 877, 776Salt and polymorphic forms of cabozantinib20309, 717, 720Formulations of cabozantinib203211, 091, ~~439 Crystalline~~ **439Crystalline** salt forms of cabozantinib203011, 091, ~~440 Pharmaceutical~~ **440Pharmaceutical** composition203011, 098, ~~015 Methods~~ **015Methods** of treatment203011, 298, ~~349 Pharmaceutical~~ **349Pharmaceutical** composition2032 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 **in** ~~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~~ **impact** the parties' claims in the **separate and ongoing** MSN II lawsuit **. In October 2023, a bench trial occurred for the MSN II case, and a judgment is expected during the first half of 2024** . 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 July 18** , **2023, we entered into a settlement and license agreement (the Teva Settlement Agreement) with Teva to end these litigations. Pursuant to the terms of the Teva Settlement Agreement, we will grant Teva a license to market its generic version of CABOMETYX in the U. S. beginning** on **January 1, 2031, if approved by the FDA and subject to conditions and exceptions common to agreements of this type. In September 2023, the parties filed a joint stipulation of dismissal with the Delaware District Court, which the Delaware District Court granted and dismissed the case without prejudice. And finally in** February ~~6,~~ 2023, we received a Paragraph IV certification notice letter regarding an ANDA submitted to the FDA by Cipla ~~Limited~~ **, Ltd. and Cipla USA, Inc.** (**individually and collectively referred to as** Cipla) requesting approval to market a generic version of CABOMETYX tablets **. In response, we filed a patent infringement lawsuit against Cipla in the Delaware District Court in March 2023, and all proceedings in our litigation against Cipla were stayed pursuant to an order of the Delaware District Court in May 2023** . 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 **composition of matter** 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. ProductPatent No. General Subject MatterPatent ExpirationCABOMETYX 2213661Composition of matter and methods of treatment20292387563Salt and polymorphic forms of cabozantinib and methods of ~~treatment2030COMETRIQ~~ **treatment20302593090Formulations of cabozantinib2031COMETRIQ** 2213661Composition of matter and methods of treatment20292387563Salt and polymorphic forms of cabozantinib and methods of ~~treatment2030~~ **treatment20302593090Formulations of cabozantinib2031** 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~~ **Product** 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~~ **product** candidates in clinical and / or preclinical development, including zanzalintinib, XB002 and ~~XL102~~ **XL309** . 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~~ **2044** , 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~~ **2023** , we had 1, ~~223~~ **310** employees, representing a ~~28~~ **7. 1** % increase in our employee workforce as compared to December 31, ~~2021~~ **2022** . Of these employees, ~~600~~ **672** are members of our research and development teams and ~~623~~ **638** are members of our commercial, general and administrative teams. Of these employees, ~~215~~ **242** hold Ph. D. degrees, ~~23~~ **31** hold M. D. (or foreign equivalent) degrees, ~~32~~ **41** hold PharmD degrees and ~~111~~ **119** 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. **We** ~~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~~ **2023** , was 59 % non- white and ~~52~~ **51** % women. In addition, as of December 31, ~~2022~~ **2023** , ~~54~~ **53** % 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 **patients,** employees ~~, patients~~ and community **. In January 2024, we announced and implemented a restructuring plan, including a reduction of our employee workforce by approximately 175 employees, or 13 % of our total headcount** . 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 **as part of our commitment to fair compensation for all employees** , **our most recent** ~~for 2022, the fourth year in a row, this~~ analysis demonstrated no gender or ethnicity- based disparities **and a gender pay parity ratio of 1: 1** . 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~~ **a wellness subsidy program, virtual and onsite fitness classes, adoption assistance** , mental health **coverage, subsidized commuter benefits** and other wellness benefits **. Our inclusive benefits are also designed to support family life with options including, among others, generous parental leave policies, grandparent leave, adoption, surrogacy and fertility programs, new parent and nursing mother support programs, mental health services, childcare tuition subsidy and tutoring services, dependent care for children and adults, family care coordination, and pet insurance** . 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~~ **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 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. 