Exelixis to Present the Preclinical Profile and Initial Clinical Pharmacokinetics of XL092, Its Next-Generation Oral Tyrosine Kinase Inhibitor

October 9, 2020

– In preclinical studies, XL092 demonstrated robust target and tumor growth inhibition –

– Clinical pharmacokinetic (PK) data suggest a significantly shorter half-life than cabozantinib –

– Phase 1 evaluation of XL092 in combination with atezolizumab now open for enrollment –

ALAMEDA, Calif.--(BUSINESS WIRE)--Oct. 9, 2020-- Exelixis, Inc. (NASDAQ: EXEL) today announced new data that support the ongoing clinical development of XL092, the company's next-generation oral tyrosine kinase inhibitor that targets VEGF receptors, MET, AXL, MER, and other kinases implicated in cancer's growth and spread. The new data will be presented in a poster discussion session (Abstract 33) as part of the 32 nd EORTC-NCI-AACR (ENA) Symposium, which is being held virtually October 24-25; abstracts for the meeting were released earlier today.

"When the XL092 program began, we wanted to develop a novel tyrosine kinase inhibitor that retained the target profile of cabozantinib, our flagship medicine that is now a global oncology franchise, while also improving on certain important characteristics," said Peter Lamb, Ph.D., Executive Vice President of Scientific Strategy and Chief Scientific Officer of Exelixis. "The data to be presented at the ENA Symposium suggest XL092 has a desirable therapeutic profile that pairs the potential for significant anti-tumor activity with a much shorter clinical half-life than cabozantinib. The data also support a potential synergistic effect for XL092 in combination with immune checkpoint inhibitors, which is why we're excited to expand our ongoing phase 1 clinical trial to include an exploration of the combination of XL092 and atezolizumab in multiple solid tumors."

The abstract released today provides a summary of results from a detailed characterization of XL092 in cancer cell lines and animal tumor models, as well as initial PK data from the ongoing phase 1 trial of the compound. Additional data will be presented in the poster discussion, which is scheduled to begin at 22:40 CEST / 4:40 p.m. EDT / 1:40 p.m. PDT on Saturday, October 24. Key findings included in the abstract are:

- XL092 is an ATP-competitive inhibitor of multiple receptor tyrosine kinases including MET, VEGFR2, AXL and MER, with IC_{50} values in cell-based assays of 15, 1.6, 3.4, and 7.2 nM, respectively.
- In xenograft studies, XL092 caused substantial tumor growth inhibition following 10 mg/kg daily oral dosing for 14 days, which was accompanied by significant inhibition of MET, AXL and VEGFR2 phosphorylation.
- When XL092 was combined with an immune checkpoint inhibitor (ICI) in a syngeneic tumor model, the combination was significantly more efficacious than either XL092 or anti-PD1 alone.
- PK data from the ongoing phase 1 clinical trial assessing daily dosing of XL092 in patients with advanced solid tumors shows a terminal half-life of 24 hours versus a 99-hour terminal half-life for cabozantinib.

The ongoing phase 1 trial (NCT03845166) is a multi-center study designed to evaluate the pharmacokinetics, safety, tolerability, and preliminary anti-tumor activity of XL092, both as a single agent and in combination with ICIs. The study protocol was recently amended to include dose-escalation and expansion cohorts for XL092 in combination with the ICI atezolizumab (TECENTRIQ®). The dose-escalation evaluation of XL092 as a single agent is ongoing, and Exelixis anticipates patient enrollment in the dose-escalation evaluation of the combination regimen imminently. As recommended doses of single-agent XL092 and XL092 in combination with atezolizumab are established, the trial will proceed to enroll expansion cohorts in patients with clear cell and non-clear cell renal cell carcinoma, hormone-receptor positive breast cancer, and metastatic castration-resistant prostate cancer.

About XL092

XL092 is a next-generation oral tyrosine kinase inhibitor that targets VEGF receptors, MET, AXL, MER, and other kinases implicated in cancer's growth and spread. In designing XL092, Exelixis sought to build upon the experience and target profile of cabozantinib, the company's flagship medicine, while improving key characteristics, including clinical half-life. The compound is the subject of an ongoing phase 1 trial (NCT03845166) evaluating its pharmacokinetics, safety, tolerability, and preliminary anti-tumor activity when administered alone and in combination with the ICI atezolizumab (TECENTRIQ®); pending positive data, further development is planned.

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: Exelixis' plans to present data that support the ongoing clinical development of XL092 in a poster discussion session as part of the 32nd ENA Symposium; the potential for XL092 to demonstrate significant anti-tumor activity with a much shorter clinical half-life than cabozantinib, as well as the potential synergistic effect for XL092 in combination with immune checkpoint inhibitors; 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 or the combination of XL092 and atezolizumab to demonstrate safety and/or efficacy in NCT03845166 and in future trials; uncertainties inherent in the product development process; the continuing COVID-19 pandemic and its impact on Exelixis' research and development operations, including Exelixis' ability to initiate new clinical trials and clinical trial sites, enroll clinical trial patients, conduct trials per protocol, and conduct drug research and discovery operations and related activities; the costs of conducting clinical trials, including the ability or willingness of Exelixis' collaboration partners to invest in the resources necessary to complete the 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; 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 6, 2020, 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.

Exelixis, the Exelixis logo, CABOMETYX, COMETRIQ and COTELLIC are registered U.S. trademarks. MINNEBRO is a Japanese trademark.

TECENTRIQ® (atezolizumab) is a registered trademark of Genentech, a member of the Roche Group.

View source version on businesswire.com: https://www.businesswire.com/news/home/20201009005112/en/

Investors Contact:
Susan Hubbard
EVP, Public Affairs and
Investor Relations
Exelixis, Inc.
(650) 837-8194
shubbard@exelixis.com

Media Contact:
Hal Mackins
For Exelixis, Inc.
415-994-0040
hal@torchcommunications.com

Source: Exelixis, Inc.