Exelixis Announces Detailed Phase 1b Results from Cohort 6 of COSMIC-021 Trial in Patients with Metastatic Castration-Resistant Prostate Cancer Presented at ESMO 2021

September 18, 2021

– New results for cabozantinib in combination with atezolizumab demonstrate a median progression-free survival in high-risk patients of 6.8 months as assessed by Blinded Independent Radiology Committee –

ALAMEDA, Calif.--(BUSINESS WIRE)--Sep. 18, 2021-- Exelixis, Inc. (Nasdaq: EXEL) today announced detailed results from the expanded cohort 6 of the phase 1b COSMIC-021 trial of cabozantinib (CABOMETYX®) in combination with atezolizumab in patients with metastatic castration-resistant prostate cancer (CRPC). Cohort 6 included patients with metastatic CRPC who had been previously treated with the novel hormone therapies (NHT) enzalutamide and/or abiraterone acetate used along with prednisone. The data are being presented during the Proffered Paper Session: GU Tumours, Prostate today at 1:30 p.m. CEST at the 2021 European Society of Medical Oncology (ESMO) Congress (LBA24).

Eligible patients in the trial had measurable disease per Response Evaluation Criteria in Solid Tumors (RECIST v 1.1) per investigator assessment, had progressed on prior NHT, and could have received prior docetaxel for metastatic hormone-sensitive disease. The analysis included 132 patients with metastatic CRPC, 101 of whom were high-risk, which was defined as having measurable visceral metastases and/or extrapelvic lymphadenopathy. The median follow-up for all patients was 15.2 months, and the primary endpoint was objective response rate (ORR) by investigator per RECIST 1.1.

As previously announced, in the high-risk patient population, investigator-assessed ORR was 27%, including 2% complete responses (CRs). The Blinded Independent Radiology Committee (BIRC)-assessed ORR was 18%, all partial responses (PRs). The disease control rate (CR + PR + stable disease) was 88% by investigator assessment and 84% by BIRC assessment.

New detailed results being presented at the 2021 ESMO Congress demonstrate that median progression-free survival per RECIST 1.1 for the high-risk population was 5.6 months (95% confidence interval [CI]: 5.4-8.2) as assessed by investigators and 6.8 months (95% CI: 5.5-9.7) as assessed by BIRC. The exploratory endpoint of overall survival for the high-risk patient population was 18.4 months (95% CI: 13.6-24.7). Tumor PD-L1 status, which was known for 75 patients, was not associated with response.

“These detailed results confirm previous findings from cohort 6 of COSMIC-021, further suggesting the promise cabozantinib in combination with atezolizumab may hold for patients with high-risk metastatic castration-resistant prostate cancer whose disease progressed following treatment with novel hormone therapy,” said Neeraj Agarwal, M.D., Professor of Medicine, Huntsman Cancer Institute, University of Utah and a trial investigator. “A significant number of these patients are looking for treatment options beyond chemotherapy, so these clinically meaningful response rates and progression-free survival results of cabozantinib in combination with atezolizumab are encouraging for this patient community and their physicians.”

The safety profile was consistent with that previously observed for each single agent. No new safety signals were observed. Discontinuation of both agents due to treatment-related adverse events (AEs) occurred in 10% of patients. Frequent treatment-related AEs were diarrhea (55%), fatigue (43%), nausea (42%) and decreased appetite (34%). Grade 3 or 4 treatment-related AEs occurred in 55% of patients (of which 3% experienced grade 4 AEs), and one grade 5 treatment-related AE was reported.

Following discussions with the U.S. Food and Drug Administration (FDA), Exelixis will not pursue a regulatory submission for the combination regimen based on cohort 6 of the COSMIC-021 trial. The CONTACT-02 study, a global phase 3 pivotal trial, initiated enrollment in June 2020 and is evaluating cabozantinib in combination with atezolizumab versus a second NHT in patients with metastatic CRPC who have been previously treated with one NHT. Pending results, CONTACT-02 may serve as a basis for future regulatory applications in this setting.

“We are pleased to provide a more detailed picture at ESMO of cabozantinib in combination with atezolizumab in patients with metastatic castration-resistant prostate cancer who are in need of additional treatment options,” said Michael M. Morrissey, Ph.D., President and Chief Executive Officer, Exelixis. “The benefits of this combination regimen are encouraging, and we remain steadfast in our commitment to addressing unmet needs for patients with this form of prostate cancer. The CONTACT-02 continues to enroll patients, and we eagerly await a future readout from this global, phase 3 pivotal trial as we advance our goal of bringing treatments to patients with advanced, difficult-to-treat cancers.”

