Exelixis Announces Dose-Escalation Results from the Phase 1 STELLAR-001 Trial Evaluating XL092 Alone and in Combination with an Immune Checkpoint Inhibitor in Patients with Advanced Solid Tumors at ESMO 2022

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– Both single-agent XL092 and XL092 in combination with atezolizumab demonstrated encouraging efficacy and safety in a heavily pretreated patient population –

– XL092 demonstrated preliminary clinical activity similar to that observed with cabozantinib in phase 1 across a range of solid tumors and dose levels, with a manageable safety profile –

– Based on the results, the 100 mg dose of XL092 was selected for the expansion phase, which is ongoing in a number of solid tumor types –

ALAMEDA, Calif.--(BUSINESS WIRE)--Sep. 10, 2022-- Exelixis, Inc. (Nasdaq: EXEL) today announced results from the dose-escalation stage of STELLAR-001, an ongoing phase 1b trial evaluating XL092 as a single-agent and in combination with atezolizumab in patients with locally advanced or metastatic solid tumors. The data are being presented on Monday, September 12 during the Poster Session (481P) at 12:00 p.m. CEST at the 2022 European Society of Medical Oncology (ESMO) Congress.

"We are pleased to present these findings from the dose-escalation stage of STELLAR-001 at ESMO, which show XL092 demonstrated preliminary clinical activity similar to that observed with cabozantinib in phase 1 across a range of solid tumors and dose levels, with a manageable safety profile," said Vicki L. Goodman, M.D., Executive Vice President, Product Development & Medical Affairs, and Chief Medical Officer, Exelixis. "We are particularly encouraged by the activity of XL092 in heavily pretreated renal cell carcinoma patients who have received prior treatment with immunotherapy and/or VEGF-targeting tyrosine kinase inhibitors, including approximately 70% of patients who received cabozantinib as a prior treatment. As we continue to enroll in the cohort-expansion stage across multiple solid tumors, we look forward to gaining additional insight into the potential of XL092 alone and in combination with immune checkpoint inhibitors as a potential new therapy for people with cancer in need of new treatment options."

STELLAR-001 enrolled patients with advanced solid tumors for which standard of care did not exist or was not effective. For this analysis, patients received XL092 either as a single-agent (n=47) or in combination with atezolizumab (n=40). The most common types of cancer for patients enrolled in the single-agent XL092 cohort were clear cell renal cell carcinoma (RCC), metastatic castration-resistant prostate cancer (CRPC) and breast cancer. The most common types of cancer for patients enrolled in the XL092 in combination with atezolizumab cohort were colorectal cancer, metastatic CRPC and sarcoma. The median duration of follow-up was 17.9 months and 6.0 months for those receiving single-agent XL092 and XL092 in combination with atezolizumab, respectively. Median age was 61 years for those receiving single-agent XL092 and 59 years for those receiving XL092 in combination with atezolizumab; 62% and 55% of patients, respectively, had an Eastern Cooperative Oncology Group score of 1. In each arm, 68% of patients had at least three prior lines of therapy.

The maximum tolerated dose was determined to be 120 mg, and the recommended dose for the expansion phase is 100 mg for both single-agent XL092 and XL092 in combination with atezolizumab. Tumor reduction was seen in 71% of patients receiving single-agent XL092 and in 56% of patients receiving XL092 in combination with atezolizumab. The objective response rate (ORR) was 10% for single-agent XL092 and 4% for XL092 in combination with atezolizumab; disease control rate (DCR) (complete response + partial response + stable disease) was 90% and 74%, respectively. Confirmed partial responses were observed in four patients treated with single-agent XL092 and one patient treated with XL092 in combination with atezolizumab.

In the 19 patients with clear cell RCC who were heavily pretreated with immunotherapy and/or VEGF-targeting tyrosine kinase inhibitors (TKIs), including 68% who received prior cabozantinib, ORR was 11%, and DCR was 95% with single-agent XL092.

