



Exelixis Reports Positive Phase 1 Data for XL281 at EORTC-NCI-AACR Symposium

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Inhibitor of RAF Kinases Shows Early Signs of Clinical Activity

GENEVA--(BUSINESS WIRE)--

Exelixis, Inc. (Nasdaq:EXEL) today reported preliminary phase 1 data from a dose-escalation trial of XL281 in patients with advanced solid malignancies. XL281 is a novel, selective, and potent small molecule inhibitor of wild-type and mutant RAF kinases that have been implicated in human cancer. Gary K. Schwartz, MD, Chief, Melanoma and Sarcoma Service, Memorial Sloan-Kettering Cancer Center, and an investigator on the phase 1 trial, presented the data in a poster session (Abstract #383) at the EORTC-NCI-AACR Symposium on Molecular Targets and Cancer Therapeutics, which is being held October 21-24 in Geneva, Switzerland. The poster will be available today on the Exelixis web site.

"XL281 demonstrates clear target inhibition and exhibits early signs of clinical activity at generally well-tolerated doses in this phase 1 population," said Michael M. Morrissey, PhD, President of Research and Development at Exelixis. "RAF is a very important target that is mutationally activated in numerous tumor types, and consequently there have been many attempts to directly inhibit this target. Based on our recent data, XL281 holds the potential to be an effective anti-cancer agent in a wide variety of tumor types."

In the trial, 29 patients have been enrolled in seven cohorts, with XL281 administered orally at doses ranging from 10 to 225 mg daily. Tumor types include colorectal cancer (N=7), papillary thyroid cancer (N=5), ovarian cancer (N=1), prostate cancer (N=1), carcinoid tumor (N=2), and melanoma (N=4).

As of October 3, 2008, one partial response (ocular melanoma) and 12 patients with stable disease (greater than or equal to 3 months) have been observed. The 5 patients with papillary thyroid cancer, two with a confirmed BRAF V600E mutation, have had stable disease (68, 64+, 53+, 26, 20 weeks, respectively). Three patients with colorectal cancer have had stable disease for 20 weeks, and two patients with carcinoid tumor have had stable disease (53+ and 22 weeks). In addition, one patient with Hurtle cell thyroid cancer and one with prostate cancer have had stable disease (31+ and 14 weeks, respectively).

Dose-limiting toxicities (DLTs) were reported in 3 of 3 patients receiving an oral daily dose of 225 mg XL281. No DLTs were observed at any of the other dose levels. No Grade 4 or 5 adverse events (AEs) considered related to XL281 have been reported. Some subjects receiving XL281 at 150 mg (either as a starting dose or following dose escalation from a lower dose) developed fatigue and weight loss after Cycle 1 and required a dose reduction to 100 mg. In the majority of these cases, fatigue was rapidly reversible following dose reduction. The most frequent treatment-related AEs have been Grade 1 or 2 fatigue, nausea, diarrhea, and vomiting. The maximum administered dose (MAD) has been established as 225 mg and the maximum tolerated dose (MTD) as 150 mg.

Pharmacokinetic analyses indicated that for the 150 mg/day cohort, XL281 accumulated approximately 1.75-fold in plasma with repeated daily dosing, with steady state reached by approximately Day 8. XL281 plasma exposure increased with increasing dose, and exceeded levels associated with anti-tumor activity in preclinical models.

In pharmacodynamic analyses, substantial modulation of the BRAF signaling pathway was observed in tumor tissue, skin, and hair, as indicated by decreases in the phosphorylation of MEK and ERK following treatment with XL281. A reduction in proliferation and an increase in apoptosis were observed in tumor tissue following treatment with XL281.

"The on-target activity of XL281, coupled with its early signs of clinical activity, is highly encouraging and suggests that this agent may be effective in a wide range of tumor types," said Gary K. Schwartz, MD, Chief, Melanoma and Sarcoma Service, Memorial Sloan-Kettering Cancer Center.

About XL281

XL281 is a novel small molecule designed to selectively inhibit RAF kinases, which lie immediately downstream of RAS and are key components of the RAS/RAF/MEK/ERK kinase signaling pathway. Genetic lesions that activate this pathway are common in human tumors, with activating mutations in KRAS occurring in 30 percent of tumors and activating mutations in BRAF occurring in approximately 60 percent of melanomas. The RAS/RAF/MEK/ERK pathway also plays a key role in the transmission of growth-promoting signals downstream of receptor tyrosine kinases. This suggests that deregulation of this pathway plays a pivotal role in the progression of many human tumors, and that inhibition of the pathway may be useful in the treatment of cancer. XL281 potentially inhibits BRAF, mutationally activated BRAF, and CRAF in vitro, and does not interact with kinases outside of the RAF family. XL281 displays high oral bioavailability in multiple preclinical species, and strongly inhibits RAS/RAF/MEK/ERK signaling in human xenograft tumor models. This translates into substantial inhibition of tumor growth in preclinical models of human tumors that overexpress receptor tyrosine kinases or harbor activating mutations in RAS or RAF.

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 3, 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 potential for XL281 to be an effective anti-cancer agent in a wide variety of tumor types. Words such as "potential," "may," 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: the potential failure of XL281 to demonstrate safety and efficacy in clinical testing; the therapeutic and commercial value of XL281; and the ability to conduct XL281 clinical trials sufficient to achieve a positive completion. These and other risk factors are discussed under "Risk Factors" and elsewhere in Exelixis' quarterly report on Form 10-Q for the quarter ended June 27, 2008, and 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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