Exelixis Announces Initial Dose-Escalation Results from the First-in-Human Phase 1 Trial Evaluating XL102 in Patients with Advanced Solid Tumors at SABCS 2022

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– In the QUARTZ-101 trial, XL102 — a novel cyclin-dependent kinase 7 inhibitor — was well tolerated at evaluated dose levels –

ALAMEDA, Calif.--(BUSINESS WIRE)--Dec. 8, 2022-- Exelixis, Inc. (Nasdaq: EXEL) today announced initial results from the ongoing dose-escalation stage of QUARTZ-101, a phase 1 clinical trial evaluating XL102, a potent, selective, irreversible and orally bioavailable small molecule cyclin-dependent kinase 7 (CDK7) inhibitor, in patients with advanced solid tumors. The data are being presented on Thursday, December 8 during the poster session (abstract P4-01-35) at 7:00 a.m. CST at the 2022 San Antonio Breast Cancer Symposium (SABCS).

“Preclinical data for XL102 showed anti-proliferative activity and an ability to induce cell death across various cancer cell lines,” said Amita Patnaik, M.D., Co-Director of Clinical Research at the START San Antonio Center for Cancer Care and lead author of the study. “With the initial dose-escalation results now in hand, I am excited to explore further in the QUARTZ-101 trial how XL102 may benefit patients with advanced solid tumors who have exhausted treatment options.”

QUARTZ-101 is enrolling patients with solid tumors that are confirmed to be inoperable, locally advanced, metastatic or recurrent. As of the September 7, 2022 data cutoff, 26 enrolled patients had been treated with single-agent oral XL102 at five dose levels: 20 mg once daily (n=3), 40 mg once daily (n=3), 80 mg once daily (n=7), 120 mg once daily (n=4) and 40 mg twice daily (n=9). The most common types of cancer for patients enrolled were hormone receptor-positive breast cancer (n=12), pancreatic cancer (n=3) and sarcoma (n=3). Median age was 63 years. Seventy-three percent of patients had an Eastern Cooperative Oncology Group score of 1, and 77% had received at least three prior lines of systemic anti-cancer therapy for metastatic disease.

“We are pleased to share these data from QUARTZ-101 at SABCS, providing a first look of our novel CDK7 inhibitor in heavily pretreated patients with advanced cancers,” said Vicki L. Goodman, M.D., Executive Vice President, Product Development & Medical Affairs, and Chief Medical Officer, Exelixis. “As the trial continues, we look forward to learning more about the potential of XL102, alone and in combination, across various cancer types that have strong unmet treatment needs, including metastatic breast cancer.”

A pharmacokinetic analysis demonstrated rapid absorption of XL102 with a T_{max} of 1-3 hours and an elimination half-life of 5-9 hours. At day 28, AUC_{0-24} was doubled with the 40 mg twice-daily dose level versus the 40 mg once-daily dose level, supporting twice-daily oral dosing. Target occupancy was exposure-dependent and prolonged relative to XL102 pharmacokinetics, consistent with covalent binding to CDK7.

The median duration of exposure was 9.1 weeks. XL102 was well tolerated at the dose levels evaluated. Dose reductions and dose delays due to a treatment-emergent adverse event (TEAE) occurred in 8% and 35% of patients, respectively; rates were highest with the 80 mg once-daily dose. The most common reasons for discontinuation were radiographic progression (42%), adverse events (12%), lack of clinical benefit (8%) and patient request (8%).

The most common TEAEs of any grade were diarrhea (42%), nausea (38%), fatigue (35%), anemia (27%) and vomiting (23%). TEAEs were generally grade 1 or 2. In the cohort of patients receiving the 40 mg twice-daily dose, one patient experienced dose-limiting toxicity (grade 4 alanine aminotransferase and grade 3 aspartate aminotransferase elevations), which was reversible and led to full recovery. Other grade 3 TEAEs were anemia, ascites, blood alkaline phosphatase increased, fatigue, gastric varices, hyperkalemia, hypertension and hypokalemia. There were no grade 5 treatment-related adverse events. The maximum tolerated dose and recommended phase 2 dose have not yet been determined.

As of data cutoff, no objective responses had been observed. Two patients with stable disease remain on study treatment as of the data cutoff: one with breast cancer and one with liposarcoma, with treatment durations of 46 and 45 weeks, respectively. One additional patient with breast cancer achieved durable stable disease as the best response and discontinued study treatment at 25 weeks. The efficacy of XL102 will be further evaluated in additional patients in the single-agent dose-escalation cohorts, in the tumor-specific cohort-expansion stage and in planned combination studies.

About QUARTZ-101

QUARTZ-101 is a phase 1, open-label dose-escalation and cohort-expansion study evaluating the safety, tolerability, pharmacokinetics, anti-tumor activity and effect on biomarkers of XL102 administered alone and in multiple combination regimens in up to 298 patients with advanced solid tumors. The study includes patients with advanced solid tumors for whom either life-prolonging therapies do not exist or available therapies are intolerable or no longer effective. The first phase is a dose-escalation stage to determine the maximum tolerated dose and/or recommended oral dose of XL102 as a single agent and in combination therapy. In the subsequent cohort-expansion stage, XL102 will be evaluated in patients with certain types of ovarian, breast and prostate cancers. The goal of the cohort-expansion stage is to evaluate the anti-tumor activity of XL102, as assessed per the Response Evaluation Criteria in Solid Tumors (RECIST) version 1.1, as well as its safety, tolerability and pharmacokinetic profile.

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

About XL102

XL102 is a potent, selective and orally bioavailable small molecule CDK7 inhibitor, which is an important regulator of the cellular transcriptional and cell cycle machinery. CDK7 helps regulate cell cycle progression, with overexpression observed in multiple cancers, such as breast, prostate and ovarian cancers. XL102 is currently being developed for advanced or metastatic solid tumors. Preclinical studies demonstrated XL102 has anti-proliferative activity and can induce cell death in multiple cancer cell lines. XL102 was in-licensed as part of a collaboration with Aurigene Discovery Technologies Limited.

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 QUARTZ-101 during the poster session at the 2022 SABCS; the therapeutic potential of XL102 as a new treatment for people with advanced solid tumors who have exhausted treatment options; Exelixis' future development plans for XL102 in the QUARTZ-101 study; 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 XL102 to demonstrate safety and/or efficacy in QUARTZ-101 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 XL102; the costs of conducting clinical trials; Exelixis' dependence on third-party vendors for the development, manufacture and supply of XL102; 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 November 1, 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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