About COSMIC-021

COSMIC-021 is a multicenter, phase 1b, open-label study that is divided into two parts: a dose-escalation phase and an expansion cohort phase. The dose-escalation phase was designed to enroll patients either with advanced renal cell carcinoma (RCC) with or without prior systemic therapy or with inoperable, locally advanced, metastatic or recurrent urothelial carcinoma (UC), (including renal, pelvis, ureter, urinary bladder and urethra) after prior platinum-based therapy. Ultimately, all 12 patients who enrolled in this stage of the trial were patients with advanced RCC. The dose-escalation phase of the study determined the recommended dose of cabozantinib to be 40 mg daily when given in combination with atezolizumab (1200 mg infusion once every three weeks).

In the expansion phase, the trial is enrolling 24 cohorts in 12 tumor types: RCC, UC, non-small cell lung cancer (NSCLC), CRPC, hepatocellular carcinoma (HCC), triple-negative breast cancer, epithelial ovarian cancer, endometrial cancer, gastric or gastroesophageal junction adenocarcinoma, colorectal adenocarcinoma, head and neck cancer, and differentiated thyroid cancer.

Four of the cohorts are exploratory single agent cohorts: two enrolled approximately 30 patients each with advanced UC or NSCLC, and one is enrolling approximately 80 patients with advanced CRPC to be treated with cabozantinib as a single-agent, and one enrolled approximately 10 patients with advanced CRPC to be treated with single-agent atezolizumab. Exploratory single agent cohorts have the option to be expanded up to 80

patients (cabozantinib) and 30 patients (atezolizumab) total.

Exelixis is the study sponsor of COSMIC-021. Both Ipsen Pharma SAS (Ipsen) and Takeda Pharmaceutical Company Limited (Takeda) have opted in to participate in the trial and are contributing to the funding for this study under the terms of the companies' respective collaboration agreements with Exelixis. Roche is providing atezolizumab for the trial.

About CRPC

According to the American Cancer Society, in 2021, approximately 250,000 new cases of prostate cancer will be diagnosed, and 34,000 people will die from the disease.[1] 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 metastatic CRPC.[2] Researchers estimate that in 2020, 43,000 people were diagnosed with metastatic CRPC, which has a median survival of less than two years.[3,4,5]

About CABOMETYX® (cabozantinib)

In the U.S., CABOMETYX tablets are approved for the treatment of patients with advanced renal cell carcinoma (RCC); for the treatment of patients with hepatocellular carcinoma who have been previously treated with sorafenib; for patients with advanced RCC as a first-line treatment in combination with nivolumab; and for adult and pediatric patients 12 years of age and older with locally advanced or metastatic differentiated thyroid cancer that has progressed following prior VEGFR-targeted therapy and who are radioactive iodine-refractory or ineligible. CABOMETYX tablets have also received regulatory approvals in the European Union and additional countries and regions worldwide. In 2016, Exelixis granted Ipsen exclusive rights for the commercialization and further clinical development of cabozantinib outside of the U.S. and Japan. In 2017, Exelixis granted exclusive rights to Takeda Pharmaceutical Company Limited for the commercialization and further clinical development of cabozantinib for all future indications in Japan. Exelixis holds the exclusive rights to develop and commercialize cabozantinib in the U.S.

CABOMETYX is not indicated as a treatment for metastatic CRPC.

IMPORTANT SAFETY INFORMATION

WARNINGS AND PRECAUTIONS

Hemorrhage: Severe and fatal hemorrhages occurred with CABOMETYX. The incidence of Grade 3 to 5 hemorrhagic events was 5% in CABOMETYX patients in RCC, HCC, and DTC studies. Discontinue CABOMETYX for Grade 3 or 4 hemorrhage and prior to surgery as recommended. Do not administer CABOMETYX to patients who have a recent history of hemorrhage, including hemoptysis, hematemesis, or melena.

Perforations and Fistulas: Fistulas, including fatal cases, occurred in 1% of CABOMETYX patients. Gastrointestinal (GI) perforations, including fatal cases, occurred in 1% of CABOMETYX patients. Monitor patients for signs and symptoms of fistulas and perforations, including abscess and sepsis. Discontinue CABOMETYX in patients who experience a Grade 4 fistula or a GI perforation.

Thrombotic Events: CABOMETYX increased the risk of thrombotic events. Venous thromboembolism occurred in 7% (including 4% pulmonary embolism) and arterial thromboembolism in 2% of CABOMETYX patients. Fatal thrombotic events occurred in CABOMETYX patients. Discontinue CABOMETYX in patients who develop an acute myocardial infarction or serious arterial or venous thromboembolic events that require medical intervention.

