Exelixis Reports Promising Interim Data from Patients with Castration-Resistant Prostate Cancer Treated with XL184

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SOUTH SAN FRANCISCO, Calif., Nov 18, 2010 (BUSINESS WIRE) -- Exelixis, Inc. (NASDAQ:EXEL) today reported interim data from the cohort of patients with metastatic castration-resistant prostate cancer (CRPC) treated with XL184 in an ongoing phase 2 adaptive randomized discontinuation trial (RDT). David C. Smith, M.D., Professor, Departments of Internal Medicine and Urology at the University of Michigan, will present the data in the Molecular-Targeted Therapies-Clinical Trials poster session (Abstract #406) on Thursday, November 18th, at the 22nd EORTC-NCI-AACR Symposium on Molecular Targets and Cancer Therapeutics in Berlin, Germany.

XL184 Activity Against Bone and Soft Tissue Lesions in CRPC

As of the November 1, 2010 cut-off date, a total of 99 patients were enrolled in the CRPC cohort, with 34 currently evaluable for tumor response per RECIST criteria and 20 with evidence of bone metastasis evaluable for changes in bone scan. The trial includes patients with (57%) and without (43%) prior docetaxel therapy.

Impact on Metastatic Bone Lesions

Nineteen of 20 patients (95%) achieved either complete or partial resolution of lesions on bone scanby independent review, with most resolving at the first post-baseline assessment at 6 weeks. Bone scans use a radiotracer imaging agent that binds to sites of new bone formation, which reflect sites of metastatic disease in bone. Multiple cases of complete or near complete resolution were observed in both docetaxel-pretreated and docetaxel-naïve subgroups. To date, a single docetaxel-pretreated patient achieved stabilization of bone scan as his best evaluation, and no patient exhibited worsening on bone scan as his best time point assessment.

Bone scan resolution was associated with investigator reported improvements in bone pain, with the majority of symptomatic patients experiencing pain relief. In addition, most patients exhibited decreases in the blood-based bone metabolism biomarkers alkaline phosphatase (ALP) and C-terminal telopeptides of type 1 collagen (CTx), which are often increased in patients with metastatic bone lesions who are at risk for skeletal morbidity. Patients with anemia at baseline exhibited maximal increases in hemoglobin levels ranging from 1.2 to 3.4 g/dL from baseline.

Impact on Soft Tissue Lesions

The week-12 disease control rate (DCR) was 71%. Tumor shrinkage was observed in 38 of 55 patients (69%) with measurable soft-tissue metastatic lesions and at least one post-baseline scan. To date, 3 of 34 patients (9%) evaluable by RECIST achieved a confirmed partial response (PR). Of note, response criteria in common use today (including RECIST) do not incorporate bone scan findings. Stable disease (SD) was reported in 25 patients (74%) including 2 unconfirmed PRs. Changes in PSA are reasonably well correlated with response to hormonally acting agents and cytotoxic chemotherapy. In contrast, XL184 treated patients experiencing tumor regression and improvement in bone pain demonstrated variable impact on PSA levels. Thus, the commonly used PSA marker does not appear to be a reliable indicator for the activity of XL184 in this disease.

Safety and Tolerability

Safety data are available for 49 patients who had at least 6 weeks of follow-up. The most common Grade greater-than or equal to 3 AEs, regardless of causality were fatigue (14%), hypertension, PPE syndrome (each 6%), hemorrhage, nausea (each 4%), diarrhea, cough, and rash (each 2%).

"CRPC is a leading cause of cancer-related death in men in the United States and Europe," said Dr. Smith. "Recent advances in systemic therapy have had at best a modest impact on survival, and virtually all patients will succumb to this disease. Bone metastases result in significant morbidity for patients with CRPC, including fractures and pain, which can substantially reduce quality of life and increase mortality. The results of this study to date suggest that XL184 has activity against both soft tissue and bone metastatic lesions. Based on this activity, further evaluation of XL184 in CRPC is clearly indicated, as the data suggest that the compound may provide clinical benefit to a population of patients with few treatment options that effectively target both components of this disease."

"The initial activity of XL184 against metastatic soft-tissue and bone lesions in CRPC patients is very encouraging," said Michael M. Morrissey, Ph.D., president and chief executive officer of Exelixis. "These data suggest that XL184 has a novel and differentiated clinical profile in CRPC, and will provide critical guidance in defining our high priority development activities for XL184 in 2011."

To access the clinical data poster mentioned in this press release, please visit www.exelixis.com.

XL184 Targets Key Pathways That Contribute to Prostate Cancer

XL184, an inhibitor of tumor growth, metastasis and angiogenesis, simultaneously targets MET and VEGFR2, key kinases involved in the development and progression of many cancers. Prominent expression of MET has been observed in primary and metastatic prostate carcinomas, with evidence for higher levels of expression in bone metastases. Overexpression of hepatocyte growth factor (HGF), the ligand for MET, has also been

observed in prostate carcinoma, and increased plasma levels of HGF are associated with decreased overall survival in CRPC. Data from preclinical studies also suggest that both HGF and MET are regulated by the androgen signaling pathway in prostate cancer, where upregulation of MET signaling is associated with the transition to androgen-independent tumor growth. Additionally, both the MET and VEGF signaling pathways also appear to play important roles in the function of osteoblasts and osteoclasts--cells in the bone microenvironment that are often dysregulated during the establishment and progression of bone metastases.

