Exelixis Initiates Phase 1/2 Trial of XL184 in Patients With Non-Small Cell Lung Cancer

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-First Combination Study of a MET and EGFR Inhibitor-

SOUTH SAN FRANCISCO, Calif., Jan 07, 2008 /PRNewswire-FirstCall via COMTEX News Network/ -- Exelixis, Inc. (Nasdaq: EXEL) today announced that it has initiated a phase 1/2 trial of XL184 in patients with non-small cell lung cancer (NSCLC) who have had progressive disease while on a regimen containing erlotinib.

XL184 is a small molecule that simultaneously inhibits the MET, RET and VEGFR receptor tyrosine kinases. In the initial phase 1 part of the study, safety and pharmacokinetics of combining XL184 with erlotinib will be evaluated. The primary endpoint of the phase 2 part of the study is overall response rate. Secondary endpoints include progression-free survival, overall survival and pharmacodynamics.

"XL184 is a potent inhibitor of MET, and MET amplification has been shown to play an important role in the development of resistance to EGFR inhibitors in NSCLC," said Michael Morrissey, Ph.D., president of research and development of Exelixis. "Our preclinical data suggest that XL184 effectively inhibits growth of cancer cells that have become resistant to EGFR inhibitors through activation of the MET signaling pathway. XL184 also potently inhibits VEGFR, which is a validated target in the treatment of NSCLC. The compound has shown encouraging anti-tumor activity in an initial phase 1 trial and we are executing a phase 2 clinical development program, and are planning on initiation of a pivotal trial for XL184 in medullary thyroid cancer in 2008."

The phase 1/2 study of XL184 is expected to enroll up to 86 NSCLC patients who have had disease progression while on erlotinib. The phase 1 portion of the study will evaluate dose escalation of XL184 in combination with erlotinib, both administered daily. Patients in the first cohort will receive a dose of XL184 that is below the maximum tolerated dose (MTD) identified in the ongoing phase 1 trial of XL184, in combination with erlotinib. Subsequent cohorts will receive erlotinib in combination with escalating doses of XL184 until the MTD is reached. In the phase 2 portion of the study, patients will be randomized to receive XL184 at the MTD alone or in combination with erlotinib. Additionally, correlative studies will evaluate MET amplification and EGFR mutational status. MET and EGFR signaling activity will be assessed in tumor and surrogate tissue.

Data from an ongoing phase 1 trial of XL184 in patients with advanced malignancies were presented in October 2007 at the 2007 AACR-NCI-EORTC International Conference on Molecular Targets and Cancer Therapeutics (Abstract #A152). Investigators reported that anti-tumor activity had been observed in a variety of cancers at doses that are not associated with significant toxicity. There were 33 patients available for safety, pharmacokinetic and tumor response analyses as of the June 22, 2007 cutoff; further data were also provided for six additional patients after the cutoff. Of seven patients with medullary thyroid cancer (MTC), three had partial responses (two confirmed and one unconfirmed) as of the date of the AACR-NCI-EORTC Conference. In addition, as of such date, six of the seven patients had tumor shrinkage and one had non-measurable disease. All seven assessable patients with MTC experienced a rapid decrease in plasma levels of calcitonin, a marker frequently elevated in MTC, and six of the seven patients had a decrease in the tumor marker carcinoembryonic antigen. All seven MTC patients remain on study. In addition, one patient with a neuroendocrine tumor has an unconfirmed partial response. In total, 15 patients with various malignancies have had stable disease lasting from 3 - 20 months, including nine patients with stable disease for more than six months.

To date, five dose-limiting toxicities (DLTs) have been reported, including Grade 3 palmar/plantar erythema (hand-foot syndrome), Grade 3 AST elevation, Grade 3 ALT elevation, and Grade 3 lipase elevation in patients dosed at 11.52 mg/kg (intermittent dosing schedule), as well as a DLT of Grade 2 mucositis in a patient dosed at 265 mg (daily dosing schedule). Serious adverse events (AEs) considered possibly or probably related to XL184 include one report each of Grade 3 fatigue and Grade 3 pulmonary embolism. Dose escalation continues in order to determine a maximum tolerated dose (MTD).

About XL184

XL184 is a novel, orally administered, small molecule anticancer compound that in preclinical models has demonstrated potent inhibition of both MET and VEGFR2. XL184 has also exhibited potent inhibition of other important receptor tyrosine kinases (RTKs) that have been implicated in various forms of cancer including RET, KIT, FLT3, and TIE2. In preclinical efficacy studies, XL184 has inhibited tumor growth and induced the regression of large tumors in a broad range of human tumor xenograft models including breast cancer, lung cancer and glioma. In laboratory studies, XL184 has demonstrated good oral bioavailability and pharmacokinetic properties.

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 for cancer and renal disease. Exelixis has established strategic corporate alliances with major pharmaceutical and biotechnology companies, including GlaxoSmithKline, Bristol-Myers Squibb Company, Genentech, Wyeth Pharmaceuticals 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, including, without limitation, statements related to the future development and potential efficacy of XL184, the future conduct of the phase 1/2 trial of XL184 and the expected timing of the initiation of a pivotal trial of XL184. Words such as "expected," "will," "planning", "suggest" and similar expressions are intended to identify forward-looking statements. These forward-looking statements are based upon Exelixis' current 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 lengthy, costly and uncertain process of clinical testing of XL184 and the potential failure of XL184 to demonstrate safety and efficacy in clinical testing. These and other risk factors are discussed under "Risk Factors" and elsewhere in Exelixis' quarterly report on Form 10-Q for the quarter ended September 30, 2007 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.

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