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Lixte Biotechnology Holdings, Inc.'s Lead Compound LB-100 Reported to Rapidly Improve Symptoms in a Rodent Model of Depression

EAST SETAUKET, NY -- (Marketwired) -- 02/03/16 -- Lixte Biotechnology Holdings, Inc. (OTCQB: LIXT) announced that neuroscientists at the French Institute of Health and Medical Research (Inserm) using a mouse model of depression have identified protein phosphatase 2A (PP2A) as a potential pharmacological target for therapy. Administration of LB-100, Lixte's proprietary inhibitor of PP2A, rapidly reduced depressive-like symptoms in these conditioned animals. The findings were published in the journal *Nature Medicine* on January 25th, 2016.

John S. Kovach, MD, founder and president of Lixte said, "Dr. Manuel Mameli, Inserm investigator, and Dr. Salvatore Lecca in his team at Inserm Unit 839, the Institut du Fer a Moulin, have identified increased activity in a specific region of the brain in mice showing depressive symptoms after stressful experience. This hyperactivity returns to normal after a single administration of LB-100. Dr. Mameli, in a press release from Inserm (<http://presse.inserm.fr/en/treating-depressive-symptoms-from-their-roots/22124/>) is quoted 'Our study unravels early cellular mechanisms able to trigger complex behavioral responses. Our study further highlights the role of the lateral habenula in the aetiology of depression. Our results provide insights on a novel potential pharmacologic target that could be studied for a therapy of mood disorders.'"

Dr. Kovach continued, "We are very interested in the findings of Dr. Mameli and his team. Their observation of rapid amelioration of the depressive symptoms by LB-100 in widely used rodent models encourages us to see if these findings translate to patients with refractory depression. As Lixte recently reported, the initial clinical study of LB-100, a Phase 1 trial in cancer patients, revealed stabilization of several types of cancer without dose-limiting toxicity, with some patients receiving LB-100 for several months. We believe a proof-of-concept clinical study of LB-100 in refractory depression is warranted. Such a trial is especially attractive because, if the results of the animal studies hold true in patients, improvement in symptoms would be expected to occur in a matter of hours rather than after weeks of treatment required by most compounds available for depressive symptoms."

"It is not surprising," Dr. Kovach added, "that a 'targeted compound' such as LB-100 which has anticancer activity would potentially have activity in non-neoplastic diseases. Many cancers have acquired genetic alterations that perturb functions of the PP2A pathway while normal tissues do not. We believe the activity of LB-100 against different types of cancer in model systems results from its targeting an already genetically disturbed PP2A pathway in the cancer but not in normal cells. Mameli and colleagues have now shown that non-genetic dysregulation of PP2A activity associated with depressive-like symptoms arises in a focal

region of the brain in mice exposed to acute stress, and that targeting this abnormal PP2A function with LB-100 eliminates symptoms and restores normal PP2A activity. As altered PP2A function is known to be present in other benign diseases, there are several, if not many, potential applications of PP2A modulation to be explored."

About Lixte Biotechnology Holdings, Inc.

Lixte is a drug discovery company that uses biomarker technology to identify enzyme targets associated with serious common diseases and then design novel compounds to attack those targets. Lixte's product pipeline encompasses two major categories of compounds at various stages of pre-clinical and clinical development that the Company believes have broad therapeutic potential not only for cancer but also for other debilitating and life-threatening diseases. Lixte's unique phosphatase inhibitor, LB-100, is completing a Phase I clinical trial at two NCI designated Comprehensive Cancer Centers and three US Oncology Research sites (see ClinicalTrials.gov: Identifier NCT01837667).

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 product demand, supply, manufacturing, costs, marketing and pricing factors 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>.

Additional information on the Company is available at www.liخته.com.

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