XBiotech Announces Publication of Breakthrough Findings for Potential Role of Interleukin-1 alpha in Risk for Heart Attacks

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Findings Demonstrate Ability of MABp1 (Bermekimab) to Block In Vitro Neutrophil Mediated Vascular Endothelial Activation and Thrombosis

AUSTIN, Texas, Aug. 27, 2018 (GLOBE NEWSWIRE) -- XBiotech Inc. (NASDAQ: XBIT) announced today the publication of findings that point toward a white blood cell-derived interleukin-1 alpha (IL-1α) as a cause of blood clots that could lead to heart attacks or strokes. The research was headed by a world-leading cardiovascular researcher, Dr. Peter Libby, Mallinckrodt Professor of Medicine at Harvard Medical School and clinical cardiologist at Brigham and Women's Hospital. Dr. Libby's team discovered that white blood cells, known as neutrophils, can release IL-1 α that could possibly lead to life threatening strokes in patients with heart disease, which offers the potential for new treatment approaches involving XBiotech's anti-IL-1 α antibody, bermekimab.

The findings describe for the first time an intriguing mechanism whereby so called neutrophil extracellular traps (NETs), released from neutrophils, are laden with IL-1α that is capable of activating cells of the artery wall in a way that in turn activates blood clotting mechanisms and recruits further white blood cells. The publication reports work done by Dr. Libby's colleagues Drs. Folco and Mawson that describes how in certain kinds of heart disease where the blood vessels become partially blocked by atherosclerotic plaques, activation of the blood vessels by IL-1α on NETs could be an important contributing factor of heart attacks. These findings are among the first to provide a clear mechanism by which neutrophils could cause heart attacks, and at the same time offer hope for a treatment by blocking IL-1α. These findings also suggest treatment opportunities for other inflammatory diseases in which neutrophils, and more specifically NETs, play a role in disease pathology, such as in cancer, pulmonary, autoimmune, and gastrointestinal diseases.

Dr. Libby stated, "Our data suggest that activation of vascular endothelial cells by NET-associated IL-1 α can not only amplify, sustain, and propagate local vascular inflammation; this process may also be involved in promoting thrombosis. We believe these findings may have very important clinical implications."

John Simard, XBiotech's President & CEO, commented, "Dr. Libby's discovery provides a new mechanism by which to understand where and why we might target IL-1α to treat inflammatory diseases. It is a fundamental advance in biology and an exciting day for us."

Dr. Libby's findings are published online in a journal of the American Heart Association (AHA). The article titled, Neutrophil Extracellular Traps Induce Endothelial Cell Activation and Tissue Factor Production Through Interleukin-1α and Cathepsin G, is featured in the August print issue of *Arteriosclerosis, Thrombosis, and Vascular Biology*.

Coronary artery thrombosis can be caused by either plaque rupture or plaque erosion[1]. Superficial plaque erosion causes up to one-third of all acute coronary syndromes[2,3]. Erosion-prone atheromatous plaques, rather than lesions with stable or rupture-prone characteristics, associate with neutrophil extracellular traps (NETs)[4]. The study performed at Dr. Libby's laboratory probed the influence of NETs on the endothelial cell (EC) functions related to erosion-associated thrombosis. These data show that exposure of human saphenous veins ECs (HSVECs) to NETs increase expression of adhesion molecules on the surface of endothelial cells such as VCAM-1 and ICAM-1, which may participate in atherogenesis. In addition, pre-treatment of NETs with bermekimab, an anti-IL-1α-neutralizing antibody, or IL-1R antagonist, but not with an anti-IL-1β-neutralizing antibody, blocked the initiation of VCAM-1, ICAM-1, and TF expression, each of which link to coronary thrombosis[5,6]. In conclusion, NETs increase thrombogenicity in vitro through a response mediated by IL-1α. These data point to a potentially important role for bermekimab therapy in treating certain kinds of heart disease and other neutrophil mediated diseases.

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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