Exelixis Reports Encouraging Phase 1 Data for the PI3K Inhibitor XL147 (SAR245408) in Combination with Paclitaxel and Carboplatin at the AACR-NCI-EORTC Conference

November 17, 2009

BOSTON--(BUSINESS WIRE)--Nov. 17, 2009-- Exelixis, Inc. (Nasdaq:EXEL) today reported interim data from an ongoing phase 1 dose-escalation trial of XL147 (SAR245408) in combination with paclitaxel and carboplatin 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. Upregulation of PI3K signaling is associated with resistance to paclitaxel and carboplatin. Jennifer Wheler, MD from the University of Texas M. D. Anderson Cancer Center, Houston, TX, and an investigator on the phase 1 trial, will present the data in a poster session (Abstract #B247) beginning at 12:30 pm, local time, on Tuesday, November 17, 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.

“Preclinical data suggest that XL147 potentiates the antitumor efficacy of paclitaxel and carboplatin without exacerbating the toxicity of this commonly used regimen,” said Michael M. Morrissey, Ph.D, president of research and development at Exelixis. “We are very encouraged by the emerging signs of clinical activity and good tolerability of the XL147/paclitaxel/carboplatin combination in this trial, including 4 confirmed partial responses in highly refractory patients with solid tumors. The results of this study thus far demonstrate the potential for enhancing anti-tumor activity by combining XL147 with two of the most commonly used chemotherapeutic agents.”

The study is evaluating escalating doses of XL147 administered daily for a 21-day cycle in combination with paclitaxel and carboplatin administered intravenously on Day 1 of the cycle. In Part A of the study, paclitaxel and carboplatin will be dose-escalated up to 175 mg/m^2 and AUC 6, respectively, with expansion at the maximum tolerated dose (MTD) in patients with endometrial and ovarian cancer. 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 non-small cell lung cancer (NSCLC).

As of October 22, 2009, 16 patients with advanced solid tumors have been enrolled. Tumor types include breast (5), cervical (2), vulvar, tonsillar, parotid, peritoneal, colorectal, esophageal, melanoma, and endometrial and tongue cancer (1 each). Patients have been treated at 6 dose levels up to 600mg XL147/AUC 6 carboplatin/175mg/m^2 paclitaxel, and the MTD has not yet been established.

As of October 22, 2009, 15 patients were evaluable for tumor response assessment. Four patients have experienced a confirmed partial response (PR) with the following maximal reductions (sum of tumor target lesions): 63% (tonsillar), 42% (cervical), 45% (esophageal), and 70% (tongue). All PRs occurred in patients who had been previously treated with a platinum-containing regimen. In addition, a platinum-naïve patient with triple-negative, inflammatory breast cancer experienced regression of cutaneous lesions after two cycles. Nine of 14 patients with measurable disease had tumor shrinkage as their best radiological response. Twelve of the 14 evaluable patients with available post-baseline scans continued on study for at least 12 weeks, with 4 patients remaining on study for at least 24 weeks.

Preliminary pharmacokinetic (PK) analyses indicate that the PK profiles of XL147, paclitaxel, and carboplatin administered in combination are similar to the PK profiles of each compound administered as a single agent. Robust pharmacodynamic modulation of the PI3K pathway was evident in tumor biopsies at plasma exposures consistent with those associated with PI3K inhibition in tumors in an ongoing single-agent phase 1 trial of XL147. The patient with cervical adenocarcinoma, who experienced a PR, had biomarker reductions ranging from 69% to 76%, and a patient with colon cancer had reductions ranging from 64% to 73%.

Fifteen patients were available for safety assessments. There have been no dose-limiting toxicities. One patient experienced a serious adverse event (Grade 4 thrombocytopenia), which was considered related to study treatment. The event resolved and study treatment was resumed without recurrence. Five patients had a dose reduction of carboplatin and/or paclitaxel; no dose reductions of XL147 were reported. Treatment-related adverse events occurring in at least 20% of patients were neutropenia (53%), fatigue (53%), anemia (47%), thrombocytopenia (47%), nausea (33%), diarrhea, peripheral neuropathy and rash (each 27%) and alopecia, anorexia and vomiting (each 20%).

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 data that suggests that XL147 potentiates the antitumor efficacy of paclitaxel and carboplatin without exacerbating the toxicity of the commonly used regimen; emerging signs of clinical activity and good tolerability of the XL147/paclitaxel/carboplatin combination; the potential for enhancing anti-tumor activity by combining XL147 with two of the most commonly used chemotherapy agents; and dose-escalation plans for the XL147 study in combination with paclitaxel and carboplatin. Words such as “suggest,” “emerging,” “demonstrate,” “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 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.

Exelixis, Inc.
Charles Butler, 650-837-7277
Vice President, Corporate Communications & Investor Relations
cbutler@exelixis.com