Exelixis Reports Encouraging Interim Data From an Ongoing Phase 1b/2 Study of XL184 With or Without Erlotinib in Patients With Non-Small Lung Cancer to be Presented at ASCO

May 20, 2010

SOUTH SAN FRANCISCO, Calif., May 20, 2010 (BUSINESS WIRE) --Exelixis, Inc. (NASDAQ:EXEL) today reported interim data from an ongoing Phase 1b/2 study of XL184 in patients with non-small cell lung cancer (NSCLC). Dr. Heather Wakelee from Stanford University School of Medicine in Stanford, CA will present the data in a poster discussion session (Abstract #3017) on Sunday, June 6 at the 2010 Annual Meeting of the American Society of Clinical Oncology in Chicago.

XL184 is a potent inhibitor of MET, a kinase which plays important roles in the proliferation, migration, and survival of cancer cells. Recent evidence indicates a key role for MET in NSCLC cells that are dependent on EGFR signaling, with expression of MET upregulated by activated EGFR, and formation of heterodimeric signaling complexes between MET and other EGFR family members. In addition, MET has been shown to play a key role in resistance to EGFR inhibitors in NSCLC, with amplification of the gene encoding MET, or strong expression of HGF (the ligand for MET), occurring frequently in cases of acquired or primary resistance, respectively. Thus, there is a compelling rationale for targeting MET in NSCLC, both with and without concurrent inhibition of EGFR.

This phase 1b/2 study is designed to evaluate the safety, tolerability, and maximum tolerated dose (MTD) of XL184 in combination with erlotinib in NSCLC patients, with the majority having demonstrated clinical features consistent with acquired resistance to erlotinib therapy (progression following an initial response or prolonged stable disease on erlotinib). The phase 1b portion of the study includes treatment cohorts that enable the evaluation of the highest tolerable dose of either XL184 or erlotinib as part of the two-drug combination. After determining one or more MTDs for the combination, the phase 2 portion of the study will assess the clinical activity in patients receiving combination MTDs or single agent XL184.

As of the cut-off date of March 25, 2010, 54 patients have been treated in five combination dose cohorts, ranging from 50 mg XL184/150 mg erlotinib to 125 mg XL184/50 mg erlotinib. The vast majority of patients (52/54) had received prior erlotinib therapy. The MTD for the erlotinib maximized arm was determined to be 50 mg XL184/150 mg erlotinib; the preliminary MTD for the XL184 maximized arm of the study is 125 mg XL184/50 mg erlotinib and the cohort is being expanded.

Thirty four of 44 (77%) patients with at least one post-baseline scan demonstrated tumor shrinkage as their best response following a median of 2 prior lines of therapy. Two patients with tumor shrinkage also showed evidence of MET copy number gain (cng). Four of 53 (8%) patients evaluable for response assessment had a confirmed partial response per RECIST criteria.

"We are very encouraged by the data generated thus far in the phase 1 portion of this study. We believe that these results with the XL184-erlotinib combination and the early single-agent XL184 signal from the NSCLC cohort seen in a separate randomized discontinuation trial, also presented at ASCO, will support phase 2 evaluation of XL184 alone and in combination with erlotinib in patients with non-small cell lung cancer," said Michael M. Morrissey, Ph.D., president of research and development at Exelixis. "The evidence of clinical activity, particularly in refractory NSCLC patients previously treated with erlotinib or with drug-resistant EGFR mutations and/or MET copy number gain is of particular note, given the poor prognoses that these patients typically experience."

Broad genotyping efforts examining archival or rebiopsied tumor tissue, plasma, and circulating tumor cells are employed in this trial. Clinical activity has been observed in erlotinib-refractory patients with and without MET cng, and in patients with and without activating EGFR mutations. Notably, stable disease as best response was observed in 7 of 9 patients with the erlotinib-resistant EGFR-T790M mutation. One patient with an L858R activating EGFR mutation and acquired resistance to erlotinib associated with MET cng was treated with 125 mg XL184/ 100 mg erlotinib and had a confirmed PR.

Pharmacokinetic analyses indicate the absence of any XL184-erlotinib drug interactions. XL184 exposure values were close to levels predicted from a single-agent study, while exposure values for erlotinib before or after XL184 administration were not significantly different.

Most adverse events (regardless of causality) were grade 1 or 2 and manageable. Most frequently occurring grade 3/4 adverse events were diarrhea (43%), fatigue (20%), dyspnea (13%), hypokalemia (7%), decreased appetite (6%), decreased weight (6%), increased transaminases (4%), peripheral edema (4%), cough (2%), hypomagnesemia (2%) and myalgia (2%). The incidence of grade 3/4 adverse events associated with VEGF inhibition was generally low, and included venous thrombosis (7%), hemorrhage (4%), hypertension (4%), rectal/peri-rectal abscess (2%), and proteinuria (0%).

The combination of XL184 and erlotinib was generally well tolerated at the MTD of 50 mg XL184/150 mg erlotinib, with 2/17 patients (12%) experiencing grade 3 diarrhea as a dose-limiting toxicity (DLT) and 1/17 patients (6%) experiencing mucositis as a DLT.

About XL184

XL184 (BMS-907351) is an investigational oral inhibitor of MET, VEGFR2, and RET that produces antiangiogenic, antiproliferative, and antiinvasive effects in preclinical tumor models. MET is mutationally activated in some tumor types, such as hereditary and sporadic papillary renal cell carcinoma and some head and neck cancers. More frequently, MET is either over-expressed or activated in the absence of mutation in glioblastomas, breast carcinomas, some gastric cancers, and other solid tumors. MET amplification has been demonstrated in some NSCLCs. Expression of VEGF has been observed in a variety of cancers and has been associated with prognostic significance. Targeting the VEGF receptor has been recognized as a potential anti-cancer strategy in multiple tumors. Dual targeting of MET and VEGFR2 blocks two of the major mechanisms tumors use to overcome hypoxia. Activated RET is involved in cell signaling cascades that regulate cell proliferation, migration, differentiation, and survival. RET is mutationally activated in papillary thyroid cancer (PTC) and in both familial and sporadic forms of medullary thyroid cancer (MTC). Exelixis is co-developing XL184 with Bristol-Myers Squibb Company, and is currently conducting multiple clinical studies with XL184.

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 XL184. Words such as "believe," "will," "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 XL184 to demonstrate safety and efficacy in clinical testing; the ability to conduct clinical trials for XL184 sufficient to achieve a positive completion; the therapeutic and commercial value of XL184; 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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