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New Clinical Findings Published in Scientific Journal Nature Validate LIXTE's Ongoing Ovarian and Colorectal Cancer Trials

Article Indicates that Inhibition of PP2A Enhances Immunotherapy Response with LIXTE's Proprietary Compound LB100

PASADENA, Calif., July 09, 2025 (GLOBE NEWSWIRE) -- LIXTE Biotechnology Holdings, Inc. ("LIXTE" or the "Company") (Nasdaq: LIXT and LIXTW), a clinical stage pharmaceutical company, today announced that the medical journal *Nature* has published findings by a team of physician-scientists that validate LIXTE's ongoing clinical trials with its proprietary compound LB100 for Ovarian and Colorectal cancers (https://www.nature.com/articles/s41586-025-09203-8).

A team led by principal investigator Amir Jazaeri, MD, professor of Gynecologic Oncology and Reproductive Medicine at The University of Texas MD Anderson Cancer Center, studied survival outcomes of Ovarian Clear Cell Carcinoma (OCCC) patients treated with immune checkpoint blockade therapy (clinicaltrials.gov identifier: NCT03026062). The ;study showed that patients having tumors with inactivating mutations in PPP2R1A - the major scaffold subunit of protein phosphatase 2A (PP2A) - had significantly better overall survival, compared with patients who did not have this mutation in their tumors.

Inactivating mutations in PPP2R1A are known to reduce the enzymatic activity of PP2A, which is the target of LIXTE's lead compound LB-100. Tumors with mutations in PPP2R1A were found to have increased the interferon gamma response pathway, which is known to be associated with improved immune checkpoint responses.

LIXTE is currently investigating the activity of LB-100 in combination with checkpoint immunotherapy in two clinical trials. The first is enrolling patients with OCCC, led by Dr. Jazaeri at MD Anderson Cancer Center, and also is open at Northwester University. In this trial, LIXTE is collaborating with GSK to test LB-100 in combination with dostarlimab (anti PD1). In the second trial, at the Netherlands Cancer Institute, LIXTE is collaborating with Roche to test LB-100 in combination with atezolizumab (anti PDL1) in colon cancer patients.

"Not only did we identify a new biomarker for improved survival with immunotherapy in ovarian cancer, but we also confirmed the correlation of this biomarker with survival benefit in other cancer types," said Dr. Jazaeri, who was co-senior author of the *Nature* article. "Since PPP2R1A mutations are relatively uncommon, we believe the same benefits may be possible by targeting the PPP2A pathway using drugs, which we currently are evaluating in a clinical trial at MD Anderson."

Bas van der Baan, LIXTE's Chief Scientific Officer, added, "This work extends a body of pre-clinical evidence indicating that LB-100 is strongly synergistic with checkpoint immunotherapy in a range of cancer types. We look forward to the first results of our clinical studies in the second half of this year."

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 demonstrated 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 enhance chemotherapies and immunotherapies and improve outcomes for patients with cancer.

LIXTE's lead compound, LB-100, is part of a pioneering effort in an entirely new field of cancer biology – activation lethality – that is advancing a new treatment paradigm. LIXTE's new approach is covered by a comprehensive patent portfolio. Proof-of-concept clinical trials are currently in progress for Ovarian Clear Cell Carcinoma, Metastatic Colon Cancer and Advanced Soft Tissue Sarcoma. Additional information about LIXTE can be found at www.lixte.com.

Forward-Looking Statement Disclaimer

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, the patent and legal costs to protect and maintain the Company's intellectual property worldwide, and the Company's ability to obtain and maintain compliance with Nasdaq's continued listing requirements, 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 resources, research results, competition from other similar businesses, and market and general economic factors.

Readers are urged to read the risk factors set forth in the Company's filings with the United States Securities and Exchange Commission at https://www.sec.gov. The Company

disclaims any intention or obligation to update or revise any forward-looking statements, whether as a result of new information, future events or otherwise.

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