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~~ **implementing** 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~~ **actions have** 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 **. There is ongoing litigation challenging CMS' s co- pay accumulator policies for non- grandfathered health plans. On September 29, 2023, a federal district court vacated provisions of the 2021 Notice of Benefit and Payment Parameter (NBPP) final rule that provided health plans with discretion whether to include manufacturer assistance toward the annual cost- sharing limit. Both parties have appealed, and the outcome of this litigation has not been determined. Additionally, CMS is proposing to require health plans to consider as essential health benefits (EHB) all prescription drugs that are covered in excess of a state' s EHB benchmark plan. If finalized, this policy would help mitigate maximizer programs** . 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 **or legal challenges** that could significantly modify the terms and scope of government- provided health insurance coverage, ranging from changes to **or litigation opposing** 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. **In** ~~HHS has notified us that it is reviewing our policy, and we have responded to HHS' request for information. Since~~ 2021, ~~numerous~~ **other** manufacturers that ~~previously~~ implemented similar contract pharmacy integrity programs ~~have~~ received enforcement letters from **the U. S. Department of Health and Human Services (** HHS **)** stating that those manufacturers' ~~actions~~ **integrity initiatives, as implemented,** 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~~ **Certain** of these **other** manufacturers are now in litigation with the government over the legality of these programs **. In November 2023** , **we received from several covered entities a 340B Administrative Dispute Resolution (ADR) petition, seeking to invoke** ~~and~~ **an administrative adjudication process overseen by the Department of Health and Human Services' Health Resources and Services Administration. The petitioners contend that the Company' s 340B Program Integrity Initiative caused them to be overcharged for CABOMETYX and COMETRIQ. No ADR proceedings have commenced as of the date of this Annual Report on Form 10- K and at this time it is unclear what, if any, liabilities we might incur if we are ultimately party to such an ADR proceeding. In addition, certain states have also enacted laws requiring manufacturers to provide the 340B Program pricing through contract pharmacy arrangements; these laws are also being challenged in ongoing litigation. We believe our 340B Program Integrity Initiative complies with the 340B Program statute, as supported by the decision in Sanofi Aventis U. S. LLC v. United States Department of Health and Human Services, and that the state laws regarding contract pharmacy arrangements are invalid. However,** depending on the outcome of ~~such~~ **the ongoing** litigation **or any specific proceedings involving us** , we may be required to modify or suspend our 340B Program Integrity Initiative. ~~Further~~ **Any negative ruling in a federal court** , ~~it is possible that~~ HHS ~~could seek to implement~~ administrative ~~proceedings~~ **proceeding,** ~~to recover overcharges and / or impose civil monetary penalties against us regarding~~ **state- level proceeding in which we are a party, or in which the compliance of** our 340B Program Integrity Initiative **is at issue** ~~. 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 **future** 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 **and sub- regulatory guidance** , ~~designed to~~ **that may impact pricing for pharmaceutical products. These initiatives include** , among ~~other~~ **others** ~~things~~ : **• efforts to reevaluate,** reduce or limit the ~~prices~~ **price** ~~of drugs and make them more affordable for~~ patients **pay (including,** for **pharmaceutical products** ~~example, by tying drug prices to the prices of drugs in other countries)~~ ; **• revisions** ~~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 **and** ~~, eliminate the~~ **other** ~~AKS discount safe harbor protection~~ **changes to the MDRP, including through a recent CMS- proposed rulemaking** for **this program, that could significantly increase** manufacturer rebate **liability** ~~arrangements with Medicare Part D plan sponsors~~ ; ~~create new AKS~~ **and • reevaluation of** 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~~ **Anti- Kickback Statute** . For instance in August 2022, President Biden signed the Inflation Reduction Act, which among other things: allows ~~for~~ CMS to ~~impose~~ **establish the** ~~price~~ **prices of** ~~controls for~~ certain single- source drugs and biotherapeutics reimbursed under Medicare Part B and Part D **(the Medicare Drug Price Negotiation Program)** ; subjects drug manufacturers to **potential** civil monetary penalties and a ~~potential~~ **significant** 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~~ **certain Part B and Part D drugs where relevant pricing metrics associated with the products** ~~increases~~ **increase faster** ~~that~~ **than** ~~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~~ **currently are** subject to various legal challenges. As of the date of this ~~Annual Report~~ **report , for example** ~~on Form 10- K~~ , CMS has **begun to implement** ~~commenced public rulemaking and issued guidance addressing certain~~ aspects of the Inflation Reduction Act ~~,~~ and ~~overtime~~ **has released revised guidance addressing the Medicare Part B and Medicare Part D inflation rebate provisions of the Inflation Reduction Act. These provisions generally require manufacturers of Medicare Part B and Part D rebatable drugs to pay inflation rebates to the Medicare program if pricing metrics associated with their products increase faster than the rate of inflation. In addition, in June 2023, CMS released revised guidance setting**

