Exelixis' Cabozantinib Demonstrates Encouraging Clinical Activity in Patients with Metastatic Ovarian Cancer

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Disease control rate of 53% at week 12, response rate of 24%
Median duration of response not yet reached

SOUTH SAN FRANCISCO, Calif., Jun 04, 2011 (BUSINESS WIRE) -- Exelixis, Inc. (NASDAQ:EXEL) reported longer follow-up data from a fully enrolled cohort of patients with advanced epithelial ovarian cancer, primary peritoneal carcinoma, or fallopian tube carcinoma treated with cabozantinib (XL184) in an ongoing phase 2 adaptive randomized discontinuation trial. Cabozantinib shows promising activity in these patients independent of prior response to platinum-based therapies.

Ronald J. Buckanovich, M.D., Ph.D., Assistant Professor, Department of Internal Medicine and Assistant Professor, Department of Obstetrics and Gynecology, University of Michigan, presented the data today in an oral session at the American Society of Clinical Oncology's 2011 Annual Meeting (Abstract #5008) in Chicago.

As of the February 11, 2011 cut-off date, accrual in this cohort was complete at 70 patients. Randomization was halted, and randomized patients were un-blinded based on an observed high rate of clinical activity.

Patient Population and Overall Response Rate

All 70 patients enrolled into the ovarian cancer cohort had minimum follow-up of at least 12 weeks and were thus evaluable for safety and the primary efficacy endpoint of response per RECIST. Approximately half of the 70 patients enrolled in the cohort were considered platinum refractory/resistant (49%), defined as a platinum-free interval of 6 months or less, and the remainder of patients (51%) had platinum-sensitive disease based on a platinum-free interval greater than 6 months. More than half the patients (57%) had received 2 or more prior lines of platinum therapy. Some patients also had additional prior lines of therapy with agents such as pegylated liposomal doxorubicin or topotecan (32%), gemcitabine (29%), and VEGF pathway inhibitors (10%). Evidence of objective tumor regression was observed in 73% of patients with at least 1 post-baseline scan. The best overall response rate per RECIST criteria was 24% (16 partial responses [PRs] and 1 complete response). The overall Week-12 disease control rate (DCR) was 53%.

"These latest results in metastatic ovarian cancer demonstrate the potential broad utility of cabozantinib beyond bone-predominant types of cancers such as castration-resistant prostate cancer. The high rates of durable response with our dual inhibitor of MET and VEGFR2 compare favorably to those of other single-agent targeted therapies and cytotoxic agents in development," said Michael M. Morrissey, Ph.D., president and chief executive officer of Exelixis. "These results underscore the potential of cabozantinib in metastatic ovarian cancer, and we are in discussions with leading cooperative groups to plan further evaluation of cabozantinib in randomized trials for this indication."

Activity in Platinum-Sensitive, -Refractory, and -Resistant Disease

Two of 11 patients (18%) with platinum refractory disease, defined as a platinum-free interval of <1 month, achieved a confirmed response (1 complete response and 1 PR). In the subset of patients with platinum-resistant disease, defined as a platinum-free interval of 1-6 months, 5 of 23 (22%) achieved a PR. Ten of 36 patients (28%) with platinum sensitive disease achieved a PR. The median duration of response has not yet been reached with 36 weeks of median follow-up. The Week-12 DCR in the platinum-refractory, -resistant, and -sensitive groups was 36%, 39%, and 67%, respectively. A total of 37 patients experienced reductions in the ovarian cancer tumor marker CA125, including 8 with decreases greater than 50%. There is no consistent concordance between CA125 changes and tumor regression.

"The continued activity of cabozantinib in a larger population of ovarian cancer patients is very encouraging, especially with respect to the clinical benefit observed in both platinum-sensitive and platinum-resistant/refractory disease. This activity profile has not been observed with other single-agent TKIs, and cabozantinib has the potential to be an important new treatment for ovarian cancer," said Ignace Vergote, M.D., Ph.D., senior author of the presentation and Chairman of the Leuven Cancer Institute at the University of Leuven, European Union. "The high rate of disease control in platinum-resistant and platinum-refractory disease suggests that cabozantinib may help to address the substantial unmet medical need faced by patients who have sub-optimal responses to platinum-based therapies. I believe that further evaluation will help to define the potential role of cabozantinib in the treatment of ovarian cancer."