The Significance of Bone Metastases in CRPC

The primary cause of morbidity and mortality in patients with CRPC is metastasis to the bone, which occurs in about 90% of cases. Bone metastases cause local disruption of normal bone remodeling, with lesions generally showing a propensity for an osteoblastic (bone-forming) phenotype on imaging. These lesions often lead to increased skeletal fractures, spinal cord compression, and severe bone pain. Osteoblastic lesions are typically visualized in CRPC patients by bone scan, which detects rapid incorporation of 99mTc-labeled methylene-diphosphonate radiotracer into newly forming bone. In addition, increased blood levels of ALP and CTx, markers for osteoblast and osteoclast activity, respectively, are often observed in CRPC patients with bone metastases, and are associated with shorter overall survival.

Broad Clinical Activity of XL184 - Randomized Discontinuation Trial

XL184 has demonstrated anti-tumor activity in 9 of 12 indications studied to date. In ongoing trials, compelling activity has been observed in medullary thyroid cancer, glioblastoma, and clear cell renal cancer. In the RDT, XL184 is being evaluated in nine different tumor types, with clear signals of activity in six: prostate, ovarian, hepatocellular, breast, non-small cell lung cancer, and melanoma. The adaptive RDT design allowed for rapid simultaneous assessment of the activity of XL184 across nine different tumor indications. As of the November 1, 2010 cut-off date, a total of 397 patients have been enrolled into the 9 disease-specific cohorts, with 273 evaluable for response, and 312 evaluable for safety. Of 273 patients evaluable for response per RECIST, 39 achieved a PR (either confirmed or unconfirmed) and 100 had SD at week 12. The week-12 DCR for the overall population was 49%, with the highest rates occurring in hepatocellular cancer (75%), CRPC (71%), ovarian cancer (64%), melanoma (45%), non-small cell lung cancer (42%) and breast cancer (42%). Of note, a breast cancer patient with evidence of bone metastasis on bone scan demonstrated evidence of resolution on bone scan accompanied by 29% reduction in tumor size. XL184 has been generally well tolerated with a consistent adverse event profile across the nine different RDT tumor types.

Conference Call and Webcast

A conference call to highlight the data from the six posters presented at the EORTC-NCI-AACR Symposium on the company's randomized discontinuation trial of XL184 will be held on November 18, at 7:30 a.m. EST / 4:30 a.m. PST. To listen to a webcast of the call, visit the Event Calendar page under Investors at www.exelixis.com.

About XL184

XL184, an inhibitor of tumor growth, metastasis and angiogenesis, simultaneously targets MET and VEGFR2, key kinases involved in the development and progression of many cancers. It has recently been shown in preclinical models that treatment with selective inhibitors of VEGF signaling can result in tumors that are more invasive and aggressive compared to control treatment. In preclinical studies, upregulation of MET has been shown to occur in concert with development of invasiveness after selective anti-VEGF therapy, and may constitute a mechanism of acquired or evasive resistance to agents that target VEGF signaling without inhibiting MET. Accordingly, treatment with XL184 in similar preclinical studies resulted in tumors that were less invasive and aggressive compared to control or selective anti-VEGF treatment. Therefore, XL184 has the potential for improving outcomes in a range of indications, including those where selective anti-VEGF therapy has shown minimal or no activity.

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. The company is leveraging its biological expertise and integrated research and development capabilities to generate a pipeline of development compounds with significant therapeutic and commercial potential for the treatment of 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 Bristol-Myers Squibb Company, sanofi-aventis, GlaxoSmithKline, Genentech (a wholly owned member of the Roche Group), Boehringer Ingelheim, 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 continued development and clinical, therapeutic and commercial potential of XL184, including the further evaluation of XL184 in CPRC and the potential for XL184 to provide clinical benefit to a population of patients with few treatment options that effectively target both soft tissue and metastatic lesions, Exelixis' belief that the novel and differentiated data in CRPC will provide critical guidance in defining the company's high priority development activities for XL184 in 2011 and Exelixis' belief that XL184 has the potential for improving outcomes in a range of indications. Words such as "suggest," "further," "may," "will," "potential," "encouraging" 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, risks related to the potential failure of XL184 to demonstrate safety and efficacy in clinical testing; Exelixis' ability to conduct clinical trials of XL184 sufficient to achieve a positive completion; the sufficiency of Exelixis' capital and other resources; the uncertain timing and level of expenses associated with the development of XL184; the uncertainty of the FDA approval process; market competition and changes in economic and business conditions. These and other risk factors are discussed under "Risk Factors" and elsewhere in Exelixis' quarterly report on Form 10-Q for the quarter ended October 1, 2010 and Exelixis' 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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