



XBiotech Announces Top-Line Results for 514G3 Antibody Therapy in Serious *Staphylococcus aureus* Infections

Apr 3, 2017

Patients Receiving 514G3 Therapy Had Reduced Hospitalization and Fewer Infection-Related Serious Adverse Events

AUSTIN, Texas, April 03, 2017 (GLOBE NEWSWIRE) -- XBiotech Inc. (NASDAQ:XBIT) announced top-line results today from its double-blind, placebo-controlled, phase I-II study evaluating the safety and efficacy of its FDA Fast Tracked true human antibody (514G3) for the treatment of *Staphylococcus aureus* bloodstream infections.

The study involved use of the Company's proprietary 514G3 antibody derived from a natural human immune response against a key virulence determinant of *S. aureus* that is present on all strains of the bacteria, including MRSA. In the study, hospitalized adult patients with confirmed blood infections were randomized 3:1 (514G3 vs placebo) during a dose escalation phase to establish a Phase II dose. The Phase II portion was randomized 2:1 at the established Phase II dose of 40 mg/kg. A total of 52 patients were enrolled: 36 received 514G3 and 16 received placebo. Thirty of the 36 patients that were given 514G3 received the established Phase II dose (40 mg/kg).

The study was the first in-human use for 514G3 using exploratory endpoints in a small population. Thus, the study was not powered to demonstrate statistically significant outcomes. Nevertheless, several key topline results from the clinical study were observed.

No drug-related adverse events were observed at any of the dose escalation levels and the 40 mg/kg Phase II dose was established without any dose-limiting toxicities (DLTs). The duration of hospitalization and incidence of serious adverse events (SAEs) were key clinical endpoints which the Company is exploring as a basis for evaluating effectiveness of the therapy. SAEs thus served as both a measure of safety and of efficacy for the 514G3 therapy. Blinded analyses for SAEs were independently performed by the study chair, treating investigators, and an independent expert. A total of 28 SAEs in 15 patients were reported during the study period including 4 deaths. There was a 49% relative risk reduction for the overall incidence of SAEs in subjects receiving 514G3 compared to those receiving placebo [(8 of 36 (22%) vs 7 of 16 (44%), respectively, (p=0.11)]. There was an even greater risk reduction in the incidence of *S. aureus* related SAEs in those that received 514G3 treatment compared to placebo, with a 56% relative risk reduction in the 514G3 group [4 of 36 (11%) vs 4 of 16 (25%), respectively, (p=0.23)]. The trend seen with overall and disease specific reduction in SAEs was a key outcome in the study and an important potential indication of 514G3 efficacy.

Another clinically important secondary endpoint was the average length of hospitalization for patients from the time they entered study. The duration of hospitalization was reduced by about 33% in the 514G3 treatment arm compared to the placebo arm [8.6±7 days vs 12.7±9 days, respectively (p=0.092)] [median 7.5 (IQR 4–9) vs median 12 (IQR 5.5–19), respectively]. Given the complexity of the co-morbidities in the population and the small study size, observing reduced hospital stay in the 514G3 group suggests a considerable impact on resolution of disease, less patient morbidity and a potential reduction in healthcare expenditures for subjects receiving the antibody therapy.

Dr. Mark E. Rupp, Principal Investigator of the study, Professor and Chief, Division of Infectious Diseases, Medical Director, Department of Infection Control & Epidemiology at the University of Nebraska, stated, "Novel treatments for serious infections due to *Staphylococcus aureus* are critically needed. Unfortunately, *S. aureus* is becoming increasingly resistant to antibiotics and, due to the expanding need for medical devices, hemodialysis, advanced surgical procedures, and an aging population, we can expect to see more and more people infected with *S. aureus*. Results from the phase I-II trial are encouraging. Despite the study being very small and 514G3-treated subjects tending to be sicker, there were fewer adverse events and shorter hospitalization associated with the 514G3 therapy.

John Simard, President & CEO of XBiotech, commented, "This first-in-human use of 514G3 used exploratory clinical endpoints to evaluate an important new antibody therapy for patients with life-threatening infections. Given the effect sizes such as reductions in SAEs and shortening of hospitalization time, in a small group with extensive co-morbidities, the study provided the signals we were hoping to see."

Other findings in this study were that randomization failed in the small sample size to provide well matched populations with respect to co-morbidities between treatment and placebo arms. Subjects who were randomized in the 514G3 treatment arm tended to be sicker and have greater numbers of serious co-morbid conditions and greater risk of complications. Seventy-eight percent of the 514G3 treated patients were admitted to the hospital via the Emergency Department vs 56% in the placebo arm. In addition, observed differences in the primary diagnosis for patients randomized to the 514G3 vs placebo arm included 4 (11%) vs 0 for stroke and 4 (11%) vs 0 for sepsis, respectively. Conversely, for 9 (56%) of the placebo arm patients vs only 11 (31%) of 514G3 patients, staphylococcus infection was associated with underlying cellulitis, which is generally a more mild form of the disease. Consequently, four deaths occurred in the treatment arm vs none in the placebo group (p=0.30). The panel of experts certified in blinded reviews that three of the deaths were unrelated to study drug. For one death, there was uncertainty. Two of the three panel experts deemed that an event for a patient admitted with an acute stroke that died one day following receiving 514G3 treatment was "possibly" related to the test article. Autopsy findings, however, revealed extensive atherosclerosis in the brain and concluded that death was sequelae of a second stroke. Dr. Rupp further related, "Although the deaths observed in the treatment arm of the study did not appear to be drug-related, this will warrant careful evaluation in larger studies. Overall, 514G3 shows promise as an innovative adjunctive approach in the treatment of serious infections due to *S. aureus*."

S. aureus bacteremia is a very serious medical problem that is associated with a 30-day mortality rate of 20%-30% despite treatment with antibiotics. *S. aureus* is becoming increasingly resistant to antibiotics and new treatment modalities are urgently needed. The CDC has graded methicillin-resistant *S. aureus* (MRSA) as a serious threat to public health and estimates that over 80,000 serious MRSA infections occur in the U.S. each year resulting in over 11,000 deaths.

About True Human™ Therapeutic Antibodies

XBiotech's True Human™ 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.

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™ 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.

Contact □
Ashley Otero
aotero@xbiotech.com
512-386-2930



XBiotech, Inc