Exelixis Reports Updated Data from Multiple Clinical Trials of the Dual PI3K and mTOR Inhibitor XL765 (SAR245409) to be Presented at ASCO

June 6, 2010

SOUTH SAN FRANCISCO, Calif., Jun 06, 2010 (BUSINESS WIRE) --Exelixis, Inc. (Nasdaq: EXEL) today reported updated interim data from three ongoing trials of XL765 (SAR245409), an orally available small molecule inhibitor of phosphoinositide-3-kinase (PI3K) and mTOR. 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 XL765 with sanofi-aventis.

"XL765 has unique clinical potential because it inhibits the signaling of both PI3K and mTOR, two important nodes in this critical pathway," said Michael M. Morrissey, Ph.D., president of research and development at Exelixis. "PI3K signaling is dysregulated in a broad spectrum of human cancers, and mTOR is a well validated target for cancer therapy. The results from these studies suggest that this novel compound may have clinical activity as a single agent and in combination with targeted agents and chemotherapy. These data support the ongoing broad phase 1/2 clinical program and further phase 2 evaluation that sanofi-aventis and Exelixis have planned for XL765."

XL765 in Patients with Advanced Malignancies

Interim results from an ongoing phase 1 dose-escalation trial of XL765 in patients with advanced malignancies (Abstract #3030) will be presented in a poster discussion session on Sunday, June 6 by Dr. Irene Brana from Vall d'Hebron University Hospital in Barcelona, Spain. The study is evaluating the safety, tolerability, and clinical activity of continuous daily dosing of XL765 administered once daily (qd) or twice daily (bid). As of May 3, 2010, 83 patients have been enrolled (31 qd and 52 bid). The maximum tolerated doses (MTDs) for qd and bid administration are 90 mg and 50 mg, respectively.

Twelve patients had been on treatment for greater-than or equal to 16 weeks with 7 patients remaining on treatment for greater-than or equal to 24 weeks. XL765 administered qd or bid was generally well tolerated. Most adverse events (AEs) were grade 1 or 2 in severity. The most frequent treatment-related grade 3 AEs were liver function test elevations which were asymptomatic and reversible. Pharmacodynamic (PD) analyses provide evidence of robust PI3K pathway inhibition, which was similar between the qd and bid regimens. Reductions in both PI3K and ERK pathway signaling in tumors were observed.

XL765 Combined with Erlotinib in Patients with NSCLC

Interim results from an ongoing phase 1b/2 study of XL765 in combination with erlotinib in patients with advanced solid tumors (Abstract #3015) will be presented in a poster session on Sunday, June 6 by Dr. Roger Cohen from Fox Chase Cancer Center in Philadelphia, PA. The study is evaluating the safety, tolerability, and clinical activity of escalating doses of XL765 in combination with daily erlotinib at 100 or 150 mg qd, with both drugs administered daily in a 28-day cycle. As of May 3, 2010, 28 patients with advanced solid tumors have been treated with XL765, on both the qd and bid regimens, across 6 dose cohorts in combination with 100 mg erlotinib.

Four non-small cell lung cancer (NSCLC) patients have been on study for greater-than or equal to 16 weeks. The maximum tolerated doses have not been determined in either the qd or bid regimen. The majority of AEs were grade 1 or 2 in severity. One patient had a dose-limiting toxicity (DLT) of grade 3 rash. PK analyses indicate that there are no major interactions between XL765 and erlotinib. PD analyses indicate robust inhibition of PI3K and EGFR pathway signaling in surrogate and tumor tissues.

XL765 Combined with Temozolomide in Patients with Glioblastoma

Interim results from an ongoing phase 1b/2 study of XL765 in combination with temozolomide (TMZ) in patients with newly diagnosed malignant glioma (Abstract #3085) will be presented in a poster session on Monday, June 7 by Dr. Leia Nghiemphu from UCLA School of Medicine in Los Angeles, CA. The study is evaluating the safety, tolerability, and clinical activity of escalating doses of XL765 administered daily in a 28-day cycle in combination with TMZ at 200 mg/m^2/day on Days 1-5 of the cycle. Patients must be on a maintenance dose of TMZ at 200 mg/m^2/day for at least one cycle prior to enrollment. As of May 3, 2010, 22 patients have been treated with XL765, in both qd and bid regimens, across 5 dose cohorts in combination with TMZ.

Eleven patients have remained on treatment for at least 16 weeks, including 1 patient with a PTEN mutation and EGFR gene amplification who remained on treatment for 62 weeks (a total of 97 weeks following chemoradiation). The maximum tolerated dose has not been established for either the qd or bid regimen. Most AEs were grade 1 or 2 in severity. DLT occurred in 2 patients: 1 patient had grade 3 brain edema and grade 4 thrombocytopenia and 1 patient had a grade 3 rash. Preliminary PK analyses indicate that the PK profiles of XL765 and TMZ administered in combination are similar to the profiles of each compound administered as a single agent. Pharmacodynamic assessments in serial skin biopsies show evidence of PI3K inhibition similar to that observed in the single agent phase 1 study in patients with advanced malignancies.

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

About XL765

XL765 (SAR245409) targets both PI3K and mTOR, key kinases in the PI3K signaling pathway. PI3K is a lipid kinase that plays a pivotal role in transmitting pro-mitotic and pro-survival signals in cells, and mTOR is a serine/threonine kinase that controls the protein translation machinery and hence, cell growth. PI3K is activated in human cancers by elevated receptor tyrosine kinase activity, by deletion of the tumor suppressor PTEN, by activating mutations in RAS, or via PI3K gene mutation or amplification. mTOR is activated by growth factors via PI3K and AKT, but is also activated in a PI3K-independent fashion in response to nutrient and energy levels. Thus, targeting both PI3K and mTOR may provide additional benefit in some tumors compared with selectively targeting PI3K. In preclinical studies, XL765 has shown attractive pharmacokinetic and pharmacodynamic properties and compelling efficacy in xenograft models, both as a single agent and in combination with other therapies. Exelixis has entered into a global license agreement with sanofi-aventis for XL765.

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 XL765. Words such as "potential," "suggest," "may," "support" 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 XL765 to demonstrate safety and efficacy in clinical testing; the ability to conduct clinical trials for XL765 sufficient to achieve a positive completion; the therapeutic and commercial value of XL765; 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.

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