Exelixis Reports Positive Phase 1 Data for PI3K Inhibitor XL147 at EORTC-NCI-AACR Symposium

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Robust Pathway Inhibition Seen in Tumor and Surrogate Tissues at Well-Tolerated Doses; Preliminary Clinical Benefit Observed in Some Patients

GENEVA--(BUSINESS WIRE)--

Exelixis, Inc. (Nasdaq:EXEL) today reported interim data from a phase 1 dose-escalation trial of XL147, a novel small molecule inhibitor of phosphoinositide-3 kinase (PI3K), which is implicated in tumor cell proliferation, survival, and resistance to chemotherapy and radiotherapy. The trial is enrolling patients with metastatic or unresectable solid tumors for which known effective measures do not exist or are no longer effective. The trial is being conducted at Vall D'Hebron University Hospital, Barcelona, Spain; Mary Crowley Medical Research Center, Dallas, Texas, USA; and Dana-Farber Cancer Institute, Boston, Massachusetts, USA. Emiliano Calvo, MD, PhD, a lead investigator in the trial while Assistant Professor and Co-Director of the Phase I Unit at Vall D'Hebron University Hospital, and currently Director of Clinical Research, START-Madrid Phase I Unit at Centro Integral Oncologico Clara Campal, presented the data in a poster session (Abstract #218) at the EORTC-NCI-AACR Symposium on Molecular Targets and Cancer Therapeutics, which is being held October 21-24 in Geneva, Switzerland. The poster will be available today on the Exelixis web site.

"We have observed robust pharmacodynamic activity in this trial, clearly demonstrating that XL147 inhibits PI3K in patients at well-tolerated doses," said Michael M. Morrissey, PhD, President of Research and Development at Exelixis. "We are particularly pleased to see the preliminary signs of clinical benefit in some patients who have received XL147. We are very encouraged by these data, and believe they support the development of this compound both as a single agent and in combination with other anti-cancer agents. Our work with XL147 is one of several approaches we are taking toward PI3K pathway inhibition. We are also developing XL765, which targets PI3K and mTOR, a downstream effector in the pathway. We believe that pursuing multiple approaches to targeting this important signaling pathway is warranted given the diverse genotypes and cancers that involve activation of this pathway."

There were 30 patients available for safety, pharmacokinetic, and tumor response analyses as of October 1, 2008. Patients have been treated with XL147 across seven dose levels, ranging from 30 mg to 900 mg daily, on 28-day cycles with a 21 days on/7 days off schedule. Of 23 evaluable subjects, 8 had achieved prolonged stable disease (greater than 3 months), 2 of whom are currently on study and 6 of whom subsequently progressed.

Results from pharmacodynamic analyses indicate that XL147 inhibits the PI3K pathway in patients at well-tolerated doses. Reductions of 70-80% in phosphorylation of PI3K pathway components including AKT, PRAS40, and S6 were observed in tumor tissues from 2 patients (leiomyosarcoma and Merkel cell carcinoma) at the 600 mg dose level. Reductions in similar end points were also observed in surrogate tissue (hair and skin) samples from patients, but to a lesser extent than observed in tumor tissue. Inhibition of PI3K pathway signaling was generally exposure-dependent. The pattern of inhibition of protein phosphorylation observed in tissue is consistent with observations from preclinical studies, and suggests that XL147 inhibits PI3K in patients.

Administration of XL147 at doses up to 600 mg has been generally well tolerated. One event of Grade 3 study drug-related dose-limiting toxicity (DLT) was reported in 1 of 3 patients at 600 mg. That cohort was expanded and no further DLTs were observed. Two events of Grade 3 study drug-related skin rash occurred in 2 of 3 subjects at 900 mg, which was determined to be the maximum administered dose (MAD). The most common treatment-related adverse events were skin rash and Grade 1 nausea. A total of 5 serious adverse events were reported in 4 patients, but none of these was considered to be related to XL147 treatment. The maximum tolerated dose (MTD) has not yet been established.

"These data are most encouraging, and demonstrate that XL147 targets the PI3K pathway in patients with a favorable initial tolerability profile," said Dr. Calvo. "The data suggest that XL147 has potential, both alone and in combination with other therapies."

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 2 and phase 1 clinical development. Exelixis has established strategic corporate alliances with major pharmaceutical and biotechnology companies, including GlaxoSmithKline, Bristol-Myers Squibb, Genentech, 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, including, without limitation, statements related to the future development path for XL147 as both a single agent and in combination with other anti-cancer agents; and the belief that pursuing multiple approaches to targeting the PI3K pathway is warranted. Words such as "believe," "potential," 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: the potential failure of XL147 to demonstrate safety and efficacy in clinical testing; the therapeutic and commercial value of XL147; and the ability to conduct XL147 clinical trials 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 June 27, 2008, and 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.