February 14, 2023

LIXTE BIOTECHNOLOGY HOLDINGS REPORTS NEWLY PUBLISHED INDEPENDENT PRE-CLINICAL RESEARCH

THE RESEARCH SHOWS THAT PP2A, THE TARGET OF LIXTE'S LEAD CLINICAL COMPOUND, LB-100, WHEN DEFICIENT, ENHANCES EFFECTS OF IMMUNE CHECKPOINT BLOCKADE OF CANCER BY A PREVIOUSLY UNAPPRECIATED MECHANISM

PASADENA, CA, Feb. 14, 2023 (GLOBE NEWSWIRE) -- LIXTE Biotechnology Holdings, Inc. ("LIXTE" or the "Company") (Nasdaq: LIXT) announced that, as recently reported in *The Journal of Clinical Investigation,* PP2A, the pharmacologic target of LIXTE's lead clinical compound, LB-100, when deficient, enhances the effects of immune checkpoint blockade of cancer in a mouse model by a previously unappreciated mechanism.

The article, entitled "PP2Ac/STRN4 negatively regulates STING-Type I interferon signaling in tumor associated macrophages," was recently published and is available online at https://www.jci.org/articles/view/162139. The authors state that "PP2A/STRN4-YAP/TAZ is a previously unappreciated mechanism that mediate[s] immunosuppression in tumor-associated macrophages and targeting PP2A/STRN4-YAP/TAZ axis can sensitize tumors to immunotherapy."

John S. Kovach, M.D., CEO and Founder of LIXTE, said, "This paper lends additional support to the potential immunotherapy application of LB-100 in cancer treatment. Dr. Winson S. Ho, Assistant Professor of Neurological Surgery at the UCSF School of Medicine, co-lead author of the article, and a former member of the LIXTE Board of Directors, bolsters the case for testing LB-100 in combination with immunotherapy in the clinic. Studies in animals show that low doses of LB-100 enhance the effectiveness of immunotherapy against a variety of cancer types by several mechanisms (Ho et al., Nature Comm 2018; Yen et al. Nature Comm 2021)."

Dr. Kovach added, "LIXTE is currently recruiting for a clinical trial in patients with previously untreated extensive stage small cell lung cancer in which LB-100 is first added to chemotherapy and an immune checkpoint blocker and then administered with the immune blocker alone in the maintenance phase of treatment (NCT04560972). We are presently

seeking to develop other collaborative clinical studies to determine whether LB-100 significantly enhances the effectiveness of immunotherapy of cancer in general."

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. Major drivers of cancer are defects in the switches that turn the biochemical pathways in cells on or off. Most cancer research over the past 30 years has focused on the "on" switches because the "off" switches, especially the master "off" switch protein phosphatase (PP2A), were believed to cause intolerable toxicity in patients. LIXTE has achieved a breakthrough with its novel, first-in-class lead clinical compound and PP2A inhibitor, LB-100, demonstrating that LB-100 is readily 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.

For more information about LIXTE, Contact:

info@lixte.com
General Phone: (631) 830-7092
Investor Phone: (888) 289-5533

or

PondelWilkinson Inc. Investor Relations
pwinvestor@pondel.com
Roger Pondel: (310) 279-5965
Laurie Berman: (310) 279-5962

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