forth the requirements and procedures for implementing the Medicare Drug Price Negotiation Program for the first round of drug pricing evaluations, which will occur in 2023 and 2024 and result in prices effective in 2026. Among other things, the revised guidance specifies how CMS intends to identify selected drugs, the factors it may consider in establishing drug prices, how it may conduct the drug pricing evaluation process and what requirements may be set for manufacturers of selected drugs. On August 29, 2023, CMS announced the list of 10 drugs selected for the first round of drug pricing evaluations. Our revenues may be significantly impacted if cabozantinib or our other product candidates are eventually selected for evaluation under this program. Furthermore, in November 2023, CMS released final guidance on the Medicare Part D Manufacturer Discount Program, and while the program will include a phase- in of the discount for certain smaller manufacturers (known as " specified manufacturers " and " specified small manufacturers ") that may apply to our company, it will ultimately require increases in manufacturer contributions toward reducing patient out- of- pocket costs. In July and August 2023, CMS also issued draft guidance on the Medicare Prescription Payment Plan, under which Medicare Part D beneficiaries may opt to make their cost- sharing payments in capped monthly installments; CMS expects that this program will most likely benefit those beneficiaries with high cost- sharing early in their respective plan years. Over time, the Inflation Reduction Act could reduce the revenues we are able to collect from sales of our products **or present challenges for payor negotiations** and **formulary access for our products, as well as** 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 **policy changes** ~~legislative proposals or executive rulemaking~~ , if implemented **as currently proposed** ~~without successful legal challenges~~ , would likely have ~~a~~ significant and far- reaching ~~impact~~ **impacts** on the biopharmaceutical industry and therefore **likely** also ~~likely~~ have a material adverse impact on our business, financial condition and results of operations. **At the state level, legislatures and regulatory agencies 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, advance notices of price increases, 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 **on Health Technology Assessment** adopted in December 2021, may further impact the price and reimbursement status of CABOMETYX and COMETRIQ when it enters into application **in January** 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 **Federal Food, Drug and Cosmetic Act (** 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~~ **a New Drug Application (** NDA **)** under section 505 (b) (2) of the FDCA **(505 (b) (2) NDA)** 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~~ **of** 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~~ **these** 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 **new chemical entity (** 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~~ **allows** 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, **they** ~~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. **Moreover, in September 2023, the FTC issued a policy statement, supported by the FDA, warning brand pharmaceutical companies that they could face legal action under the FTC Act if they improperly list patents in the Orange Book, and in November 2023, it subsequently initiated challenges against patents held by brand pharmaceutical companies and listed in the Orange Book under FDA' s patent listing dispute process.** Risks Related to Growth of Our Product Portfolio and Research and Development 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 **potential** 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~~ **investigational oncology assets** and technologies. However, the in- licensing and acquisition of ~~product candidates~~ **investigational oncology assets** and technologies is a highly competitive area, and many other companies are pursuing the same or similar ~~product candidates~~ **investigational oncology assets** 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~~ **investigational oncology assets** 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~~ **investigational oncology assets** and technologies, the competitive business environment may result in higher acquisition or licensing costs, and our investment in these potential ~~products~~ **product candidates** 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~~ **licensors** for the continued development of ~~the~~ **any product candidates and / or technologies that we have** in- licensed ~~technology~~ and ~~their~~ **such licensors'** 