

**UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
WASHINGTON, D.C. 20549**

FORM 8-K

CURRENT REPORT
PURSUANT TO SECTION 13 OR 15(d) OF THE
SECURITIES EXCHANGE ACT OF 1934

Date of Report (Date of earliest event reported): February 14, 2023

LIXTE BIOTECHNOLOGY HOLDINGS, INC.

(Exact name of registrant as specified in its charter)

DELAWARE
(State or other jurisdiction
of incorporation)

001-39717
(Commission
File Number)

20-2903526
(I.R.S. Employer
Identification Number)

680 East Colorado Boulevard, Suite 180
Pasadena California 91101
(Address of principal executive offices)

(631) 830-7092
(Registrant's telephone number, including area code)

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions (See General Instruction A.2. below):

- ☐ Written communications pursuant to Rule 425 under the Securities Act of 1933 (17 CFR 230.425)
- ☐ Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)
- ☐ Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))
- ☐ Pre-commencement communications pursuant to Rule 13e-4(e) under the Exchange Act (17 CFR 240.13e-4(e))

Securities registered pursuant to Section 12(b) of the Act:

Title of Each Class	Trading Symbol(s)	Name of each exchange on which registered
Common Stock, par value \$0.0001 per share	LIXT	The NASDAQ Stock Market, LLC
Warrants to Purchase Common Stock, par value \$0.0001 per share	LIXTW	The NASDAQ Stock Market, LLC

Item 8.01. Other Events.

On February 14, 2023, the Company issued a press release regarding newly published independent pre-clinical research on the potential immunotherapy application of Lixte's lead compound, LB-100, in cancer treatment.

Item 9.01. Financial Statements and Exhibits.

(d) There is filed as part of this report the exhibit listed on the accompanying Index to Exhibits, which exhibit is incorporated herein by reference.

2

SIGNATURES

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned hereunto duly authorized.

Date: February 15, 2023

LIXTE BIOTECHNOLOGY HOLDINGS, INC.

By: /s/ JOHN S. KOVACH

John S. Kovach, Chief Executive Officer

3

INDEX TO EXHIBITS

Exhibit No.	Description
99.1	Press Release regarding newly published independent pre-clinical research on the potential immunotherapy application of Lixte's lead compound, LB-100 in cancer treatment.
104	Cover Page Interactive Data File (embedded within the Inline XBRL document)



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 – (February 14, 2023) — 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 "PP2A/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.

1

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

2