Exelixis Reports Additional Data From the Phase I Trial of XL999 in Patients With Advanced Solid Tumors

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PRAGUE, Czech Republic, Nov. 8 /PRNewswire-FirstCall/ -- Exelixis, Inc. (Nasdaq: EXEL) announces that updated data from a Phase I trial of XL999, an investigational cancer therapy, administered weekly or every two weeks by intravenous (IV) infusion were reported today. Consistent with previously reported results from this study, XL999 showed preliminary evidence of antitumor activity. Cardiac failure and elevated hepatic transaminases were identified as dose-limiting toxicities. Dr. Monica M. Mita of the Institute for Drug Development in San Antonio and an investigator in the study presented the data in a poster (Abstract #83) at the 18th EORTC-NCI-AACR Symposium on Molecular Targets and Cancer Therapeutics, which is being held November 7-10 in Prague, Czech Republic.

As of October 1, 2006, 45 patients had been enrolled and reported on in the Phase I trial and were evaluable for safety and tumor response assessments. Three dosing regimens were studied: weight based bi-weekly, weight based weekly, and fixed dose weekly dosing. Of these patients, 23 received weight-based dosing of XL999 administered every 2 weeks, with a maximum tolerated dose (MTD) established at 3.2 mg/kg; 15 patients received weekly weight-based dosing of XL999 (seven patients at 3.2 mg/kg and eight at 2.4 mg/kg); and seven patients received a weekly fixed dose of 200 mg XL999.

Three patients have had partial responses (one each squamous cell cancer in the liver, renal cell cancer and thyroid cancer [unconfirmed]). Ten other patients have had stable disease for 3 to 25.5+ months (thyroid cancer [2], renal cell carcinoma [2], and one each cystoid adenoma, esophageal cancer, gastrointestinal stromal tumor, colorectal cancer, carcinoid and hepatocellular carcinoma).

The weekly weight-based and fixed dose dosing safety characteristics of XL999 have been similar in nature but less severe at lower doses than previously reported for the bi-weekly dosing regimen (Papadopoulos et al, 2005, Proceedings of the 17th EORTC-NCI-AACR Symposium on Molecular Targets and Cancer Therapeutics). The reported dose-limiting toxicity at 6.4 mg/kg for the bi-weekly dosing regimen was fatal cardiac failure and elevated transaminases. In the weekly weight-based dosing cohorts at 3.2 mg/kg XL999, one patient developed a reversible decrease in left ventricular ejection fraction, elevated troponins, and ECG changes on day 1, and another patient treated at 2.4 mg/kg XL999 had asymptomatic grade 1 hypotension with nonspecific ECG changes. At weekly 200 mg fixed dosing, serious adverse events considered related to study drug include one patient with grade 3 hypotension, grade 3 ECG changes, and grade 3 increased troponin, and one patient with grade 2 cardiac failure, grade 2 ECG changes, grade 3 dyspnea, and grade 3 increased troponin. All cardiac events occurred with the first dose of XL999.

A Phase II clinical program for XL999 was initiated in December 2005 and is ongoing. The Phase II program is composed of six trials that will evaluate XL999 in colon, ovarian and non-small cell lung cancer (NSCLC), renal cell carcinoma, acute myelogenous leukemia (AML) and multiple myeloma. As announced on November 2, 2006, enrollment in the Phase II trial has been suspended pending further review of data relating to cardiovascular adverse events. Through the end of September, 117 patients had been dosed with XL999, of whom 12 (10.3%) experienced serious adverse cardiovascular events. However, 4 of the 14 patients enrolled during October also experienced such events, which raised a concern with the company's internal safety monitoring committee. The company therefore decided to suspend enrollment of new patients pending further review of the data. Because 115 of the 131 subjects enrolled in the XL999 clinical program to date have received repeated doses of XL999 (every week or every other week) ranging from 2 doses (2 weeks) to 53 doses (approximately 2 years) with no reported cardiac toxicities, the company has elected to allow patients already enrolled to continue to receive XL999.