The activity of single-agent XL092, as measured by the percent of patients with reduction in tumor size (RTS), was similar to that observed with cabozantinib in phase 1 (trial identifier: XL184-011): XL092 demonstrated a 71% RTS versus a 74% RTS with cabozantinib; a greater than 30% RTS was seen in 15% of patients treated with XL092 versus 18% of those treated with cabozantinib.

Grade 3/4 treatment-emergent adverse events (AEs) occurred in 60% of those receiving single-agent XL092 and 38% of those receiving XL092 in combination with atezolizumab. The most common (≥5%) grade 3/4 treatment-emergent AEs for those receiving single-agent XL092 were hypertension (19%), diarrhea (9%) and fatigue (6%); for those receiving XL092 in combination with atezolizumab, they were hypertension (13%), abdominal pain (5%), fatigue (5%) and thrombocytopenia (5%). There were no grade 5 treatment-related AEs.

"These results show manageable tolerability along with promising early indications of activity for XL092, alone and in combination with atezolizumab, even in this heavily pretreated population of patients with a broad range of advanced tumors," said Manish R. Sharma, M.D., Associate Director of Clinical Research at START Midwest and lead author of the study. "We will continue enrolling for the expansion stage of this trial as we look to identify potential new therapies and combinations for our cancer patients."

About STELLAR-001

STELLAR-001 is a global, open-label phase 1b study of Exelixis' novel TKI XL092 as a single agent or in combination with atezolizumab or avelumab in patients with inoperable locally advanced or metastatic solid tumors. The trial plans to enroll 800 patients and is divided into two parts: a dose-escalation stage and an expansion cohort stage.

The expansion cohorts evaluating XL092 as a single agent or in combination with atezolizumab include patients with: RCC with clear cell histology, RCC with non-clear cell histology, breast cancer that is hormone receptor-positive and HER-2 negative, CRPC and CRC. The expansion cohorts evaluating XL092 in combination with avelumab will enroll patients with urothelial carcinoma.

More information about the trial is available at ClinicalTrials.gov.

About XL092

XL092 is a next-generation oral TKI that inhibits the activity of receptor tyrosine kinases implicated in cancer growth and spread, including VEGF receptors, MET, AXL and MER. These receptor tyrosine kinases are involved in both normal cellular function and in pathologic processes such as oncogenesis, metastasis, tumor angiogenesis, and resistance to multiple therapies, including immune checkpoint inhibitors. In designing XL092, Exelixis sought to build upon its extensive experience with and the target profile of cabozantinib, the company's flagship medicine, while improving key characteristics, including pharmacokinetic half-life. XL092 is currently being developed for the treatment of advanced solid tumors, including genitourinary cancers, as a monotherapy and in combination with immune checkpoint inhibitors. XL092 is the first internally discovered Exelixis compound to enter the clinic following the company's reinitiation of drug-discovery activities.

About CABOMETYX® (cabozantinib)

In the U.S., CABOMETYX tablets are approved for the treatment of patients with advanced RCC; for the treatment of patients with hepatocellular carcinoma (HCC) 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 (DTC) 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 Pharma SAS 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.

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. For more information about Exelixis, please visit www.exelixis.com, follow @ExelixisInc on Twitter or like Exelixis, Inc. on Facebook.

Forward-Looking Statements

This press release contains forward-looking statements, including, without limitation, statements related to: the presentation of data from STELLAR-001 during the Poster Session at the 2022 ESMO Congress; the therapeutic potential of XL092, both alone and in combination with immune checkpoint inhibitors, as a therapy for cancer patients in need of new treatment options; 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; complexities and the unpredictability of the regulatory review and approval processes in the U.S. and elsewhere; Exelixis' continuing compliance with applicable legal and regulatory requirements; the potential failure of XL092 as a single agent or in combination with atezolizumab to demonstrate safety and/or efficacy in STELLAR-001 and in future 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 XL092; the costs of conducting clinical trials; Exelixis' dependence on third-party vendors for the development, manufacture and supply of XL092; Exelixis' ability to protect its intellectual property rights; market competition; changes in economic and business conditions, including as a result of the COVID-19 pandemic and other global events; 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 9, 2022, 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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