Hypertension and Hypertensive Crisis: CABOMETYX can cause hypertension, including hypertensive crisis. Hypertension was reported in 37% (16% Grade 3 and <1% Grade 4) of CABOMETYX patients. Do not initiate CABOMETYX in patients with uncontrolled hypertension. Monitor blood pressure regularly during CABOMETYX treatment. Withhold CABOMETYX for hypertension that is not adequately controlled with medical management; when controlled, resume at a reduced dose. Permanently discontinue CABOMETYX for severe hypertension that cannot be controlled with anti-hypertensive therapy or for hypertensive crisis.

Diarrhea: Diarrhea occurred in 62% of CABOMETYX patients. Grade 3 diarrhea occurred in 10% of CABOMETYX patients. Monitor and manage patients using antidiarrheals as indicated. Withhold CABOMETYX until improvement to ≤ Grade 1, resume at a reduced dose.

Palmar-Plantar Erythrodysesthesia (PPE): PPE occurred in 45% of CABOMETYX patients. Grade 3 PPE occurred in 13% of CABOMETYX patients. Withhold CABOMETYX until improvement to Grade 1 and resume at a reduced dose for intolerable Grade 2 PPE or Grade 3 PPE.

Hepatotoxicity: CABOMETYX in combination with nivolumab can cause hepatic toxicity with higher frequencies of Grades 3 and 4 ALT and AST elevations compared to CABOMETYX alone. Monitor liver enzymes before initiation of and periodically throughout treatment. Consider more frequent monitoring of liver enzymes than when the drugs are administered as single agents. For elevated liver enzymes, interrupt CABOMETYX and nivolumab and consider administering corticosteroids.

With the combination of CABOMETYX and nivolumab, Grades 3 and 4 increased ALT or AST were seen in 11% of patients. ALT or AST >3 times ULN (Grade ≥2) was reported in 83 patients, of whom 23 (28%) received systemic corticosteroids; ALT or AST resolved to Grades 0-1 in 74 (89%). Among the 44 patients with Grade ≥2 increased ALT or AST who were rechallenged with either CABOMETYX (n=9) or nivolumab (n=11) as a single agent or with both (n=24), recurrence of Grade ≥2 increased ALT or AST was observed in 2 patients receiving CABOMETYX, 2 patients receiving nivolumab, and 7 patients receiving both CABOMETYX and nivolumab. Withhold and resume at a reduced dose based on severity.

Adrenal Insufficiency: CABOMETYX in combination with nivolumab can cause primary or secondary adrenal insufficiency. For Grade 2 or higher adrenal insufficiency, initiate symptomatic treatment, including hormone replacement as clinically indicated. Withhold CABOMETYX and/or nivolumab and resume CABOMETYX at a reduced dose depending on severity.

Adrenal insufficiency occurred in 4.7% (15/320) of patients with RCC who received CABOMETYX with nivolumab, including Grade 3 (2.2%), and Grade 2 (1.9%) adverse reactions. Adrenal insufficiency led to permanent discontinuation of CABOMETYX and nivolumab in 0.9% and withholding of CABOMETYX and nivolumab in 2.8% of patients with RCC.

Approximately 80% (12/15) of patients with adrenal insufficiency received hormone replacement therapy, including systemic corticosteroids. Adrenal insufficiency resolved in 27% (n=4) of the 15 patients. Of the 9 patients in whom CABOMETYX with nivolumab was withheld for adrenal insufficiency, 6

reinstated treatment after symptom improvement; of these, all (n=6) received hormone replacement therapy and 2 had recurrence of adrenal insufficiency.

Proteinuria: Proteinuria was observed in 8% of CABOMETYX patients. Monitor urine protein regularly during CABOMETYX treatment. For Grade 2 or 3 proteinuria, withhold CABOMETYX until improvement to ≤ Grade 1 proteinuria, resume CABOMETYX at a reduced dose. Discontinue CABOMETYX in patients who develop nephrotic syndrome.

Osteonecrosis of the Jaw (ONJ): ONJ occurred in <1% of CABOMETYX patients. ONJ can manifest as jaw pain, osteomyelitis, osteitis, bone erosion, tooth or periodontal infection, toothache, gingival ulceration or erosion, persistent jaw pain, or slow healing of the mouth or jaw after dental surgery. Perform an oral examination prior to CABOMETYX initiation and periodically during treatment. Advise patients regarding good oral hygiene practices. Withhold CABOMETYX for at least 3 weeks prior to scheduled dental surgery or invasive dental procedures, if possible. Withhold CABOMETYX for development of ONJ until complete resolution, resume at a reduced dose.

