



XBiotech Presents Pivotal Phase III Data Showing Xilonix(TM) Demonstrated Significant Clinical Response in Advanced Colorectal Cancer Patients Refractory to Further Treatment

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(GLOBE NEWSWIRE via COMTEX) --- Improved clinical response seen for multiple symptoms associated with disease progression and overall survival, with notable lack of toxicity

- Xilonix is the first antibody therapy to neutralize biological activity of interleukin-1 alpha (IL-1alpha), a potent anti-inflammatory signaling molecule known to promote the growth and spread of tumors

- Xilonix granted accelerated review by the European Medicines Agency (EMA); an approval decision could come as early as fourth quarter 2016

AUSTIN, Texas, July 02, 2016 (GLOBE NEWSWIRE) -- XBiotech Inc. (NASDAQ:XBITE), developer of next-generation True Human(TM) antibody therapies, today presented positive results from a pivotal Phase III trial of Xilonix(TM), the company's lead monoclonal (IgG1k) antibody immunotherapy for the treatment of advanced colorectal cancer (CRC). In the study, Xilonix-treated patients with advanced disease and multiple symptoms known to inversely correlate with overall survival experienced a 76% relative increase in clinical response rate (CRR), a novel measure of anti-cancer activity, after 8 weeks of therapy compared to placebo (33% vs. 19%, respectively; $p=0.0045$). In addition, clinical response correlated with improved overall survival. Among responders (in both treatment and placebo arms), clinical response was associated with a 2.7-fold increase in overall survival (11.5 versus 4.2 months in responders vs. non-responders, respectively). Overall survival was not compared between treatment arms because after 8 weeks, all patients were eligible to receive study drug. Treatment with Xilonix was well tolerated, with an adverse event profile comparable to placebo. The data were presented at the 18th European Society of Medical Oncology (ESMO) World Congress on Gastrointestinal Cancer in Barcelona, Spain.

The study's primary endpoint, CRR, was developed in collaboration with the European Medicines Agency (EMA) Scientific Advice Working Group as a means to determine efficacy of Xilonix as an anti-cancer therapy in patients with advanced colorectal cancer. The CRR measured debilitating symptoms (pain, fatigue, appetite loss and muscle loss) that are key indicators of health status and are associated with poor prognosis for survival. 1, 2, 3, 4, 5, 6

"In this first-of-its-kind study, not only did treatment with Xilonix demonstrate clinical benefit but it was also very well-tolerated, suggesting Xilonix has the potential to meet the real and urgent need for more effective, less toxic therapies for patients with advanced colorectal cancer," said Dr. Tamas Hickish, Chair of the Xilonix European Phase III Study and Consultant Medical Oncologist, Dorset Cancer Centre, Visiting Professor, Bournemouth University, UK. "In addition, this study provides evidence that novel endpoints based on symptom recovery can serve as a predictor of overall survival benefit and thus may be used to evaluate an anti-tumor agent in this disease."

In addition to increased overall survival, responders gained more lean body mass compared to non-responders ($p<0.0007$), had reduced fatigue and pain ($p<0.001$) and improved appetite ($p<0.001$). Control of thrombocytosis and systemic inflammation (IL-6), which are known prognosticators of overall survival, were also significantly improved in responders vs. non-responders ($p<0.0002$ and $p<0.0007$, respectively).

There was a notable lack of toxicity associated with Xilonix treatment in the study. The most common adverse events (AEs) reported were abdominal pain, peripheral edema, fatigue, anemia, constipation, decrease in weight, asthenia, decreased appetite and nausea. The majority of these events were characterized as mild to moderate and appeared to be related to the underlying disease. The prevalence of AEs was similar in both treatment and placebo groups. While the study was not powered to demonstrate a difference in serious adverse events (SAEs) between treatment and placebo groups, there was a 26% relative risk reduction of SAEs in the treatment arm vs. placebo ($p=0.062$), a unique and notable finding.

"There is an urgent need for new forms of anti-tumor, disease-modifying cancer therapies that effectively control disease while being less toxic," said John Simard, XBiotech Founder, President and Chief Executive Officer. "We believe these data demonstrate that our True Human monoclonal antibody targeting interleukin-1 alpha has the potential to meet this critical need."

Study Methodology

In the double-blind placebo-controlled Phase III study, 309 patients were randomized (2:1) to receive Xilonix plus best supportive care (BSC) versus placebo plus BSC. Study participants had failed all available chemotherapy and had metastatic disease with one or more symptoms of metabolic dysfunction and functional impairment (i.e., elevated systemic inflammation, unintentional weight loss, pain, fatigue, anorexia). Patients were required to have an Eastern Cooperative Oncology Group (ECOG) function status of only 1 or 2. Elderly patients (>70 years of age) were eligible as well, in contrast to many studies of anti-cancer therapies in advanced disease.

