Exelixis Reports Encouraging Phase 1 Data for the PI3K Inhibitor Xl147 (SAR245408) in Combination with Erlotinib at the AACR-NCI-EORTC Conference

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BOSTON--(BUSINESS WIRE)--Nov. 18, 2009-- Exelixis, Inc. (Nasdaq:EXEL) today reported interim data from an ongoing phase 1 dose-escalation trial of XL147 (SAR245408) in combination with the EGFR inhibitor erlotinib in patients with advanced solid tumors. XL147 is a selective, 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. The pathway also has been implicated as a mediator of resistance to epidermal growth factor receptor (EGFR) inhibitors. Neil Faulkner, MD from the Karmanos Cancer Institute, Wayne State University, Detroit, MI, an investigator on the phase 1 trial, will present the data in a poster session (Abstract #C197) beginning at 12:30 pm, local time, on Wednesday, November 18, 2009, at the AACR-NCI-EORTC International Conference on Molecular Targets and Cancer Therapeutics, which is being held November 15-19 in Boston. XL147 is being developed with sanofi-aventis.

“The PI3K signaling pathway is frequently dysregulated in a broad spectrum of human tumors, and we believe that XL147 has substantial potential for treating diverse cancers,” said Michael M. Morrissey, Ph.D., president of research and development at Exelixis. “We chose to evaluate XL147 in combination with erlotinib given the data suggesting that PI3K may play a role in resistance to EGFR inhibitors. The results of this phase 1 study thus far are encouraging, and preliminary data demonstrate that the combination regimen simultaneously inhibits PI3K and EGFR signaling. In collaboration with sanofi-aventis, we will continue to evaluate XL147 alone and in combination with a variety of other therapies, with a goal to provide cancer patients and oncologists with new therapeutic options that may overcome resistance mechanisms in cancer.”

The study is evaluating escalating doses of XL147, administered daily for 21 days of a 28-day cycle, in combination with erlotinib, administered daily. As of October 6, 2009, 21 patients with advanced solid tumors had been enrolled in the trial. Tumor types include non-small cell lung cancer (NSCLC) (8), colorectal cancer (5), hepatocellular carcinoma, head and neck squamous cell carcinoma, biliary tract, carcinoid, ethmoid, esophageal, kidney and adenoid cystic cancer (1 each). Patients have been treated at 7 dose levels up to 600 mg XL147/150 mg erlotinib, and the maximum tolerated dose has not yet been reached.

As of October 22, 2009, 20 patients were evaluable for tumor response assessment. One patient with adenoid cystic carcinoma had a documented decrease of metastatic disease. One patient with NSCLC who had not previously been treated with erlotinib had a confirmed partial response with a 59% decrease of metastatic disease after Cycle 3. One patient with head and neck cancer had a documented decrease of disease and shrinkage of the primary tumor bulk. Ten of 20 evaluable patients remained on study for at least 12 weeks, including three patients on study for more than 24 weeks.

Preliminary pharmacokinetic (PK) analyses indicate that the PK profiles of XL147 and erlotinib administered in combination are similar to the PK profiles of each compound administered as a single agent. Pharmacodynamic assessments of blood, skin, and tumor samples demonstrate robust and simultaneous inhibition of signaling through the PI3K pathway and through EGFR, the target of erlotinib, after administration of the combination. Tumor biopsy samples from a patient with an ethmoid tumor showed marker reductions ranging from 39% to 44%.

Sixteen patients were evaluable for safety assessments. Six patients have experienced serious adverse events (SAE), including one patient treated at the 600 mg XL147/150 mg erlotinib dose who experienced a drug rash and eosinophilia and systemic symptoms (Grade 4). This was considered to be an SAE and a dose-limiting toxicity possibly related to study treatment. The patient subsequently developed respiratory failure and fatal multi-organ failure. Treatment-related adverse events occurring in at least 10% of patients were rash (44%), nausea (31%), fatigue and vomiting (each 25%), and diarrhea (19%) and anorexia (13%).

To access the clinical data poster mentioned in this press release, please visit www.exelixis.com.

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. Exelixis has entered into a global license agreement with sanofi-aventis for XL147.

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 (acquired by Pfizer Inc.), and Daiichi-Sankyo. For more information, please visit the company’s web site at www.exelixis.com.

Exelixis Forward-Looking Statements

This press release contains forward-looking statements, including, without limitation, statements related to the potential for XL147 in the treatment of

diverse cancers; the role of PI3K in resistance to EGFR inhibitors; the continued evaluation of XL147 alone and in combination with a variety of other therapies; and the goal to provide cancer patients and oncologists with new therapeutic options that may overcome resistance mechanisms in cancer. Words such as “believe,” “potential,” “may,” “will,” “continue,” “goal,” 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 and Exelixis’ ability to conduct clinical trials of XL147 sufficient to achieve a positive completion. These and other risk factors are discussed under “Risk Factors” and elsewhere in Exelixis’ quarterly report on Form 10-Q for the quarter ended October 2, 2009 and Exelixis’ other filings 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.

Source: Exelixis, Inc.

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