Exelixis Reports Encouraging Phase 1 Data To Be Presented at ASCO for XL147, a Selective Inhibitor of PI3K

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-Pharmacodynamic Data Indicate Robust Inhibition of PI3K Pathway at Well-Tolerated Doses-

SOUTH SAN FRANCISCO, Calif.--(BUSINESS WIRE)--Jun. 1, 2009-- Exelixis, Inc. (Nasdaq:EXEL) today reported encouraging data from an ongoing Phase 1 dose-escalation trial of XL147 in patients with solid tumors. XL147 is an orally available small molecule inhibitor of phosphoinositide-3-kinase (PI3K). Activation of the PI3K pathway is a frequent event in human tumors, promoting cell proliferation, survival, and resistance to chemotherapy and radiotherapy. Geoffrey Shapiro, MD, PhD, Director, Early Drug Development Center, at the Dana-Farber Cancer Institute, an investigator on the Phase 1 trial, will present the data in an oral session (Abstract #3500) beginning at 1:30 p.m. local time on Monday, June 1, 2009, at the American Society of Clinical Oncology Annual Meeting, which is being held May 29-June 2 in Orlando.

“The robust pharmacodynamic results in this trial clearly demonstrate that XL147 inhibits PI3K pathway signaling in human tumors at well-tolerated doses,” said Michael M. Morrissey, Ph.D., president of research and development at Exelixis. “XL147 inhibits a critical signaling pathway that influences multiple components of malignancy, and could be beneficial in combination with various anti-cancer agents. We are encouraged by these data, which clearly support an aggressive development plan for XL147 in major tumor types.”

The study is evaluating a 28-day dosing cycle with either an intermittent dosing schedule (21 days on/7 days off; doses from 30 mg to 900 mg) or a continuous daily dosing (CDD, doses of 100 mg and 400 mg) schedule. Sixteen of 43 (37%) evaluable patients including 5 of 13 (38%) patients with non-small cell lung cancer (NSCLC) had remained on study for 12 or more weeks. Most patients’ cancer had progressed following treatment with multiple regimens. Three of the patients with NSCLC were progression-free for more than 6 months. One of these NSCLC patients had a partial response with a 33% reduction in the size of their target lesion. This patient had previously received four prior treatment regimens and has remained on study with XL147 for more than 70 weeks.

Adverse events have generally been of Grade 1 or 2 severity and manageable. Skin rash was reported in 12 patients and was Grade 1 or 2 in eight patients. Four patients in the 21 days on/7 days off dosing schedule experienced dose-limiting Grade 3 rash (1 patient each in the 400 and 600 mg cohorts, and 2 patients in the 900 mg cohorts). Other frequent adverse events reported included fatigue (25%) and cough (22%). The maximum tolerated dose (MTD) for the 21 days on/7 days off dosing schedule is 600 mg. No dose-limiting toxicities have been reported for the 100 and 400 mg cohorts on the CDD schedule, and additional patients are being enrolled.

Pharmacodynamic analyses demonstrated substantial reductions in biomarkers of PI3K pathway signaling in multiple tumor types across a range of well-tolerated doses. These analyses also demonstrated inhibition of the ERK signaling pathway in tumors, in contrast to the induction of this pathway observed with inhibitors that selectively target TORC1. Pharmacodynamic target modulation was also observed in hair and skin, with robust pathway inhibition noted in samples at the lowest doses administered in the study (30-60 mg 21 days on/7 days off). Target inhibition appeared to be exposure-dependent, and was progressive with time in cases where serial samples were obtained.

Pharmacokinetic analyses demonstrate that XL147 exposure increased dose-proportionally over 24 hours from 30 to 400 mg on the 21 days on/7 days off dosing schedule. Exposures were similar at the 400, 600 and 900 mg doses. Repeated dosing of XL147 resulted in a 5- to 13-fold accumulation, and steady-state levels were reached 15 to 21 days after initiation of dosing.

Exelixis looks forward to working with sanofi-aventis to collaborate on the recently signed strategic alliance for the development of this potential candidate. Exelixis and sanofi-aventis have entered into a global license agreement for XL147. The effectiveness of the license is subject to antitrust clearance under the Hart-Scott-Rodino Antitrust Improvements Act and other customary regulatory approvals.

About XL147

XL147 selectively targets PI3K. Upregulation of PI3K activity is one of the most common characteristics of human tumor cells and can result from activation of growth factor receptors, mutational activation or amplification of the PI3K gene, downregulation of the PTEN lipid phosphatase, or activating mutations in RAS. Activation of PI3K results in stimulation of AKT and mTOR kinases, resulting in promotion of tumor cell proliferation and survival. This survival signal plays a significant role in conferring resistance to chemotherapy and radiotherapy by inhibiting apoptotic cell death. In preclinical cancer models, administration of XL147 leads to tumor growth inhibition or regression and has been shown to enhance the activity of EGFR-targeted agents and cytotoxic drugs.

About Exelixis

Exelixis, Inc. is a development-stage biotechnology company dedicated to the discovery and development of novel small molecule therapeutics for the treatment of cancer and other serious diseases. The company is leveraging its fully integrated drug discovery platform to fuel the growth of its development pipeline, which is primarily focused on cancer. Currently, Exelixis’ broad product pipeline includes investigational compounds in phase 3, phase 2, and phase 1 clinical development. Exelixis has established strategic corporate alliances with major pharmaceutical and biotechnology companies, including Bristol-Myers Squibb, sanofi-aventis, GlaxoSmithKline, Genentech, Boehringer Ingelheim, Wyeth Pharmaceuticals, and Daiichi-Sankyo. For more information, please visit the company’s web site at www.exelixis.com.

Forward-Looking Statements

This press release contains forward-looking statements by Exelixis, including, without limitation, statements related to the future development path and therapeutic potential of XL147; and the anticipated effectiveness of the global license agreement between Exelixis and sanofi-aventis for XL147.

Words such as “suggest,” “looks forward” and similar expressions are intended to identify forward-looking statements. These forward-looking statements are based upon Exelixis' current plans, assumptions, beliefs and expectations. Forward-looking statements involve risks and uncertainties. Exelixis' actual results and the timing of events could differ materially from those anticipated in such forward-looking statements as a result of these risks and uncertainties, which include, without limitation, risks related to the potential failure of XL147 to demonstrate safety and efficacy in clinical testing; the therapeutic and commercial value of XL147; the uncertainty of the FDA approval process; market competition; and Exelixis' dependence on its relationship with its collaboration partners. These and other risk factors are discussed under “Risk Factors” in Exelixis’ Quarterly Report for the quarter ended April 3, 2009 and Exelixis’ other reports filed with the Securities and Exchange Commission. Exelixis expressly disclaims any duty, obligation or undertaking to release publicly any updates or revisions to any forward-looking statements contained herein to reflect any change in Exelixis' expectations with regard thereto or any change in events, conditions or circumstances on which any such statements are based.

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