The study's primary endpoint measured CRR after 8 weeks of therapy. This novel endpoint was developed in consultation with the EMA, which has provided a regulatory path to encourage and expedite the development of anti-cancer agents that improve patient health status while prolonging life. These guidelines enable development of anti-cancer agents based on an effect that improves debilitating symptoms in patients, particularly where the effect is the result of an anti-tumor mechanism and the clinical measures are considered prognosticators for overall survival.⁷

CRR was assessed using dual-energy X-ray absorptiometry to determine lean body mass (LBM) and using the standard European Organization for Research and Treatment of Cancer (EORTC) quality of life questionnaire (QLQ-C30) to capture patients' own assessment of their fatigue, pain and anorexia from baseline to week 8. To be classified as responders, patients had to maintain or improve LBM and maintain or improve in at least two of the three categories of pain, fatigue and anorexia. Secondary endpoints evaluated paraneoplastic thrombocytosis and systemic inflammation, both

known correlates for survival in colorectal cancer. Median overall survival was also assessed. Patients receiving placebo were allowed to receive study drug after completion of the 8-week protocol, therefore overall survival was not compared between arms. Rather, the overall survival analysis compared responders vs. non-responders.

About Colorectal Cancer

Colorectal cancer is the second leading cause of malignancy in the industrialized world.⁸ Because the incidence of colorectal cancer increases with economic development and aging, incidence is rising worldwide.⁹ In Europe, approximately 470,000 patients will be diagnosed with colorectal cancer this year, and half will progress and ultimately succumb to the disease.¹⁰ Disease progression is associated with significant morbidity, functional impairment and failure of multiple therapies, often with substantial toxicities. People with advanced disease are thus symptomatic and often unable to tolerate further treatment-related side effects, leaving an urgent need for more effective, less toxic therapies for these patients.

About Xilonix(TM) and Interleukin-1 alpha (IL-1alpha)

Xilonix(TM) is the first monoclonal antibody to specifically target and neutralize interleukin-1 alpha (IL-1alpha), one of the most potent inflammatory signaling molecules. The IL-1 pathway in general, and IL-1alpha in particular, is a desirable target for anti-cancer therapy because of its potential role in both local and systemic effects of cancer.^{11,12} IL-1alpha in the tumor microenvironment is known to promote angiogenesis (the growth and spread of tumors), as well as mediate symptoms such as metabolic dysregulation (e.g., loss of weight and muscle mass), fatigue and anxiety associated with advanced cancer.

About True Human(TM) Therapeutic Antibodies

Unlike previous generations of antibody therapies, XBiotech's True Human(TM) antibodies are derived without modification from individuals who possess natural immunity to certain diseases. With discovery and clinical programs across multiple disease areas, XBiotech's True Human antibodies have the potential to harness the body's natural immunity to fight disease with increased safety, efficacy and tolerability.

The first of these therapies, Xilonix(TM), for advanced colorectal cancer, is in Phase III clinical trials in the United States with a Fast Track designation by the U.S. Food and Drug Administration (FDA). In Europe, Xilonix Phase III clinical trials have been completed and the therapy is under accelerated review following the validation of its Market Authorization Application by the European Medicines Agency (EMA).

About XBiotech

XBiotech is a fully integrated global biosciences company dedicated to pioneering the discovery, development and commercialization of therapeutic antibodies based on its True Human(TM) proprietary technology. XBiotech currently is advancing a robust pipeline of antibody therapies to redefine the standards of care in oncology, inflammatory conditions and infectious diseases. Headquartered in Austin, Texas, XBiotech also is leading the development of innovative biotech manufacturing technologies designed to more rapidly, cost-effectively and flexibly produce new therapies urgently needed by patients worldwide. For more information, visit www.xbiotech.com.

Cautionary Note on Forward-Looking Statements

This press release contains forward-looking statements, including declarations regarding management's beliefs and expectations that involve substantial risks and uncertainties. In some cases, you can identify forward-looking statements by terminology such as "may," "will," "should," "would," "could," "expects," "plans," "contemplate," "anticipates," "believes," "estimates," "predicts," "projects," "intend" or "continue" or the negative of such terms or other comparable terminology, although not all forward-looking statements contain these identifying words. Forward-looking statements are subject to inherent risks and uncertainties in predicting future results and conditions that could cause the actual results to differ materially from those projected in these forward-looking statements. These risks and uncertainties are subject to the disclosures set forth in the "Risk Factors" section of certain of our SEC filings. Forward-looking statements are not guarantees of future performance, and our actual results of operations, financial condition and liquidity, and the development of the industry in which we operate, may differ materially from the forward-looking statements contained in this press release. Any forward-looking statements that we make in this press release speak only as of the date of this press release. We assume no obligation to update our forward-looking statements whether as a result of new information, future events or otherwise, after the date of this press release.

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