Exelixis and BMS Report Phase 2 Data to Be Presented at ASCO for XL184 in Patients with Previously Treated Glioblastoma Multiforme

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SOUTH SAN FRANCISCO, Calif. & PRINCETON, N.J.--(BUSINESS WIRE)--May. 31, 2009-- Exelixis, Inc. (Nasdaq:EXEL) and Bristol-Myers Squibb Company (NYSE:BMY) today reported encouraging data from an ongoing phase 2 trial of XL184 in patients with previously treated glioblastoma multiforme (GBM) (study XL184-201).

XL184 is an orally administered small molecule inhibitor of receptor tyrosine kinases including MET, VEGFR2, and RET. Overexpression of MET and VEGFR2, as well as the ligands which activate these receptors, has been shown to correlate with poor prognosis in GBM, which is the most common and aggressive form of brain tumor. In addition, phosphorylated RET has been described in some cases of GBM.

Exelixis is co-developing XL184 with Bristol-Myers Squibb Company. John De Groot, MD, of The MD Anderson Cancer Center, and an investigator on the Phase 2 GBM trial, will present the data in a poster session (Abstract #2047) from 8 a.m. to 12 p.m. local time on Sunday, May 31, 2009, at the American Society of Clinical Oncology (ASCO) Annual Meeting, which is being held May 29-June 2 in Orlando.

The exploratory study is evaluating the safety, tolerability and clinical activity of XL184 at a continuous daily dose of 175 mg in patients with previously treated GBM. To date, 46 patients who make up the intent to treat (ITT) population have been enrolled in the trial, including 30 (65%) in first relapse and 16 (35%) in second or third relapse. Importantly, the trial did not exclude patients previously treated with an antiangiogenic agent.

Tumor response, as determined by an independent radiology facility (IRF), using MacDonald criteria were reported. By ITT analysis, 7 of 35 (20%) of the antiangiogenic naïve patients had a confirmed partial response. The overall rate of response in all patients, including the refractory population of previously treated patients with an antiangiogenic therapy, was 15%. The median duration of response by IRF was 2.9 months (range = 1.9-8.6 months). In an exploratory analysis, among 35 patients with at least one post baseline MRI scan, 12 (34%) had tumor shrinkage ≥50% as their best response as determined by investigator, including 1 patient who had received prior antiangiogenic therapy.

The efficacy evaluable population was defined as patients having received at least 1 dose of XL184 and either had at least 1 post-baseline tumor assessment per investigator or failed to return for any tumor assessments because of death or clinical determination of progression. In the anti-angiogenic naïve population, 7 of 31 (23%) of efficacy evaluable patients had a confirmed partial response by IRF. The 6-month progression-free survival (PFS) rate in patients receiving no prior antiangiogenic therapy was 23%, with 10 patients censored for PFS at the time of analysis, and the median PFS interval was 3.6 months.

“These initial data from our ongoing GBM program are encouraging, and suggest that XL184 could have utility in this underserved indication,” said Michael M. Morrissey, Ph.D., president of research and development at Exelixis. “We believe that these data support continued evaluation of XL184 in patients with GBM, and we intend to enroll additional patients in this study to better assess the compound’s anti-tumor activity and safety profile in this difficult to treat patient population.”

All 46 patients were evaluated for safety. Most adverse events were of Grade 1 or 2 severity. The most frequently occurring Grade 3 and Grade 4 adverse events were: fatigue (30%), alanine aminotransferase increase (9%), confusional state (9%), lipase increase (9%), lymphopenia (9%), convulsion (7%), headache (7%), and hypophosphatemia (7%). Adverse events of special interest were: hypertension (all incidences, 39%; Grade 3/4, 7%), palmar-plantar erythrodysesthesia (30%; 7%), bleeding events (28%; 9%), proteinuria (26%; 0%), pulmonary embolism (9%; 7%) and craniotomy wound dehiscence (4%; 2%).

In the study, 87% of patients had a dose interruption of XL184, median average daily dose was 122 mg/day. XL184 will be evaluated at a lower dose of 125 mg daily in order to provide continuous and sustained exposure to the drug in this previously treated glioblastoma population.

Correlative tumor profiling and biomarker evaluation and vascular imaging data from this trial will also be presented in two additional posters in the same poster session. Abstract 2048, entitled “Neurovascular imaging in GBM patients quantifies early physiologic changes after treatment with XL184, an inhibitor of multiple receptor tyrosine kinases: results from a Phase 2 study” will be presented by Gregory Sorensen, MD, from the Massachusetts General Hospital, Boston, MA, and abstract 2049, entitled “Correlative tumor molecular profiling and plasma biomarker analysis in a phase 2 study of XL184 in patients with progressive or recurrent glioblastoma multiforme” will be presented by Samuel DePrimo, PhD, Exelixis Inc, South San Francisco, CA.

About XL184

XL184 (BMS-907351) is a small molecule designed to inhibit MET, VEGFR2, and RET. MET is a receptor tyrosine kinase that plays a key role in cellular proliferation, migration, and angiogenesis. These biological processes contribute to the transformation, progression, survival, and metastasis of cancer cells. MET is mutationally activated in some tumor types, such as hereditary and sporadic papillary renal cell carcinoma and some head and neck cancers. More frequently, MET is either over-expressed or activated in the absence of mutation in glioblastomas, breast carcinomas, some gastric cancers, and other solid tumors. MET amplification has been demonstrated in some NSCLCs. Expression of VEGF has been observed in a variety of cancers and has been associated with prognostic significance. Targeting the VEGF receptor has been recognized as a potential anti-cancer strategy in multiple tumors. Dual targeting of MET and VEGFR2 blocks two of the major mechanisms tumors use to overcome hypoxia. Activated RET is involved in cell signaling cascades that regulate cell proliferation, migration, differentiation, and survival. RET is mutationally activated in papillary thyroid cancer (PTC) and in both familial and sporadic forms of medullary thyroid cancer (MTC). Exelixis is co-developing XL184 with Bristol-Myers Squibb Company, and is currently conducting multiple clinical studies for XL184.

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 Bristol-Myers Squibb, sanofi-aventis, GlaxoSmithKline, Genentech, Boehringer Ingelheim, Wyeth Pharmaceuticals, and Daiichi-Sankyo. For more information, please visit the company's web site at www.exelixis.com.

About Bristol-Myers Squibb

Bristol-Myers Squibb is a global biopharmaceutical company whose mission is to extend and enhance human life. For more information, visit www.bms.com.

Exelixis Forward-Looking Statements

This press release contains forward-looking statements by Exelixis, including, without limitation, statements related to the future development path and therapeutic potential of XL184. Words such as "suggest," "believe," "intend," "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 XL184 to demonstrate safety and efficacy in clinical testing; the therapeutic and commercial value of XL184; the uncertainty of the FDA approval process; market competition; and Exelixis' dependence on its relationship with its collaboration partners. These and other risk factors are discussed under "Risk Factors" in Exelixis' Quarterly Report for the quarter ended April 3, 2009 and Exelixis' other reports filed 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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