

Exelixis Describes the Discovery of Novel Cancer Targets at AACR

New Insights Into Interdependence of Two Cancer Signaling Pathways

SOUTH SAN FRANCISCO, Calif., March 29 /PRNewswire-FirstCall/ --

Exelixis, Inc. (Nasdaq: EXEL) today described the identification of two enzyme targets that play a functional role in key signaling pathways involved in cancer. Exelixis has also presented novel insights into how one of these targets lies at the intersection of the PTEN and beta-catenin signaling pathways, which has implications on which patient populations to target with future drugs designed to inhibit these kinases. Exelixis is currently generating small molecule inhibitors against these kinase targets as potential anti-cancer agents. Exelixis Senior Vice President, Research, Greg Plowman, M.D., Ph.D., presented these findings at the 95th Annual Meeting of the American Association of Cancer Research, in a session entitled, "Signaling Pathways Revisited."

Exelixis' work in the discovery of these novel cancer targets was performed as part of the company's broad oncology research collaboration with Bristol-Myers Squibb, Inc.

"Exelixis' identification of targets that provide a link between the PTEN and beta-catenin signaling could lead to the creation of new classes of cancer therapeutics," said Dr. Plowman. "We believe that Exelixis is at the forefront of translating novel biological insights into drug discovery strategies and identifying ways to use this information to improve the quality and efficiency of drug development. Exelixis' focus on 'Spectrum Selective Kinase Inhibitors'(TM) that specifically target key players in multiple signaling pathways with highly potent small molecule inhibitors is a major advance in this strategy. We are excited by the potential application of these insights in the clinical oncology setting."

About PTEN and beta-catenin

PTEN is recognized to be the most highly mutated tumor-suppressor gene discovered since p53. Exelixis performed multiple genetic screens in several model systems, including *C. elegans*, *Drosophila* and cell lines, resulting in the identification of multiple targets involved in tumor cell biology, including a specific kinase target that, when inhibited, was shown to impact signaling through the PTEN pathway. Exelixis' high throughput screening efforts have identified potent small molecule inhibitors against this kinase. Structural biology efforts have solved the structure of the target and co-crystal structures of the kinase in complex with three distinct chemical scaffolds. The company plans to advance these compounds into further lead optimization.

Mutations within the beta-catenin pathway have been implicated in multiple tumor types, including colon, gastric and hepatocellular tumors and melanoma. Despite high interest in this important pathway over the last two decades, few significant drug development targets have been identified. Exelixis' genetic screening efforts have identified key targets within the beta-catenin signaling pathway that, when inactivated, interrupt cell signaling and cause apoptosis in cancer cells. Of particular interest is a specific kinase target against which Exelixis has generated potent small molecule inhibitors that are progressing into lead optimization.

About Exelixis

Exelixis, Inc. is a leading genomics-based drug discovery company dedicated to the discovery and development of novel therapeutics. The company is leveraging its fully integrated gene-to-drug platform to fuel the growth of its proprietary drug pipeline. Exelixis' development pipeline includes: XL119 which is anticipated to enter a Phase 3 clinical trial as a potential treatment for bile duct tumors; XL784, an anticancer compound that has completed a Phase 1 clinical trial; XL647, for which an IND application has been submitted; XL999 and XL844, anticancer compounds that are

potential IND candidates; and multiple compounds in preclinical development. Exelixis has established broad corporate alliances with major pharmaceutical and biotechnology companies, including GlaxoSmithKline and Bristol-Myers Squibb Company. After completion of Phase 2a clinical trials, GlaxoSmithKline has the right to elect to develop a certain number of the cancer compounds identified in this release, other than XL119, thus potentially triggering milestone payments and royalties from GlaxoSmithKline and co-promotion by Exelixis. The company has also established agricultural research collaborations with Bayer CropScience, Dow AgroSciences and Renessen LLC. Other partners include Merck & Co., Inc., Schering-Plough Research Institute, Inc., Cytokinetics, Inc., Elan Pharmaceuticals, Inc. and Scios Inc. For more information, please visit the company's web site at www.exelixis.com.

This press release contains forward-looking statements, including without limitation all statements related to the discovery and application of potentially novel biological insights to Exelixis' drug discovery programs, plans to commence a Phase 3 clinical trial of XL119, including the expected structure of this clinical trial, and plans to advance its compounds in preclinical and clinical development, and lead optimization including XL119, XL784, XL647, XL999, XL844 and other early-stage compounds, as well as the therapeutic and commercial potential of these compounds. Words such as "believes," "anticipates," "plans," "expects," "intend," "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, risks related to the uncertainty of the preclinical development and clinical trials process and whether our compounds will demonstrate safety and efficacy, and related to the ability of the company to initiate the planned Phase 3 clinical trial of XL119. These and other risk factors are discussed under "Risk Factors" and elsewhere in the company's annual report on Form 10-K, as amended, for the year ended December 31, 2003 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.

NOTE: Exelixis and the Exelixis logo are registered U.S. trademarks. Spectrum selective kinase inhibitor is a trademark of Exelixis, Inc.