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 **of resources** , 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 trials are inherently risky and may reveal that cabozantinib, despite its approval for certain indications, or a new product candidate **, such as zanzalintinib** , 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 **, zanzalintinib** 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 **our** 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~~ **demonstrate potentially superior** safety or efficacy **profiles as** compared to cabozantinib **, zanzalintinib** 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. **Further, with the passage of the Food and Drug Omnibus Reform Act of 2022 (FDORA), Congress clarified the FDA' s authority to conduct inspections by expressly permitting inspection of facilities involved in the preparation, conduct or analysis of clinical and non- clinical studies submitted to FDA, as well as of other persons holding study records or otherwise involved in the study process, which could delay or add complexity to our clinical trials.** The ongoing ~~Russo~~ **Russia** - ~~Ukrainian~~ **Ukraine** ~~War has~~ **war and Israel- Hamas war have** had ~~a~~ modest ~~impact~~ **impacts** 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~~ **impacts** on the ability of clinical sites and ~~their~~ **enrolled** patients to adhere to trial protocols for in- office clinical visits and other procedures, our ability to supply clinical sites with cabozantinib **, zanzalintinib** 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~~ **These issues** ~~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 **have relied and may in the future** rely on ~~our~~ collaboration partners to ~~fund~~ **share** a significant portion of **the expenses associated with** 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 **, zanzalintinib** or our other product candidates and, as a result, **the burden of clinical trial expenses** we **incur associated with our business plans** may be **materially greater than** ~~unable to execute our current~~ **currently anticipated** ~~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~~ **due to** a ~~result~~ **number** of factors ~~relating to a particular clinical trial~~ , including, ~~among others~~ **but not limited to** : 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 **, such as zanzalintinib** , 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 **government** 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 **of** ~~for this initiative is to advance~~ **advancing** 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~~ **For example** , in ~~part due~~ **early 2023, the FDA issued a draft guidance intended** to ~~questions raised by~~ **assist sponsors in identifying the optimal dosages for** ~~the~~ **these** ~~process underlying the~~ **products during clinical development and prior to applying for** approval ~~of~~ **for a new indication** ~~an~~ **and** ~~Alzheimer' s disease~~ **usage as well as another draft guidance intended to provide recommendations to sponsors of anti- cancer** ~~drug~~ **drugs** ~~, government authorities and other stakeholders have been scrutinizing~~ **or biological products on considerations for designing trials intended to support accelerated approval. In response to scrutiny of** 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 FDORA (incorporated in** the 2023 Appropriations Act **)** revised **this** ~~the accelerated approval~~ pathway **to** ~~. Although this legislation did not change the standard for accelerated approval, it~~ , among other things: ~~requires~~ - **require** the FDA to specify the conditions for required post- marketing trials; ~~permits~~ - **permit** the FDA to require such trials to be underway prior to approval, or within a specific period after approval; ~~requires~~ - **require** 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~~ - **make** the failure to conduct required post- marketing trials with due diligence and the failure to submit the required reports prohibited acts; and ~~details~~ - **detail** procedures the FDA must follow to withdraw an accelerated approval on an expedited **basis. This legislation did not, however, change the standard for accelerated approval. Even prior to this legislation, the FDA had held Oncologic Drugs Advisory Committee meetings to discuss accelerated approvals for which confirmatory trials have not verified clinical benefit, resulting in voluntary withdrawals of certain products and indications approved on an accelerated** 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 **grants an accelerated** ~~approves~~ **approval for** cabozantinib ~~for~~ **in** one or more new indications or ~~approves~~ **for** one of our other product candidates, including zanzalintinib, ~~for use,~~ such **accelerated** 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 **or a comparable authority in another jurisdiction** in connection with a specific **accelerated** approval in accordance with the timelines and conditions set forth by the FDA **or comparable authority** 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 drug discovery, clinical development, business development and commercialization activities grow more quickly than the revenues we generate.