Exelixis Reports Encouraging Phase 1 Data To Be Presented at ASCO for XL765, a Dual Inhibitor of PI3K and mTOR

June 1, 2009

-Pharmacodynamic Data Indicate Robust Inhibition of PI3K Pathway With Daily or Twice-Daily Dosing-

SOUTH SAN FRANCISCO, Calif.--(BUSINESS WIRE)--Jun. 1, 2009-- Exelixis, Inc. (Nasdaq:EXEL) today reported encouraging data from an ongoing Phase 1 dose-escalation trial of XL765 in patients with solid tumors. XL765 is a novel small molecule inhibitor of PI3K and mTOR, kinases which are implicated in tumor cell proliferation, survival, and resistance to chemotherapy and radiotherapy. Patricia LoRusso, DO, Medical Director, Phase I Clinical Trials, Karmanos Cancer Institute, and an investigator on the Phase 1 trial, will present the data in an oral session (Abstract #3502) beginning at 2:00 p.m. local time on Monday, June 1, 2009, at the American Society of Clinical Oncology Annual Meeting, which is being held May 29-June 2 in Orlando.

“The data from this trial demonstrate that XL765 is a potent inhibitor of PI3K and mTOR that provides robust PI3K pathway inhibition in tumors at well-tolerated doses,” said Michael M. Morrissey, Ph.D., president of research and development at Exelixis. “We are encouraged by these preliminary results and the finding that a number of patients remained on study without disease progression for more than 16 weeks, with one patient on study more than 41 weeks. The pharmacodynamic effects observed across diverse tumor types suggest that XL765 may have utility in a variety of cancers.”

The study is evaluating continuous daily dosing of XL765 administered once or twice daily. Six of 50 patients were on study for approximately 16 or more weeks. Four of these 6 patients, including 1 patient each with appendiceal, rectal, and colon cancer with KRAS mutations in their tumors, were on study for 24 weeks or more. Most patients had previously received multiple treatment regimens.

Adverse events have generally been of Grade 1 or 2 severity and manageable. The most frequently occurring adverse events were: nausea (all incidences, 36%; Grade3/4, 4%), diarrhea (32%; 0%), fatigue (28%; 6%), anorexia (26%; 4%), vomiting (22%; 2%) and transaminase increase (22%; 6%). For the twice-daily dosing schedule, the preliminary maximum tolerated dose (MTD) has been established at 50 mg, and additional patients are being enrolled in this dose cohort. The daily dosing schedule is currently evaluating a 90 mg dose and a preliminary MTD has not yet been determined.

Pharmacodynamic analyses demonstrate substantial reductions in biomarkers of PI3K and mTOR activity in multiple tumor types. These analyses also demonstrate inhibition of the ERK signaling pathway in tumors, in contrast to the induction of this pathway observed with inhibitors that selectively target TORC1. Pharmacodynamic target modulation was also observed in hair, skin, and blood samples, with robust pathway inhibition noted in samples at the lowest dose administered in the study (15 mg twice daily). Pharmacodynamic effects in peripheral blood cells exhibited an exposure-dependent trend, while data from serial hair samples suggest that inhibition is progressive in a time-dependent manner. The pharmacodynamic effects observed in blood cell and skin samples were comparable between the daily and twice-daily dosing schedules. XL765 had a small but significant effect on fasting plasma insulin levels after multiple doses, but had minimal to no effect on glucose levels.

Pharmacokinetic analyses indicate that the maximal concentration and exposure of XL765 increased with dose. Repeated dosing of XL765 resulted in low to moderate accumulation.

Exelixis looks forward to working with sanofi-aventis to collaborate on the recently signed strategic alliance for the development of this potential candidate. Exelixis and sanofi-aventis have entered into a global license agreement for XL765. The effectiveness of the license is subject to antitrust clearance under the Hart-Scott-Rodino Antitrust Improvements Act and other customary regulatory approvals.

About XL765

XL765 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.

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, 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 by Exelixis, including, without limitation, statements related to the future development path and therapeutic potential of XL765; and the anticipated effectiveness of the global license agreement between Exelixis and sanofi-aventis for XL765. Words such as “suggest,” “may,” “looks forward” 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 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 3, 2009 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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