Safety and Tolerability

Safety data are available for the 70 patients in the Lead-In phase of the study. The most common grade 3 or 4 adverse events (AEs), regardless of causality, were diarrhea (10%), fatigue (9%), PPE syndrome (7%), vomiting (4%), abdominal pain (3%), hypomagnesemia (3%), and nausea, constipation, rash, increased transaminase, and hypertension (each 1%). Two cabozantinib-related grade 5 AEs, one enterocutaneous fistula and one intestinal perforation, were reported after the Lead-In phase. At least one dose reduction was reported in 37% of patients. Less frequent important medical events, regardless of causality, were hemorrhage (11% all grades, 0% grade 3 or 4), venous thrombosis (6%, 4%), and gastrointestinal perforation (6%, 0%).

To access the clinical data mentioned in this press release, please visit www.exelixis.com/sites/default/files/pdf/ASCO_2011-XL184-Ovarian.pdf

Conference Call and Webcast

An investor briefing webcast will be held in conjunction with the 2011 ASCO Annual Meeting. The webcast will be held on Monday, June 6, 2011, from 6:00-8:00 p.m. CT, and may be accessed by visiting the Event Calendar page under Investors at www.exelixis.com. An archived replay will be available on the Event Calendar page under Investors at www.exelixis.com and via phone until 11:59 p.m. EDT/8:59 p.m. PDT on July 6, 2011. Access numbers for the replay are: 1-888-286-8010 (domestic) and 1-617-801-6888 (international). The replay passcode is 15003148.

About Cabozantinib

Cabozantinib is a potent, dual inhibitor of MET and VEGFR2. Cabozantinib is an investigational agent that provides coordinated inhibition of metastasis and angiogenesis to kill tumor cells while blocking their escape pathways. The therapeutic role of cabozantinib is currently being investigated across several tumor types. MET is upregulated in many tumor types, thus facilitating tumor cell escape by promoting the formation of more aggressive phenotypes, resulting in metastasis. MET-driven metastasis may be further stimulated by hypoxic conditions in the tumor environment, which are often exacerbated by selective VEGF-pathway inhibitors. In preclinical studies, cabozantinib has shown powerful tumoricidal, antimetastatic and antiangiogenic effects, including:

- Extensive apoptosis of malignant cells
- Decreased tumor invasiveness and metastasis
- Decreased tumor and endothelial cell proliferation
- Blockade of metastatic bone lesion progression
- Disruption of tumor vasculature

About Exelixis

Exelixis, Inc. is a biotechnology company committed to developing small molecule therapeutics for the treatment of cancer. Exelixis is focusing its resources and development efforts exclusively on cabozantinib, its most advanced solely-owned product candidate, in order to maximize the therapeutic and commercial potential of this compound. Exelixis believes cabozantinib has the potential to be a high-quality, differentiated pharmaceutical product that can make a meaningful difference in the lives of patients. Exelixis has also established a portfolio of other novel compounds that it believes have the potential to address serious unmet medical needs. 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 cabozantinib; promising activity shown by cabozantinib in ovarian cancer patients independent of prior response to platinum-based therapies; the potential broad utility of cabozantinib beyond bone-predominant types of cancers; the potential of cabozantinib in metastatic ovarian cancer; discussions with leading cooperative groups to plan further evaluation of cabozantinib; the belief that cabozantinib has the potential to be an important new treatment for ovarian cancer; the suggestion that cabozantinib may help to address the substantial unmet medical need faced by patients who have sub-optimal responses to platinum-based therapies; and the belief that further evaluation will help to define the potential role of cabozantinib in the treatment of ovarian cancer. Words such as "encouraging," "promising," "demonstrate," "potential," "plan," "suggest," "may," "believe," "will," 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 cabozantinib to demonstrate safety and efficacy in clinical testing; Exelixis' ability to conduct clinical trials of cabozantinib sufficient to achieve a positive completion; the availability of data at the referenced times, the sufficiency of Exelixis' capital and other resources; the uncertain timing and level of expenses associated with the development of cabozantinib; 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 April 1, 2011 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.

SOURCE: Exelixis, Inc.

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