Exelixis Reports Encouraging Phase 1 Data for XL184 at ASCO

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Greater Than 50% Response Rate and 100% Disease Control Rate Observed in Patients with Medullary Thyroid Cancer

CHICAGO, June 1 /PRNewswire-FirstCall/ -- Exelixis, Inc. (Nasdaq: EXEL) reported encouraging new data from an ongoing phase 1 clinical trial of XL184, a novel small molecule inhibitor of MET, VEGFR2, and RET, in patients with advanced malignancies. The maximum tolerated dose (MTD) for XL184 has been determined to be 175 mg/day given orally daily. Based on initial signs of clinical activity in a number of patients with medullary thyroid cancer (MTC) during the dose-escalation phase, the trial has been expanded to treat an additional 20 patients with MTC at the MTD. Ravi Salgia, MD, PhD, Associate Professor of Medicine and Director of the Thoracic Oncology Research Program at the University of Chicago Medical Center, and a lead investigator in the trial, presented the data today in the Developmental Therapeutics: Molecular Therapeutics oral abstract session (Abstract #3522) at the 44th Annual Meeting of the American Society of Clinical Oncology (ASCO).

Sixty patients were evaluated for safety, pharmacokinetics, and tumor response as of the May 1, 2008 cutoff; further data also were provided for nine additional patients after the cutoff. Across all tumor types, 10 patients had partial responses as determined by RECIST criteria: 9 partial responses were observed in patients with MTC (5 confirmed), and 1 in a patient with a neuroendocrine tumor. An additional 25 patients with various tumor types had stable disease for at least 3 months, including 8 patients with MTC. The disease control rate (percentage of patients with partial responses or prolonged stable disease >3 months) in patients with MTC was 100%, with 53% of evaluable MTC patients (9 of 17) experiencing partial responses. With a single exception, all of the evaluated MTC patients had reductions in the MTC-associated plasma markers calcitonin and carcinoembryonic antigen. Most of the MTC patients in the trial had previously failed other treatments, including tyrosine kinase inhibitors with anti-RET activity (e.g., vandetanib, sorafenib, motesanib), chemotherapeutics, immunotherapy, radioactive iodine, and radiotherapy.

"Patients with medullary thyroid cancer are a highly underserved population as there is no active approved therapy available at this time. Targeted therapeutics, such as dual inhibitors of RET and VEGFR2, are the first compounds showing activity in this disease. The phase 1 results of XL184, the first such molecule in this class also to inhibit the oncogenic MET receptor, were reported today by Drs. Salgia and Kurzrock, and are remarkable, both in terms of the high frequency of responses and how rapidly they occur," said Steven I. Sherman, MD, Chair and Professor, Department of Endocrine Neoplasia and Hormonal Disorders, University of Texas M.D. Anderson Cancer Center, Houston, Texas. "I am looking forward to the phase 3 trial of XL184 in this indication and believe that studies like this will importantly advance the care of patients with medullary thyroid cancer."

The data indicate that XL184 was generally well-tolerated at the MTD of 175 mg QD (capsule). Adverse events related to study drug included diarrhea, nausea, fatigue, mucositis, anorexia, elevation of liver enzymes, hypertension, vomiting, hair hypopigmentation, and palmar-plantar erythema. Dose-limiting toxicities included palmar-plantar erythema, elevation of liver enzymes, lipase elevation, and mucositis.

Pharmacokinetic analyses indicate that the half-life of XL184 was approximately 100 hours (range 59-136 hours), with exposure at the MTD exceeding that required for efficacy in preclinical models. Pharmacodynamic analyses demonstrated statistically significant changes at the MTD in plasma markers including VEGF-A, PlGF, and soluble VEGFR2, similar to the effects of other anti-angiogenic agents, and consistent with the anti-VEGFR activity of XL184. In addition, decreases in soluble MET were measured in 4 of 7 patients at the MTD who were analyzed for this endpoint.

"We believe the results for XL184 are remarkable and strongly support our plan to initiate a pivotal trial this summer in patients with MTC. Based on these data, we believe that XL184 is in a strong position to become the best-in-class therapy in MTC," said Michael M. Morrissey, PhD, President of Research and Development at Exelixis. "Given the potent activity of XL184 against MET, RET, and VEGFR2, and the observed long-lasting disease stabilization in a variety of tumor types in this phase 1 trial, we will continue to explore the compound's utility as a single agent, or in combination with other therapies, in tumor types like lung cancer, glioblastoma, and potentially many others."

Investor and Analyst Briefing at ASCO, Monday, June 2, 6 pm

Exelixis will host an investor and analyst briefing on Monday, June 2, at 6:00 p.m. at the Hyatt McCormick Place (Regency C&D - 2nd Floor). At this event, Exelixis will provide a review of its data presented at ASCO and describe additional data on XL147, a PI3K inhibitor, and XL281, an inhibitor of RAF. The event will be webcast and may be accessed in the Event Calendar page under Investors at www.exelixis.com. An archived replay of this webcast will be available until 9:00 p.m. PT/12:00 a.m. ET on July 2, 2008. Access numbers for this replay are: 1-888-286-8010 (domestic) and +1-617-801-6888 (international); the replay passcode is: 42662164.

About XL184

XL184 inhibits MET, RET, and VEGFR2, which are key drivers of tumor growth, metastasis, survival, and angiogenesis. In pharmacodynamic studies in mice, oral administration of XL184 resulted in balanced and durable inhibition of these targets. The compound has also shown activity against common mutant forms of RET and MET. XL184 has exhibited dose-dependent tumor growth inhibition and tumor regression in a variety of tumor models, including breast cancer, colon cancer, MTC, non-small cell lung cancer, and glioblastoma. A pivotal phase 3 trial of XL184 in patients with MTC is planned to begin in the summer of 2008. Phase 1/2 and 2 studies of XL184 in non-small cell lung cancer and glioblastoma multiforme are ongoing.

About Medullary Thyroid Cancer

The American Cancer Society estimates that MTC accounts for 5% of all thyroid cancers. MTC occurs in sporadic and inherited forms (approximately 80% and 20% of MTC, respectively), and is frequently associated with genetic activation of RET. The inherited form usually appears at a younger age, while dietary iodine deficiency and radiation exposure are risk factors for the sporadic form. MTC may metastasize to lymph nodes or other organs before it is ever diagnosed. Additionally, MTC does not take up radioactive iodine, which is commonly used to treat other types of thyroid cancers and to diagnose metastases. As a result, MTC is more difficult to treat than other thyroid cancers. There are no approved therapies for MTC; however, common treatments for MTC include surgery to remove malignant tissue, radiation therapy, and chemotherapy, all of which are associated with potential side effects, some of which may be long-term.

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 web site at www.exelixis.com .

Forward-Looking Statements

This press release contains forward-looking statements, including without limitation statements related to the future development and potential efficacy of XL184 and the timing of the initiation of pivotal trials for XL184. Words such as "hope," "plan," "continue," "will," "believe," 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 XL184 to demonstrate safety and efficacy in clinical testing, our ability to initiate and complete pivotal trials for XL184 at the referenced times; the timing and level of expenses associated with the growth of proprietary programs and other collaborations; the therapeutic and commercial value of XL184 and our other compounds; our relationship with our partners; 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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