"We continue to believe in the potential of XL999 as a novel cancer therapy," said Gisela M. Schwab, M.D., senior vice president and chief medical officer of Exelixis. "We are placing patients' safety first and are diligently analyzing the clinical data available for XL999 to determine the appropriate next steps in the development of this novel cancer therapy."

Additional Information

Exelixis' clinical investigators will discuss clinical data on XL999, XL880, XL820 and XL184 in conjunction with data presentations at the conference. The discussion will take place in Prague at 6:00 p.m. (local time) / 12:00 p.m. (ET) / 9:00 a.m. (PT) on Thursday, November 9, 2006. The discussion will be webcast and archived and may be accessed in the Event Calendar page under Investors at www.exelixis.com. Additionally, the XL999 poster presented at the conference may be accessed in the Pipeline page at www.exelixis.com upon the conclusion of the conference.

About the Trial

This Phase I, nonrandomized, open-label, dose-finding trial is being conducted in patients aged 18 years or older with histologically confirmed advanced solid malignancy that is metastatic or unresectable and for which alternative therapies do not exist or are no longer effective. Patients were enrolled in successive cohorts to receive escalating doses of XL999 administered by intravenous infusion. Each 2-week treatment cycle consisted of a 4-hour infusion of XL999 administered either every 2 weeks or weekly. Patients received weekly XL999 at either a weight-based dose or a fixed dose of 200 mg. Patients receiving a fixed-dose therapy underwent intensive cardiovascular monitoring. Primary endpoints of the study were to determine the MTD of XL999; assess the safety and tolerability of XL999 administered weekly or every 2 weeks as a 4-hour IV infusion with weight-based (mg/kg) or fixed dosing to patients with solid tumors; assess the safety and tolerability of XL999 administered weekly as a 4-hour IV infusion with weight-based (mg/kg) dosing; and to assess a fixed-dose schedule with intensive cardiac monitoring. The secondary endpoint was to evaluate plasma pharmacokinetics of repeat dosing of XL999. Tumor response rate was also included as an exploratory endpoint.

About XL999

XL999 is a potent inhibitor of key receptor tyrosine kinases (RTKs) implicated in the development and maintenance of tumor vasculature and in the

proliferation of some tumor cells. It inhibits the FGFR, VEGFR and PDGFR RTKs and has exhibited excellent activity in target-specific cellular functional assays. In addition, in preclinical studies XL999 is a potent inhibitor of FLT3, an important driver of leukemia cell proliferation in some patients with AML. In several preclinical models of human tumors, including breast, lung, colon and prostate cancer, XL999 demonstrated potent inhibition of tumor growth, and also caused regression of large well- established tumors.

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 III (XL119, exclusively out-licensed to Helsinn Healthcare S.A.), Phase II, and Phase I 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 Sankyo. For more information, please visit the company's web site at www.exelixis.com.

This press release contains forward-looking statements, including, without limitation, statements related to clinical development plans for XL999. Words such as "believes," "anticipates," "plans," "expects," "intends," "will," "slated," "goal" 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, analysis of data from the XL999 program may show that XL999 cannot be administered safely at a therapeutic dose; additional serious adverse events in the XL999 program; failure to resume enrollment in the XL999 program in a timely manner or at all; regulators or institutional review boards may not authorize or may delay, suspend or terminate the clinical trial program for XL999 due to the observed adverse cardiovascular or other effects; the ability to conduct clinical trials sufficient to achieve a positive completion; the uncertainty of the FDA approval process; and the therapeutic and commercial value of the company's compounds. These and other risk factors are discussed under "Risk Factors" and elsewhere in our quarterly report on Form 10-Q for the quarter ended September 30, 2006 and other filings with the Securities and Exchange Commission. The company expressly disclaims any obligation or undertaking to release publicly any updates or revisions to any forward- looking statements contained herein to reflect any change in the company's expectations with regard thereto or any change in events, conditions or circumstances on which any such statements are based.

SOURCE Exelixis, Inc.
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