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Recently Published Independent Research Reveals New Mechanisms by Which LIXTE Biotechnology's Lead Clinical Compound, LB-100, Increases Effectiveness of Cancer Immunotherapy

Results Add to Growing Body of Evidence that Inhibiting PP2A with LB-100 May Be a General Method for Enhancing the Effectiveness of Immunotherapy in Refractory Cancers

PASADENA, CA, May 30, 2023 (GLOBE NEWSWIRE) -- LIXTE Biotechnology Holdings, Inc. ("LIXTE" or the "Company") (Nasdaq: LIXT) today announced that a recently published article in the journal *Cancer Research* showed that PP2A, the pharmacologic target of LIXTE's lead clinical compound, LB-100, when inactivated in pre-clinical models of glioma, activates a complex intracellular signaling system, the cGAS-STING pathway. This leads to an activation of interferon signaling, an increase in MHC class I expression on tumor cells, an increase in $CD8^+$ killer T cell proliferation, while at the same time reducing immunosuppressive tumor associated macrophages. Consequently, as shown in the article, PP2A inactivation sensitized the immunologically "cold" glioblastoma cells to immune checkpoint blockade therapy in vivo.

The May 23, 2023 article in the journal *Cancer Research*, entitled "PP2Ac Deficiency Enhances Tumor Immunogenicity by Activating STING-Type I Interferon Signaling in Glioblastoma," by Mondal et al. from the Department of Neurological Surgery, University of California, San Francisco.

John S. Kovach, M.D., CEO and Founder of LIXTE, said, "The case for combining LB-100 with immunotherapy is ever more compelling. We reported last year on emerging clinical evidence that PP2A inhibition may sensitize clear cell ovarian cancer patients to checkpoint inhibitors (https://ir.lixte.com/news-events/press-releases/detail/77/inactivating-mutations-in-scaffold-component-of-pp2a-the). We currently have one active multi-center trial in which LB-100 is combined with immunotherapy and chemotherapy in small cell lung cancer (NCT04560972), and are finalizing additional trials of LB-100 with immunotherapy for treatment of immunologically unresponsive tumors."

Dr. Kovach continued, "Lixte has long been interested in determining whether LB-100 potentiates standard treatment of glioblastomas. Thanks to the work of Mondal et al., we are now keenly interested in assessing whether LB-100 facilitates immunotherapy of primary brain tumors, among other immunologically 'cold' tumors for which more effective treatments are needed."

Rene Bernards, Professor of Molecular Carcinogenesis at the Netherlands Cancer Institute

and member of the LIXTE Board of Directors, commented, “Our own recent research provides yet another reason to combine LB-100 with immunotherapy as phospho-proteomic analysis of LB-100 treated colon cancer cells identifies mRNA processing as a major pathway perturbed by LB-100. As a consequence of LB-100 exposure, colon cancer cells contain a significant amount of incorrectly spliced mRNAs, which is a known source of neo-antigens that can help turn an immunologically ‘cold’ tumors ‘hot’ and vulnerable to immunotherapy.”

About LIXTE Biotechnology Holdings, Inc.

LIXTE Biotechnology Holdings, Inc. is a clinical-stage pharmaceutical company focused on new targets for cancer drug development and on developing and commercializing cancer therapies. LIXTE has achieved a breakthrough demonstrating that its first-in-class lead clinical PP2A inhibitor, LB-100, is well-tolerated in cancer patients at doses associated with anti-cancer activity. Based on extensive published preclinical data (see www.lixte.com), LB-100 has the potential to significantly improve outcomes for patients undergoing various chemotherapies or immunotherapies. LIXTE's new approach has no known competitors and is covered by a comprehensive patent portfolio. Initial proof-of-concept clinical trials are in progress.

Forward-Looking Statements

This announcement contains certain forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, and Section 21E of the Securities Exchange Act of 1934. For example, statements regarding the Company's financial position, business strategy and other plans and objectives for future operations, and assumptions and predictions about future activities, including the continuing development of proprietary compounds, the planning, funding, coordination and potential results of clinical trials, and the patent and legal costs to protect and maintain the Company's intellectual property worldwide, are all forward-looking statements. These statements are generally accompanied by words such as "intend," anticipate," "believe," "estimate," "potential(ly)," "continue," "forecast," "predict," "plan," "may," "will," "could," "would," "should," "expect" or the negative of such terms or other comparable terminology. The Company believes that the assumptions and expectations reflected in such forward-looking statements are reasonable, based on information available to it on the date hereof, but the Company cannot provide assurances that these assumptions and expectations will prove to have been correct or that the Company will take any action that the Company may presently be planning. However, these forward-looking statements are inherently subject to known and unknown risks and uncertainties. Actual results or experience may differ materially from those expected or anticipated in the forward-looking statements. Factors that could cause or contribute to such differences include, but are not limited to, regulatory policies, available cash, research results, competition from other similar businesses, and market and general economic factors. This discussion should be read in conjunction with the Company's filings with the United States Securities and Exchange Commission at https://www.sec.gov.

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