Impaired Wound Healing: Wound complications occurred with CABOMETYX. Withhold CABOMETYX for at least 3 weeks prior to elective surgery. Do not administer CABOMETYX for at least 2 weeks after major surgery and until adequate wound healing. The safety of resumption of CABOMETYX after resolution of wound healing complications has not been established.

Reversible Posterior Leukoencephalopathy Syndrome (RPLS): RPLS, a syndrome of subcortical vasogenic edema diagnosed by characteristic findings on MRI, can occur with CABOMETYX. Evaluate for RPLS in patients presenting with seizures, headache, visual disturbances, confusion, or altered mental function. Discontinue CABOMETYX in patients who develop RPLS.

Thyroid Dysfunction: Thyroid dysfunction, primarily hypothyroidism, has been observed with CABOMETYX. Based on the safety population, thyroid dysfunction occurred in 19% of patients treated with CABOMETYX, including Grade 3 in 0.4% of patients.

Patients should be assessed for signs of thyroid dysfunction prior to the initiation of CABOMETYX and monitored for signs and symptoms of thyroid dysfunction during CABOMETYX treatment. Thyroid function testing and management of dysfunction should be performed as clinically indicated.

Hypocalcemia: CABOMETYX can cause hypocalcemia. Based on the safety population, hypocalcemia occurred in 13% of patients treated with CABOMETYX, including Grade 3 in 2% and Grade 4 in 1% of patients. Laboratory abnormality data were not collected in CABOSUN.

In COSMIC-311, hypocalcemia occurred in 36% of patients treated with CABOMETYX, including Grade 3 in 6% and Grade 4 in 3% of patients.

Monitor blood calcium levels and replace calcium as necessary during treatment. Withhold and resume at reduced dose upon recovery or permanently discontinue CABOMETYX depending on severity.

Embryo-Fetal Toxicity: CABOMETYX can cause fetal harm. Advise pregnant women and females of reproductive potential of the potential risk to a fetus. Verify the pregnancy status of females of reproductive potential prior to initiating CABOMETYX and advise them to use effective contraception during treatment and for 4 months after the last dose.

ADVERSE REACTIONS

The most common (≥20%) adverse reactions are:

CABOMETYX as a single agent: diarrhea, fatigue, PPE, decreased appetite, hypertension, nausea, vomiting, weight decreased, constipation.

CABOMETYX in combination with nivolumab: diarrhea, fatigue, hepatotoxicity, PPE, stomatitis, rash, hypertension, hypothyroidism, musculoskeletal pain, decreased appetite, nausea, dysgeusia, abdominal pain, cough, and upper respiratory tract infection.

DRUG INTERACTIONS

Strong CYP3A4 Inhibitors: If coadministration with strong CYP3A4 inhibitors cannot be avoided, reduce the CABOMETYX dosage. Avoid grapefruit or grapefruit juice.

Strong CYP3A4 Inducers: If coadministration with strong CYP3A4 inducers cannot be avoided, increase the CABOMETYX dosage. Avoid St. John's wort.

USE IN SPECIFIC POPULATIONS

Lactation: Advise women not to breastfeed during CABOMETYX treatment and for 4 months after the final dose.

Hepatic Impairment: In patients with moderate hepatic impairment, reduce the CABOMETYX dosage. Avoid CABOMETYX in patients with severe hepatic impairment.

Please see accompanying full Prescribing Information https://www.cabometyx.com/downloads/CABOMETYXUSPI.pdf.

You are encouraged to report negative side effects of prescription drugs to the FDA. Visit www.FDA.gov/medwatch or call 1-800-FDA-1088.

About Exelixis

Founded in 1994, Exelixis, Inc. (NASDAQ: EXEL) is a commercially successful, oncology-focused biotechnology company that strives to accelerate the discovery, development and commercialization of new medicines for difficult-to-treat cancers. Following early work in model system genetics, we established a broad drug discovery and development platform that has served as the foundation for our continued efforts to bring new cancer therapies to patients in need. Our discovery efforts have resulted in four commercially available products, CABOMETYX® (cabozantinib), COMETRIQ® (cabozantinib), COTELLIC® (cobimetinib) and MINNEBRO® (esaxerenone), and we have entered into partnerships with leading pharmaceutical companies to bring these important medicines to patients worldwide. Supported by revenues from our marketed products and collaborations, we are committed to prudently reinvesting in our business to maximize the potential of our pipeline. We are supplementing our existing therapeutic assets with targeted business development activities and internal drug discovery — all to deliver the next generation of Exelixis medicines

and help patients recover stronger and live longer. Exelixis is a member of the Standard & Poor's (S&P) MidCap 400 index, which measures the performance of profitable mid-sized companies. In November 2020, the company was named to *Fortune*'s 100 Fastest-Growing Companies list for the first time, ranking 17th overall and the third-highest biopharmaceutical company. For more information about Exelixis, please visit www.exelixis.com, follow @ExelixisInc on Twitter or like Exelixis, Inc. on Facebook.