** Although we reported net income of $ **207. 8 million and $** 182. 3 ~~million and $ 231. 1~~ million for the fiscal years ended December 31, **2023 and** 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 **and commercialization** 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 **zanzalintinib and** 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. 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~~ **products or product** 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 **and development** 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; • **our research and in- licensing partners' failure to retain essential staff, which is crucial for fulfilling their obligations under our agreements; • the possibility that our research and in- licensing partners' technology may be superseded or otherwise no longer be competitive; •** 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 **or regions** 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~~ **Good Practice guidelines (GxP)** . 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~~ **or for zanzalintinib or our other** 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..... 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~~ **who** 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. 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 ~~our own current GMP~~ 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 ~~mostly~~ 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 ~~are~~ **continue to** ~~expanding~~ --- **expand** ~~internal CMC development laboratories to augment~~ our ~~external network focusing on our product candidates.We expect this to enable us to maximize application of our internal expertise and scientific know- how and advance our product candidates more efficiently and with greater technical precision,speed,agility and quality,while working in close collaboration with our expanding external manufacturing and~~ supply chain ~~network~~ through additional third- party contract manufacturers,distributors and suppliers.To establish and manage our ~~manufacturing network and~~ 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 ~~legal and~~ regulatory requirements ~~,including the FDA' s current GMP,the EC' s Guidelines on GDP,as well as other stringent regulatory requirements enforced by the FDA or foreign regulatory agencies,as applicable.These third parties are also subject to routine inspections by the FDA and foreign regulatory agencies~~ .Although we maintain significant resources to directly and effectively oversee the activities and relationships with the **companies** ~~third parties~~ in our ~~network~~ **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** ~~hostilities in Eastern Europe and the Middle East or other global events~~ ,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.** 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. **We also conduct clinical trial activities outside the**

United States and are therefore subject to applicable laws in the countries where those operations take place. 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 **; • federal Civil Monetary Penalties law, including the beneficiary inducement provisions; • the Eliminating Kickbacks in Recovery Act** ; • 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; • **laws and regulations in effect in foreign jurisdictions where drug manufacturers, or third- party entities operating on behalf of drug manufacturers (including clinical research organizations), are conducting clinical trial activities; •** 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 **; and • European countries' national laws mandating public disclosure of transfers of value to healthcare professionals, healthcare organizations and other entities active in the healthcare sector, as well as requirements for prior review and / or approval of agreements with healthcare professionals** . In addition, we **are** ~~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 **periodic** donations to independent charitable foundations that help financially needy patients. These types of programs **are** designed to **provide financial** ~~assist~~ **assistance to** patients ~~with~~ **who might otherwise be unable to** ~~afford~~ --- **afford** pharmaceuticals **that they have been prescribed by their physicians and** 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~~ **arrangements** , 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 **MDRP** ~~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~~ **arrangements**) was challenged and vacated by a federal court in May 2022 ~~(~~ and **was not appealed. Additionally, in May 2023,** CMS ~~did not appeal). However, it is possible that CMS could issue~~ **issued a** new **proposed** rulemaking ~~or guidance~~ that would ~~affect~~ **repeal** the **changes implemented by** ~~amount of rebates owed under~~ the **court- vacated December 2020 final rule regarding co- payment assistance programs. The May 2023 CMS proposed rulemaking would, however, adopt significant new changes in the MDRP. The changes, if finalized as drafted, could ultimately have significant impacts on our** Medicaid **rebate** ~~program or otherwise limit our ability~~ **liability and potential exposure** to **penalties for MDRP participation** ~~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 **reimbursement and other product** support **programs** , 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 **and other product support** 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~~ **CCPA** 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 **became** ~~will be~~ enforceable in **certain** ~~most key~~ respects **in** ~~beginning on~~ July ~~1,~~ 2023 **, with the CPRA' s implementing regulations currently subject to a stay of enforcement until one year from their issuance** . 