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LIXTE BIOTECHNOLOGY ANNOUNCES APPROVAL OF A PHASE 1B/2 RANDOMIZED TRIAL OF DOXORUBICIN +/- LB-100 IN ADVANCED SOFT TISSUE SARCOMAS TO BE CONDUCTED BY THE SPANISH SARCOMA GROUP

PASADENA, CA, Oct. 13, 2022 (GLOBE NEWSWIRE) -- LIXTE Biotechnology Holdings, Inc. (Nasdaq: LIXT), ("LIXTE" or the "Company"), a clinical-stage pharmaceutical company focused on developing and commercializing cancer therapies, announced that the Spanish Agency for Medicines and Health Products (Agencia Española de Medicamentos y Productos Sanitarios, AEMPS) has authorized a Phase 1b/randomized Phase 2 study of LB-100, the Company's lead clinical compound, plus doxorubicin versus doxorubicin alone, the global standard for initial treatment of advanced soft tissue sarcomas (ASTS).

Dr. John Kovach, the founder and CEO of LIXTE, said, "The purpose of this clinical trial is to obtain information with respect to the efficacy and safety of LB-100 combined with doxorubicin in soft tissue sarcomas. Doxorubicin alone has been the cornerstone of first line treatment of ASTS for over 40 years, with little therapeutic gain from adding cytotoxic compounds to or substituting other cytotoxic compounds for doxorubicin. In animal models, LB-100 has consistently enhanced the anti-tumor activity of doxorubicin without apparent increases in toxicity. The interim analysis of this clinical trial will be done before full accrual is completed to determine whether the study has the possibility of showing superiority of the combination of LB-100 plus doxorubicin compared to doxorubicin alone. A positive study would have the potential to change the standard therapy for this disease after four decades of failure to improve the marginal benefit of doxorubicin alone."

Dr. Kovach continued, "This study was designed and will be carried out by the Spanish Sarcoma Group (Grupo Español de Investigación en Sarcomas, or GEIS). GEIS was formed in 1994 by oncologists from four hospitals and has grown to include members from more than 60 medical centers across Spain. For relatively uncommon but life-threatening diseases like ASTS, GEIS has shown that it is essential for many institutions to collaborate

and accrue a large enough group of patients needed to timely evaluate promising new treatments. We are delighted that GEIS has chosen to study whether LIXTE's lead clinical compound, LB-100, can significantly improve the anti-tumor activity of doxorubicin, the current clinical standard, an only marginally effective treatment for previously untreated ASTS. The clinical trial is expected to begin later this year or during the first quarter of 2023; up to 170 patients will be entered onto the trial, which is expected to be completed within two and a half years. This rapid rate of patient accrual is only possible through the collaborative efforts of GEIS oncologists."

Dr. Javier Martín-Broto, Coordinating Investigator of the trial, medical oncologist at the Fundación Jiménez Díaz University Hospital (Madrid) and GEIS Co-Founder, commented, "Although there has been an increase in overall survival in advanced sarcoma in recent years, this gain has not been accompanied by advances in first line therapy. Anthracyclines, and specifically doxorubicin, is still the standard initial treatment. The growing list of negative phase III trials indicates to us that sarcoma therapy is in crisis. It is true that sarcoma encompasses more than 60 different subtypes and, for some of them, substantial advances have emerged. But it is also true that the most frequent sarcoma subtypes desperately need a turning point. One promising topic of research is the combination of doxorubicin with drugs that are able to impair the mechanisms of DNA repair. LB-100 has demonstrated synergistic action in in vivo preclinical mesenchymal tumors. GEIS will lead a European initiative to conduct a Phase 1/randomized II trial exploring the combination of doxorubicin plus LB-100 in first line of advanced soft tissue sarcomas."

Dr. Kovach added, "We believe that authorization of this trial by AEMPS should facilitate approval of other LB-100 protocols in EU countries."

About LIXTE Biotechnology Holdings, Inc.

LIXTE Biotechnology Holdings, Inc. (Nasdaq: LIXT), 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 http://www.sec.gov/edgar.shtml.

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