Exelixis Forward-Looking Statements

This press release contains forward-looking statements, including, without limitation, statements related to: the presentation of data from cohort 6 of COSMIC-021 at ESMO 2021; the therapeutic potential of cabozantinib in combination with atezolizumab for patients with high-risk metastatic CRPC whose disease progressed following treatment with novel hormone therapy; Exelixis' plan not pursue a regulatory submission for the combination of cabozantinib and atezolizumab based on cohort 6 of COSMIC-021; Exelixis' commitment to addressing unmet needs for patients with metastatic CRPC and its belief that, pending results, CONTACT-02 may serve as a basis for future regulatory applications in the metastatic CRPC setting; Exelixis' goal of bringing treatments to patients with advanced, difficult-to-treat cancers; and Exelixis' plans to reinvest in its business to maximize the potential of the company's pipeline, including through targeted business development activities and internal drug discovery. Any statements that refer to expectations, projections or other characterizations of future events or circumstances are forward-looking statements and are based upon Exelixis' current plans, assumptions, beliefs, expectations, estimates and projections. Forward-looking statements involve risks and uncertainties. Actual results and the timing of events could differ materially from those anticipated in the forward-looking statements as a result of these risks and uncertainties, which include, without limitation: the availability of data at the referenced times; the potential failure of cabozantinib in combination with atezolizumab to demonstrate safety and/or efficacy in clinical testing; unexpected concerns that may arise as a result of the occurrence of adverse safety events or additional data analyses of clinical trials evaluating cabozantinib; uncertainties inherent in the product development process; complexities and the unpredictability of the regulatory review and approval processes in the U.S. and elsewhere; Exelixis' dependence on its relationships with its cabozantinib collaboration partners, including the level of their investment in the resources necessary to successfully commercialize cabozantinib or atezolizumab or the combination of these two drugs in the territories where approved; the continuing COVID-19 pandemic and its impact on Exelixis' product development and commercial activities; Exelixis' continuing compliance with applicable legal and regulatory requirements; Exelixis' dependence on third-party vendors for the development, manufacture and supply of cabozantinib; Exelixis' ability to protect its intellectual property rights; market competition, including the potential for competitors to obtain approval for generic versions of CABOMETYX; changes in economic and business conditions, including as a result of the COVID-19 pandemic; and other factors affecting Exelixis and its development programs discussed under the caption "Risk Factors" in Exelixis' Quarterly Report on Form 10-Q filed with the Securities and Exchange Commission (SEC) on August 5, 2021, and in Exelixis' future filings with the SEC. All forward-looking statements in this press release are based on information available to Exelixis as of the date of this press release, and Exelixis undertakes no obligation to update or revise any forward-looking statements contained herein, except as required by law.

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[1] American Cancer Society: Cancer Facts & Figures 2021. Available at: https://www.cancer.org/content/dam/cancer-org/research/cancer-facts-and-statistics/annual-cancer-facts-and-figures/2021/cancer-facts-and-figures-2021.pdf. Accessed September 2021.

[2] American Society of Clinical Oncology. Cancer.Net. Treatment of Metastatic Castration-Resistant Prostate Cancer. September 8, 2014. Available at: https://www.cancer.net/research-and-advocacy/asco-care-and-treatment-recommendations-patients/treatment-metastatic-castration-resistant-prostate-cancer. Accessed September 2021.

[3] Scher, H.I., Solo, K., Valant, J., Todd, M.B., Mehra, M. Prevalence of Prostate Cancer Clinical States and Mortality in the United States: Estimates Using a Dynamic Progression Model. *PLOS ONE*. 2015; 10: e0139440.

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[5] Moreira, D. M., Howard, L. E., Sourbeer, K. N., et al. Predicting Time From Metastasis to Overall Survival in Castration-Resistant Prostate Cancer: Results From SEARCH. *Clin Genitourin Cancer*. 2017; 15: 60–66.e2.

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