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~~ **cybersecurity incidents or threats** . 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 **cybersecurity incidents and threats, including** 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 **or other cybersecurity incidents** 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. 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 **certain** ~~" unfriendly~~ countries ~~"~~ (including the U. S.) in response to sanctions relating to the ongoing ~~Russo~~ **Russia** - ~~Ukrainian~~ **Ukraine** ~~War~~ **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~~ **human capital needs** , 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~~ **In January 2024, we announced** and **implemented a restructuring plan, including a reduction** ~~expect to continue to experience growth in the number~~ of our **employee workforce by approximately 175** employees ~~and in the scope of our~~ **or** ~~operations, in particular as~~ **13 % of our total headcount. As** we continue to grow our pipeline of product candidates ~~. This~~ **, our clinical development organization and related functions may** ~~growth~~ **grow, which may** ~~places~~ **place** significant demands on our management and resources, and our current and planned personnel and operating practices may not be adequate to support ~~our~~ **such** growth. To effectively manage our ~~growth~~ **evolving human capital needs** , we must continue to improve existing, and **when necessary,** 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~~ **can do so** effectively ~~manage our~~ **or avoid** ~~growth without~~ experiencing operating inefficiencies or control deficiencies. We continue to ~~increase~~ **rely on** our management personnel to oversee our ~~expanding~~ operations, and **retaining and** recruiting ~~and retaining~~ qualified individuals is difficult. If we are unable to manage our ~~growth~~ **human capital needs** effectively, or **if** we are unsuccessful in **retaining or** recruiting qualified management personnel, there could be a material adverse impact on our business, financial condition and results of 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 **, zanzalintinib** and our other product candidates, successfully executing upon our commercialization plan for the cabozantinib franchise and **continuing** 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. **In addition, our reduction in force announced in January 2024, and any future restructuring plans intended to improve operational efficiencies and operating costs, may adversely affect our ability to attract and retain employees.** ~~Further~~ **Furthermore** , 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; • **the announcement of a repurchase of our common stock; •** 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 **a** 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, **the Federal Reserve interest rate increases,** as well as policies governing foreign trade and healthcare spending and delivery, or the ongoing ~~Russo- Ukrainian War~~ **hostilities in Eastern Europe and the Middle East** , 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. **Governments, investors and other stakeholders are increasingly focusing on environmental, social and governance (ESG) practices and disclosures. Expectations in this area are rapidly evolving and growing, and new ESG laws and regulations are expanding mandatory disclosure, reporting and diligence requirements. We manage, track and report on our ESG goals and objectives, including in our Corporate Values & Sustainability Report or as may be required in our annual and quarterly reports. Our efforts to accomplish and report on these goals and objectives subjects us to risks, any of which could have a material adverse impact on our business, including specifically market perception and the market price of our common stock. Such risks may be outside of our control and the criteria by which our ESG practices and disclosures are assessed may change due to the evolving regulatory requirements affecting ESG standards and disclosures, which could result in increased expectations for us with respect to ESG matters and cause us to undertake costly initiatives to satisfy such new criteria. Our failure or perceived failure to pursue or achieve our ESG goals and objectives, or to maintain our ESG practices that meet evolving stakeholder expectations or expanding legal requirements, could have a material adverse impact on our market perception and stock price, as well as expose us to government enforcement actions and private litigation.**