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Preclinical Results of LIXTE Biotechnology's Collaboration with Netherlands Cancer Institute Reveal Novel Mechanism by which LIXTE's Lead Clinical Compound LB-100 Enhances Effectiveness of Immunotherapy and Chemotherapy

Results Provide Striking Molecular Evidence that Inhibiting PP2A with LB-100 Sensitizes Cancer Cells to Immunotherapy and Chemotherapy

PASADENA, CA, July 17, 2023 (GLOBE NEWSWIRE) -- LIXTE Biotechnology Holdings, Inc. ("LIXTE" or the "Company") (Nasdaq: LIXT and LIXTW) today announced that a recently posted article in BioRxiv (https://www.biorxiv.org/content/10.1101/2023.07.12.548685v1), based on the results of a collaboration between the Company and the Netherlands Cancer Institute, shows that inhibition of PP2A in colon cancer cells, using LIXTE's lead clinical compound LB-100, leads to major changes in the way cancer cells process their mRNAs.

Based on this finding, cancer cells are predicted to produce a significant number of aberrant proteins that can be recognized by the immune system. This newly discovered mechanism, by which LB-100 turns immunologically "cold" tumors "hot," adds to several additional mechanisms that have recently been described through which LB-100 sensitizes cancer cells to immune checkpoint blockade.

John S. Kovach, M.D., CEO and Founder of LIXTE, said, "The case for combining LB-100 with immunotherapy is based on extensive pre-clinical data. The new findings provide a clear mechanistic underpinning for why this synergy is being seen. This data further supports our focus on developing LB-100 in combination with checkpoint blockade antibodies and strengthens our expectation that our current and upcoming clinical trials combining LB-100 with immune checkpoint blockade will be effective in treating cancer."

The Company said the new research also shows that disruption of proper mRNA maturation induced by LB-100 leads to a reduced ability of the cancer cells to deal with DNA damage. This finding concurs with multiple pre-clinical studies demonstrating synergy between LB-100 and radiotherapy or different chemotherapies in various cancer models.

The July 13, 2023 *BioRxiv* article, titled "PP2A Inhibition Instructs Spliceosome Phosphorylation to Create Splicing Vulnerability in Colon Adenocarcinoma," was authored by Dias et. al. from the Netherlands Cancer Institute, in a collaboration that LIXTE initiated in

2021 with a team of scientists headed by René Bernards, a Professor of Molecular Carcinogenesis at the Netherlands Cancer Institute and a member of the LIXTE Board of Directors.

Prof. Bernards said, “There is strong scientific evidence to support the notion that incorrectly spliced mRNAs, as we see in cells treated with LB-100, are a rich source of neo-antigens that can render cancer cells much more sensitive to immunotherapies. Other companies are developing drugs that target mRNA splicing for this reason, but we are not aware of any that have reached the clinic. That LB-100 has such an unexpectedly strong effect on mRNA splicing is a nice surprise that further supports its use in combination with 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 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 pre-clinical 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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