XBiotech Announces First Patient in Clinical Study to Evaluate Bermekimab in Systemic Sclerosis

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Bermekimab Blocks Key Inflammatory Pathway in Systemic Sclerosis, a Devastating Disease with Currently No Approved Therapies

AUSTIN, Texas, Oct. 02, 2019 (GLOBE NEWSWIRE) -- XBiotech (NASDAQ: XBIT) announced the first patient was enrolled in a clinical study evaluating bermekimab therapy in adults with systemic sclerosis (SSc), otherwise known as scleroderma, a devastating inflammatory syndrome characterized by chronic inflammation in the blood vessels, skin, and other organs. The randomized double-blind, placebo-controlled trial will evaluate efficacy of weekly bermekimab monotherapy versus placebo. The primary endpoint of the study will be measured at 12 weeks, and will assess SSc disease severity using a combination of rheumatological, clinical, and physiological measures. The study will randomize patients 1:1 to receive either weekly subcutaneous injections of bermekimab or placebo. The study will also include an open label weekly bermekimab treatment regimen during weeks 13-24, where patients will continue to be evaluated using the same endpoints.

SSc is characterized by systemic inflammation that results in injury to blood vessels, and fibrosis of the skin and internal organs[1]. Skin lesions can be severe, resulting in disfiguration and debilitating pain. In addition, patients suffering from SSc have substantially reduced life expectancy due to the fibrosis that occurs in vital organs and chronic inflammation of the blood vessels[2].

While the cause of SSc is unknown, pathogenesis of the disease is understood to involve errant activation of fibroblasts. In normal organs and tissues, fibroblast cells play a crucial role in building the structural framework of connective tissue that holds the organs and tissues together. Fibroblasts produce the extracellular matrix substances that actually enable the organ structure. When fibroblasts are errantly activated in SSc, they become hyperactive and produce excessive extracellular matrix, which is the basis for fibrosis.

An initial step in the SSc disease process is believed to be the release of the potent inflammatory cytokine interleukin-1 alpha (IL-1α) from keratinocytes in the epidermis[3]. The release of IL-1α results in the production of a myriad of other inflammatory cytokines, including IL-6, TNF, IL-8, IL-10, and others from surrounding tissues[4,5,6,7]. Blocking IL-1α could abrogate the pathological cascade that occurs in this disease. Bermekimab specifically binds and neutralizes IL-1α.

Errant IL-1α production has been repeatedly shown to occur in cells of patients with SSc ([8,9]). IL-1α levels are elevated in SSc patients[10,11], including in the skin and in lung fluids of SSc patients with pulmonary fibrosis; and when IL-1α production is induced in normal fibroblasts, these take on the characteristics of SSc fibroblasts[12].

Evangelos Giamarellos-Bourboulis, MD, PhD, Professor of Internal Medicine, Attikon University Hospital and principle investigator of the study, commented, “We have long suspected a role for IL-1 α in the pathogenesis of systemic sclerosis. There are thus strong fundamental principles behind our use of bermekimab in treating the disease. We hope that this study will finally lead to an effective treatment approach for patients with systemic sclerosis.”

The most common affected organs in SSc are the skin, the gastrointestinal tract, the lungs, and the heart. Capillary endothelium is involved, leading to ischemia and digital necrosis. Patients develop an interstitial lung disease (ILD) prototype dominated by pulmonary hypertension (PHA) and failed gas exchange. Almost all patients also have signs of intestinal dysmotility leading to gastrointestinal reflux and bloating[13]. Hallmarks of SSc are fibrosis of the skin and internal organs and vasculopathy. SSc is the only rheumatic disorder accompanied by substantial lethality; so far no specific treatment targeting the mechanism of pathogenesis is available.

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 technologyXBiotech 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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[1] Varga J, Abraham D (2007) Systemic sclerosis. A prototypic multisystem fibrotic disorder. J Clin Invest 117:557–67.

[2] Steen VD, Medsger TA Jr. Severe organ involvement in systemic sclerosis with diffuse scleroderma. Arthritis Rheum 2000; 43: 2437–2444.

[3] Werner S, Krieg T, Smola H. Keratinocyte-fibroblast interactions inwound healing. J Invest Dermatol 2007; 127: 998 1008.

[4] Engelhardt E, Toksoy A, Goebeler M, Debus S, Bröcker EB, Gillitzer R. Chemokines IL-8, GROa, MCP-1, IP-10, and Mig are sequentially and differentially expressed during phase-specific infiltration of leukocyte subsets in human wound healing. Am J Pathol 1998; 153: 1849–1860.

[5] Uchi H, Terao H, Koga T, Furue M. Cytokines and chemokines in the epidermis. J Invest Dermatol 2000; 24S: 529-538.

[6] Gillitzer R, Goebeler M. Chemokines in cutaneous wound healing. J Leukoc Biol 2001; 69: 513–521.

[7] Gillitzer R, Goebeler M. Chemokines in cutaneous wound healing. J Leukoc Biol 2001; 69: 513–521.

[8] Kawaguchi Y, Hara M, Wright TM. Endogenous IL-1a from systemic sclerosis fibroblasts induces IL-6 and PDGF-A. J Clin Invest 1999; 103: 1253–1260.

[9] Kawaguchi Y. IL-1a gene expression and protein production by fibroblasts from patients with systemic sclerosis. Clin Exp Immunol 1994; 97: 445–450.

[10] Duan H, Fleming J, Pritchard DK et al. (2008) Combined analysis of monocyte and lymphocyte messenger RNA expression with serum protein profiles in patients with scleroderma. Arthritis Rheum 58:1465–74.

[11] Maekawa T, Jinnin M, Ohtsuki M, Ihn H. Serum levels of interleukin-1α in patients with systemic sclerosis. J Dermatol. 2013 Feb;40(2):98-101. doi: 10.1111/1346-8138.12011. Epub 2012 Oct 18.

[12] Kawaguchi Y, McCarthy SA, Watkins SC, Wright TM. Autocrine activation by interleukin 1a induces the fibrogenic phenotype of systemic sclerosis fibroblasts. J Rheumatol 2004; 31: 1946– 1954.

[13] Denton CP, Khanna D, Systemic sclerosis. Lancet 2017; 390: 1685-1699.

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