Mesothelioma Articles

Encouraging Phase I Trial Results for XL647 in Patients with Advanced Solid Malignancies Presented at ASCO

ATLANTA, June 3 /PRNewswire-FirstCall/ -- Exelixis, Inc. (NASDAQ: EXEL) announces that updated results from a Phase I trial of XL647 in patients with advanced solid malignancies were reported today. XL647 is an orally bioavailable small molecule inhibitor of HER2, EGFR, VEGFR and EphB4. Study results demonstrate that XL647 is well tolerated and shows evidence of biologic and clinical activity. A maximum tolerated dose (MTD) has been identified. Results of the Phase I trial of XL647 were presented in a poster, titled "A Phase I Dose-Escalation and Pharmacokinetic (PK) Study of a Novel Spectrum Selective Kinase Inhibitor, XL647, in Patients with Advanced Solid Malignancies (ASM)," (Abstract # 3044) in a poster discussion session at the 42nd Annual Meeting of the American Society of Clinical Oncology (ASCO). The conference is taking place June 2 to 6 in Atlanta.

As of March 15, 2006, a total of 40 patients have been treated across 9 dose levels ranging from 0.06 to 7.0 mg/kg, in a liquid formulation and then a tablet formulation and are evaluable for safety endpoints.

As reported by the investigators one patient (non-small cell lung cancer [NSCLC]) has had a partial response and 12 others (NSCLC [3], chordoma [2], adenoid cystic carcinoma [2], adrenocortical carcinoma, colorectal, ovarian, mesothelioma and head and neck cancer) have had prolonged stable disease >3.5 months.

"We are pleased to see the favorable safety and tolerability data with XL647 in Phase I. The evidence of clinically relevant activity of XL647 in tumors where we would expect to see activity, like non-small cell lung cancer, is very encouraging," said George A. Scangos, Ph.D., president and chief executive officer of Exelixis. "Based on these promising results, we expect to initiate a Phase II development program for XL647 this summer."

"The Phase I trial of XL647 has provided important information on the safety, tolerability, PK profile and clinical activity of this multi-RTK inhibitor," said Dr. Alex Adjei, Professor of Oncology, Mayo Clinic and an author on the study. "These data provide a compelling rationale for evaluating XL647 in Phase II trials."

The first two patients treated at the 7.0 mg/kg dose experienced dose limiting toxicities (DLTs) of grade 3 diarrhea, which resolved upon a reduction in dose to 4.68 mg/kg. Expansion of the 4.68 mg/kg cohort to 6 patients occurred without further DLTs, and this is considered the MTD. One serious adverse event of grade 4 pulmonary embolism was considered potentially related to study treatment in a patient treated at the 0.28 mg/kg dose. One patient at the 3.12 mg/kg dose had an asymptomatic QTc prolongation on electrocardiogram.

About the Trial

The primary objective of the Phase I dose escalation trial was to establish a MTD and to assess safety and tolerability of oral administration of XL647. Secondary objectives included PK analyses and tumor response. The study enrolled patients with advanced solid malignancies in successive cohorts to receive XL647 orally as a single dose on day 1, followed by 5 continuous daily doses starting on day 4. Patients then continued to receive dosing for 5 continuous days followed by a break with cycles repeated every 14 days. Patients were allowed to stay on-study in the absence of unacceptable toxicity until evidence of disease progression.

About XL647

XL647 is a potent inhibitor of multiple RTKs implicated in driving tumor cell proliferation and tumor vascularization (blood vessel formation). XL647 inhibits the EGF, HER2, and VEGF RTKs, each of which is a target of currently approved cancer therapies. In addition, XL647 inhibits EphB4, an RTK that is highly expressed in many human tumors and plays a role in promoting angiogenesis. In a broad array of preclinical tumor models including breast, lung, colon and prostate cancer, XL647 demonstrated potent inhibition of tumor growth and causes tumor regression. In cell culture models, XL647 retains significant potency against mutant EGFRs that are resistant to current EGFR inhibitors.

About Exelixis

Exelixis, Inc. is a biotechnology company dedicated to the discovery and development of novel therapeutics that will potentially enhance the care and lives of patients with cancer and other serious diseases. The company is leveraging its fully integrated gene-to-drug platform to fuel the growth of its proprietary drug pipeline. Exelixis' development pipeline covers cancer and metabolism and is comprised of the following compounds: XL119 (becatecarin), for which a multinational Phase III clinical trial in bile duct tumor is ongoing and which has been exclusively licensed to Helsinn Healthcare S.A.; XL784, which is being advanced in a Phase II trial as a treatment for renal disease; XL999, an anticancer compound currently in Phase II clinical trials for a variety of solid tumors and hematologic malignancies; XL647, XL880, XL820, XL844 and XL184, anticancer compounds currently in Phase I clinical trials; and multiple compounds in preclinical development for diseases including cancer and various metabolic and cardiovascular disorders. Exelixis has established broad corporate alliances with major pharmaceutical and biotechnology companies including GlaxoSmithKline (GSK) and Bristol-Myers Squibb Company. Pursuant to a product development and commercialization agreement between Exelixis and GSK, GSK has the option, after completion of clinical proof-of-concept by Exelixis, to elect to develop a certain number of compounds in Exelixis' product pipeline, which may include XL784 and the cancer compounds identified in this press release (other than XL119), thus potentially triggering milestone payments and royalties from GSK and co- promotion rights by Exelixis. For more information, please visit the company's web site at http://www.exelixis.com.

This press release contains forward-looking statements. 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, the potential failure of product candidates to demonstrate safety and efficacy in clinical testing; the ability of Helsinn Healthcare S.A. to conduct the Phase III clinical trial of XL119 sufficient to achieve FDA approval; the ability to complete and initiate trials at the referenced times; the ability to conduct clinical trials sufficient to achieve a positive completion; the ability to file INDs at the referenced times; the ability of Exelixis to advance additional preclinical compounds into clinical development; 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 March 31, 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: http://www.exelixis.com