Exelixis Reports Updated Data from Multiple Clinical Trials of the PI3K Inhibitor XL147 (SAR245408) to be Presented at ASCO

June 7, 2010

SOUTH SAN FRANCISCO, Calif., Jun 07, 2010 (BUSINESS WIRE) --Exelixis, Inc. (Nasdaq:EXEL) today reported updated interim data from three ongoing trials of XL147 (SAR245408), 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 agents targeting epidermal growth factor receptor (EGFR) family members. The presentations will be made at the 2010 Annual Meeting of the American Society of Clinical Oncology, which is being held June 4-8 in Chicago. Exelixis is developing XL147 with sanofi-aventis.

"XL147 is the leading class I selective PI3K inhibitor and has significant clinical and commercial potential in a variety of cancer indications," said Michael M. Morrissey, Ph.D., president of research and development at Exelixis. "The results of the studies being presented at ASCO continue to highlight the potential utility of XL147 as a single agent or in combination with other therapies that are mainstays of cancer treatment. These data provide the foundation for the broad phase 2 program that is currently underway for XL147, including new trials in metastatic breast and endometrial cancers."

XL147 in Patients with Advanced Malignancies

Interim results from an ongoing phase 1 dose-escalation trial of XL147 in patients with advanced malignancies (Abstract #3004) will be presented in a Clinical Science Symposium at 8:30 am on Monday, June 7 by Dr. Gerald Edelman from the Mary Crowley Medical Research Center in Dallas, TX. Patients are treated once daily on either an intermittent schedule (21 days on/7 days off; 21/7) or a continuous daily dosing schedule (CDD). Both a capsule and a tablet formulation are being evaluated. As of April 1, 2010, 78 patients with advanced solid tumors have been enrolled. The maximum tolerated doses (MTDs) for both the 21/7 and CDD schedules with the capsule formulation are 600 mg. The MTD for the tablet formulation has not been determined. Enrollment of lymphoma patients has been initiated.

Seventy-five patients were evaluable for antitumor activity. Of these, 14 have been on treatment greater-than or equal to 16 weeks, including 10 on treatment greater-than or equal to 24 weeks and 4 on treatment greater-than or equal to 40 weeks. One patient with non-small cell lung cancer (NSCLC) who had received 4 prior treatment regimens had a partial response (PR) after 56 weeks on study. Safety data were available for 62 patients. Most adverse events (AEs) were grade 1 or 2 in severity. Dose-limiting toxicities (DLTs) were skin rash and hypersensitivity. Pharmacokinetic (PK) analyses indicate that exposure increased dose-proportionally from 30 to 400 mg with the capsule formulation, and that exposures were similar for the 400 mg, 600 mg, and 900 mg doses. Mean half-life was 5 days. Pharmacodynamic (PD) analyses indicate robust inhibition of PI3K and ERK pathway signaling.

XL147 Combined with Carboplatin and Paclitaxel in Patients with Advanced Solid Tumors

Interim results from an ongoing phase 1b/2 study of XL147 in combination with carboplatin and paclitaxel in patients with advanced solid tumors (Abstract #3078) will be presented in a poster session on Monday, June 7 by Dr. Anne Traynor from the University of Wisconsin Carbone Cancer Center in Madison, WI. The study is evaluating the safety, tolerability, and clinical activity of escalating doses of XL147 administered daily in combination with paclitaxel and carboplatin administered intravenously on Day 1 of each 21-day cycle. In Part A of the study, paclitaxel and carboplatin have been dose-escalated to 175 mg/m^2 and AUC 6, respectively. As of March 31, 2010, 24 patients have been enrolled and treated using an XL147 capsule formulation. MTD determination using an XL147 tablet formulation has recently been initiated. Cohorts of patients with endometrial cancer and ovarian cancer will be enrolled at the MTD. In Part B, paclitaxel and carboplatin will be dose-escalated up to 225 mg/m^2 and AUC 6, respectively, with expansion at the MTD in patients with NSCLC.

Twenty two patients were evaluable for tumor response. One patient has experienced a confirmed complete response (CR) and 4 have had confirmed PRs. All responses occurred in patients who were previously treated with a platinum-containing regimen. Fourteen of the 22 evaluable patients remained on treatment greater-than or equal to 12 weeks, with 5 patients on treatment greater-than or equal to 24 weeks. In addition, a platinum-naïve patient with triple-negative inflammatory breast cancer experienced regression of cutaneous lesions after 2 cycles. Safety data were available for 19 patients. Most AEs were grade 1 or 2 in severity. Three DLTs have been reported: 2 patients with a history of drug allergies experienced grade 3 allergic reactions, which resolved after discontinuation of study treatment, and 1 patient experienced grade 3 rash without symptoms of allergic reaction, which resolved following XL147 interruption. PK analyses indicate that there are no major interactions between XL147, paclitaxel, and carboplatin. PD analyses of matched tumor biopsies provide evidence for inhibition of PI3K pathway signaling.

XL147 Combined with Erlotinib in Patients with Advanced Solid Tumors

Interim results from an ongoing phase 1b/2 study of XL147 in combination with erlotinib in patients with advanced solid tumors (Abstract #3070) will be presented in a poster session on Monday, June 7 by Dr. Cristian Moldovan from Institut Goustave Roussy in Villejuif, France. The study is evaluating the safety, tolerability, and clinical activity of escalating doses of XL147 administered daily for 21 days of a 28-day cycle, in combination with erlotinib administered daily. As of April 1, 2010, 28 patients with advanced solid tumors had been enrolled in the trial and treated at 7 dose levels up to 600 mg XL147/150 mg erlotinib. The preliminary MTD is 400 mg XL147/150 mg erlotinib.

Twenty-six patients were evaluable for tumor response. One patient with NSCLC who had prior chemotherapy but was erlotinib naïve achieved a PR and a 59% decrease of metastatic disease after Cycle 3, with a 24-week duration of response. Seven additional patients had SD greater-than or equal to 8 weeks, 4 of which remained on treatment for greater-than or equal to 24 weeks. Safety data were available for 22 patients. Most AEs were grade 1 or 2 in severity. One patient had a DLT of drug rash with eosinophilia and systemic symptoms (DRESS syndrome) at 600 mg XL147/150 mg erlotinib. The patient subsequently died from progressive disease and DRESS. PK analyses indicate that there are no major interactions between XL147 and erlotinib. PD analyses indicate robust inhibition of PI3K and EGFR pathway signaling in surrogate and tumor tissues.

To access the abstracts and clinical data posters 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, promoting 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 biological expertise and integrated research and development capabilities to generate a pipeline of development compounds with significant therapeutic and commercial potential for the treatment of cancer and potentially other serious diseases. 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 Company, sanofi-aventis, GlaxoSmithKline, Genentech (a wholly owned member of the Roche Group), Boehringer Ingelheim, and Daiichi-Sankyo. For more information, please visit the company's web site at http://www.exelixis.com.

Forward-Looking Statements

This press release contains forward-looking statements by Exelixis, including, without limitation, statements related to the continued development and therapeutic potential of XL147. Words such as "potential," "will" 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 ability to conduct clinical trials for XL147 sufficient to achieve a positive completion; 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 2, 2010 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.

SOURCE: Exelixis, Inc.

Exelixis, Inc.
Charles Butler, 650-837-7277
Vice President
Corporate Communications
& Investor Relations
cbutler@exelixis.com
DeDe Sheel, 650-837-8231
Associate Director,
Investor Relations
dsheel@exelixis.com