Exelixis Announces Promising Initial Dose-Escalation Results from the First-in-Human Phase 1 JEWEL-101 Trial Evaluating XB002 in Patients with Advanced Solid Tumors at ENA 2022

October 26, 2022

– XB002, a next-generation tissue factor-targeting antibody-drug conjugate, was well-tolerated at multiple dose levels –

– Pharmacokinetic analysis confirmed XB002 was stable with low levels of free payload –

ALAMEDA, Calif.--(BUSINESS WIRE)--Oct. 26, 2022-- Exelixis, Inc. (Nasdaq: EXEL) today announced promising initial results from the ongoing dose-escalation stage of JEWEL-101, a phase 1 study evaluating XB002, Exelixis' next-generation tissue factor-targeting antibody-drug conjugate. The data are being presented on Friday, October 28 during the Antibody-drug Conjugates Poster Session (abstract 256) at 10:00 a.m. CEST at the 34th Symposium on Molecular Targets and Cancer Therapeutics hosted by the European Organisation for Research and Treatment of Cancer (EORTC), the National Cancer Institute (NCI) and the American Association for Cancer Research (AACR).

"Following promising preclinical data, it is encouraging to see that XB002 was well-tolerated across multiple dose levels with a pharmacokinetic analysis supporting the ability of XB002 to remain stable after infusion and reach its target before releasing its cytotoxic payload," said Susanna Ulahannan, M.D., M.Med., Assistant Professor of Medicine in the Section of Hematology/Oncology, University of Oklahoma College of Medicine and Associate Director of Oklahoma TSET Phase 1 Program, OU Health Stephenson Cancer Center at the OU Health Sciences Center. "As the dose-escalation phase progresses, and we initiate enrollment into tumor specific cohorts, I look forward to learning more about how XB002 may benefit people with advanced solid tumors, in particular in tumor types with high unmet need."

JEWEL-101 is enrolling patients with advanced solid tumors for which therapies are unavailable, ineffective or intolerable. A total of 19 patients were enrolled across five initial escalating doses: 0.16 mg/kg (n=3), 0.5 mg/kg (n=3), 1.0 mg/kg (n=6), 1.5 mg/kg (n=3) and 2.0 mg/kg (n=4). The most common types of cancer for patients enrolled were pancreatic cancer, colorectal cancer, cervical cancer and prostate cancer. Median age was 63 years, and 63% of patients had an Eastern Cooperative Oncology Group score of 1. Seventy-nine percent of patients had at least three prior lines of therapy.

"We are pleased to present the first clinical profile of XB002 at ENA 2022, representing an important milestone for our first biologic in clinical development," said Vicki L. Goodman, M.D., Executive Vice President, Product Development & Medical Affairs, and Chief Medical Officer, Exelixis. "We are eager to proceed to the expansion cohort stage of JEWEL-101 once the recommended dose is determined, as we aim to further understand the activity of this molecule as a potential new treatment for people who have difficult-to-treat tumors with limited treatment options."

The recommended dose and maximum tolerated dose for XB002 have not yet been determined. As of the data cutoff, there were no dose-limiting toxicities. The primary reasons for treatment discontinuation included radiographic progression (47%), treatment-emergent adverse events (AEs; 11%), lack of clinical benefit (11%) and patient request other than AEs (16%).

A pharmacokinetic analysis demonstrated that XB002 exposure increased more than or proportionately to a dose increase from 0.16 mg/kg to 2.0 mg/kg. XB002 total antibody and intact antibody-drug conjugate pharmacokinetics were similar, suggesting XB002 is stable after infusion. Levels of free payload remained low (<1 ng/mL) at all dose levels. At 2.0 mg/kg, mean $AUC_{0\text{-}t}$ was 121 µg·day/mL for intact antibody-drug conjugate and 4.21 ng·day/mL for free payload; mean C_{max} was 46.6 µg/mL and 0.809 ng/mL, respectively.

Grade 3 treatment-emergent AEs were experienced by 42% of patients; there were no grade 4 or 5 treatment-emergent AEs. Treatment-related AEs were experienced by 63% of patients; all were grade 2 or lower, except for one grade 3 event (hypertension), and improved or resolved prior to the next XB002 dose. Serious AEs were experienced by 16% of patients, and all were considered unrelated to XB002; two patients had grade 3 events (COVID-19 pneumonia and diarrhea), and one patient had grade 2 bacteremia. No bleeding events occurred despite the use of anticoagulant agents in 8 patients (42%).

Ocular treatment-emergent AEs were experienced by 42% of patients, with noninfective conjunctivitis (26%) and dry eye (16%) considered related to XB002 treatment. Incidence of ocular events was higher at the 2 mg/kg dose level (75%) than at the other dose levels (33%). No corneal toxicity was observed. All ocular events were reversible with supportive care, which included lubricating, vasoconstrictive, corticosteroid and/or antibiotic eyedrops.

No objective responses were observed. Three patients with stable disease remain on treatment with XB002: one each with metastatic castration-resistant prostate cancer, appendiceal adenocarcinoma and pancreatic adenocarcinoma, at treatment durations of 42 weeks, 10 weeks and 7 weeks, respectively. One additional patient with uterine carcinosarcoma who achieved stable disease as the best response discontinued XB002 at 15 weeks. In the upcoming cohort-expansion stage, the efficacy of XB002 will be further evaluated as a single agent and in combination with nivolumab.

About JEWEL-101

JEWEL-101 is an open-label, multicenter, first-in-human phase 1 study of Exelixis' next-generation antibody-drug conjugate XB002 in patients with advanced solid tumors. The trial plans to enroll approximately 450 patients and is divided into two parts: a dose-escalation stage and an expansion cohort stage. Expansion cohorts are planned for cervical cancer, ovarian cancer, non-small cell lung cancer, prostate cancer, pancreatic cancer and several other cancers.

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

About XB002

XB002 is a next-generation antibody-drug conjugate that targets tissue factor, which is overexpressed in a variety of solid tumors. After binding to tissue factor on tumor cells, XB002 is internalized, and the cytotoxic agent is released, resulting in targeted tumor cell death. XB002 is currently being developed for advanced solid tumors. Preclinical findings demonstrate that XB002 binds tissue factor without affecting the coagulation cascade — a limitation of prior tissue-factor-targeting molecules.

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 JEWEL-101 during the Antibody-drug Conjugates Poster Session at ENA 2022; the therapeutic potential of XB002 as a new treatment for people with difficult-to-treat tumors with limited treatment options; Exelixis' future development plans for XB002 in the JEWEL-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 XB002 as a single agent or in combination with atezolizumab to demonstrate safety and/or efficacy in JEWEL-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 XB002; the costs of conducting clinical trials; Exelixis' dependence on third-party vendors for the development, manufacture and supply of XB002; 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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