Exelixis Presents Clinical Data Supporting the Safety and Initial Clinical Activity of XL228 in Chronic and Acute Leukemia

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Compound Inhibits Mutant Forms of BCR-ABL That Cause Resistance to Current CML and ALL Therapies

COPENHAGEN, Denmark, June 13, 2008 /PRNewswire-FirstCall via COMTEX News Network/ -- Exelixis, Inc. (Nasdaq: EXEL) today reported preliminary phase 1 data from an ongoing trial of XL228 in patients with chronic myelogenous leukemia (CML) or Philadelphia chromosome-positive acute lymphocytic leukemia (Ph+ALL) who are resistant to or intolerant of the approved BCR-ABL inhibitors imatinib and dasatinib. XL228 is a small molecule inhibitor of BCR-ABL, SRC, and insulin-like growth factor type 1 receptor (IGF1R), which are associated with cancer cell proliferation, survival, and metastasis. The compound also potently inhibits the T315I mutant form of BCR-ABL, which is resistant to all currently approved inhibitors. Dr. Jorge Cortes, Professor of Medicine, Deputy Chair, Department of Leukemia, University of Texas, MD Anderson Cancer Center, Houston, Texas, and an investigator on the phase 1 trial, presented the data in a poster session (Abstract #1260) at the 13th Congress of the European Hematology Association.

Seventeen subjects have received at least one dose of XL228, of whom 16 had completed Cycle 1 as of May 15, 2008. The trial is evaluating a treatment cycle consisting of 4 weekly 1-hour IV infusions of XL228 at doses ranging from 0.45 mg/kg to 7.2 mg/kg. Thirteen of the 17 subjects (76.5%) have BCR-ABL mutations, including seven (41.2%) with the T315I mutation. At the 3.6 and 7.2 mg/kg doses (either as part of Cohorts 4 and 5 or through dose escalation from a previous cohort), all subjects have demonstrated stable or decreasing white blood cell counts. A CML patient with an F317L BCR-ABL mutation in lymphoid blast crisis experienced a marked decrease in peripheral blast counts on XL228 (7.2 mg/kg) and hydroxyurea which was maintained despite decreasing use of hydroxyurea. Two patients have demonstrated prolonged stable disease for more than 8 months.

"The data presented today provide evidence that XL228 inhibits wild type and clinically relevant mutant forms of BCR-ABL at well tolerated doses," said Michael M. Morrissey, PhD, President of Research and Development at Exelixis. "To date, all patients dosed at or above 3.6 mg/kg have experienced decreases in leukocytes, and/or decreased use of hydroxyurea resulting in prolonged stable disease. Importantly, initial signs of clinical activity have been observed in patients with mutant forms of BCR-ABL, including the imatinib-, dasatinib-, and nilotinib-resistant BCR-ABL mutant T315I. These data suggest that XL228 may have important clinical utility for patients with CML or Ph+ALL, including those resistant or intolerant to current therapeutics."

Currently available safety data show that adverse events are generally of Grade 1 or 2 severity and manageable. One Grade 3 event of tumor lysis syndrome in a patient with lymphoid blast crisis receiving concurrent treatment with hydroxyurea was considered a dose-limiting toxicity (DLT) at 7.2 mg/kg. The maximum tolerated dose (MTD) has not been reached, and dose escalation is ongoing.

Pharmacokinetic results indicate that XL228 has a mean terminal half-life ranging from 15 to 44 hours, with exposure increasing in a slightly greater than dose-proportional manner. Pharmacodynamic analyses demonstrate moderate decreases in phosphorylated CrkL in subjects dosed at 1.8 and 3.6 mg/kg, which reversed between 2 and 24 hours post-infusion. CrkL is a binding partner and substrate of BCR-ABL, and decreases in phosphorylation of CrkL are indicative of BCR-ABL kinase inhibition. XL228 also inhibits IGF1R and the insulin receptor, and plasma insulin was increased at the end of the XL228 infusion on Day 1 and Day 8, with an average 10-fold increase in subjects dosed at 3.6 mg/kg. By 4 hours post-infusion, insulin levels returned to near-normal range. Modest increases in glucose post-infusion also were observed, and these returned to near baseline by 4 hours post-infusion.

About XL228

XL228 is a protein kinase inhibitor with potent activity against wild-type and the T315I mutant forms of BCR-ABL, with additional activity against IGF1R, SRC, and Aurora A. These targets play crucial roles in cancer cell proliferation, survival, and metastasis. XL228 blocks downstream signaling from BCR-ABL T315I in cell lines and modulates phosphorylated CrkL levels in mouse xenografts consistent with inhibitory activity against BCR-ABL in vivo. XL228 has exhibited activity in a variety of solid tumor xenograft models.

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 website 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 utility of XL228. Words such as "may" and similar expressions are intended to identify forward-looking statements. These forward-looking statements are

based upon our current plans, assumptions, beliefs and expectations. Forward-looking statements involve risks and uncertainties. Our 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 XL228 and our other compounds to demonstrate safety and efficacy in clinical testing; the therapeutic and commercial value of XL228 and our other compounds; and our ability to enter into new collaborations, continue existing collaborations and receive milestones and royalties under our collaborative agreements. These and other risk factors are discussed under "Risk Factors" and elsewhere in our quarterly report on Form 10-Q for the quarter ended March 28, 2008, and other filings with the Securities and Exchange Commission. We expressly disclaim any duty, obligation or undertaking to release publicly any updates or revisions to any forward-looking statements contained herein to reflect any change in our expectations with regard thereto or any change in events, conditions or circumstances on which any such statements are based.

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