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LIXTE BIOTECHNOLOGY HOLDINGS, INC. REPORTS THAT ITS LEAD CLINICAL COMPOUND, LB-100, CAN KILL CANCER CELLS THROUGH HYPER-STIMULATION OF CELL PROLIFERATION SIGNALS IN PRE-CLINICAL MODELS

--THE STUDY ESTABLISHES A NOVEL CONCEPT OF "TUMOR SUPPRESSIVE DRUG RESISTANCE"

--THE COMBINATION OF LB-100 WITH INHIBITORS OF CELLULAR STRESS RESPONSE MODULATORS WAS HIGHLY EFFECTIVE IN KILLING CANCER CELLS IN SEVERAL PRE-CLINICAL CANCER MODELS

--RESISTANCE TO THIS THERAPY CAN RESULT IN THE LOSS OF THE ONCOGENIC PROPERTIES OF CANCER CELLS

PASADENA, CA, Feb. 07, 2023 (GLOBE NEWSWIRE) -- LIXTE Biotechnology Holdings, Inc. ("LIXTE" or the "Company") (Nasdaq: LIXT) noted that a team of scientists headed by Professor Rene Bernards at the Netherlands Cancer Institute, Amsterdam and member of the Board of Directors of LIXTE reported that in three difficult to treat cancer types, LIXTE's lead clinical compound, LB-100, combined with an inhibitor of the WEE1 kinase, causes unexpectedly effective cancer cell killing. Most surprisingly, when cancer cells acquire resistance to this combination therapy, they have highly reduced cancer-causing capacity in animal models. This observation indicates that this LB-100 combination therapy can force cells to give up their cancer-causing properties to acquire drug resistance.

John S. Kovach, M.D., CEO and Founder of LIXTE, and a co-author of thereport in BioRxiv (https://www.biorxiv.org/content/10.1101/2023.02.06.527335v1) entitled "Paradoxical activation of oncogenic signaling as a cancer treatment strategy" commented, "Over the past 20 years, efforts to develop better cancer therapies have focused on inhibiting the stimulatory effects of the oncogenes, but such therapies often deliver only modest benefit to patients with advanced cancer due to development of resistance. Dr. Matheus

Henrique Dias, working in the laboratory of Professor Rene Bernards at the Netherlands Cancer Institute, Amsterdam, and an international team of collaborators, have now shown that treatment of cancer cells with Lixte's unique lead clinical compound, LB-100, rather than inhibiting, further stimulates the signals that drive cancer cell proliferation, but paradoxically, impeding cell proliferation."

Dr. Kovach continued, "The authors also show that combination of LB-100 with an inhibitor of WEE1, a regulator of stress responses in the cell, leads to highly efficient cancer cell death in three hard-to-treat cancer models: colorectal, pancreatic, and bile duct carcinomas. The Bernards' group contends that this paradoxical result stems from the fact that the survival of cancer cells depends on a balance between activated oncogenic pathways driving tumorigenesis and engagement of stress-response programs that counteract the inherent toxicity of such aberrant signaling. Normal cells, which are not in proliferation overdrive in the first place, apparently can tolerate transient overstimulating signaling much better than cancer cells. The combination of LB-100 and WEE1 inhibition suppressed the growth of patient-derived tumors refractory to conventional therapies and was associated with only modest toxicity in animal models."

Dr. Kovach concluded, "Intriguingly, the authors present evidence to indicate that cancer cells that become resistant to this LB-100 combination therapy do so by losing some important cancer cell characteristics and are less cancerous in animal models. This "tumor suppressive drug resistance" still needs to be demonstrated in patients. However, given the safety profile in animal models of LB-100 in combination with WEE1 inhibition, this hypothesis should be readily testable in the clinic."

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.

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