Filed pursuant to Rule 424(b)(5)
Registration Statement No. 333-278874

PROSPECTUS SUPPLEMENT
(To Prospectus Dated May 2, 2024)

LIXTE BIOTECHNOLOGY HOLDINGS, INC.
2,366,503 Shares of Common Stock, Pre-Funded Warrants to Purchase up to 258,859 Shares of
Up to 258,859 Shares of Common Stock Underlying the Pre-Funded Warrants

We are offering 2,366,503 shares of our common stock, par value $0.0001 per share ("Common Stock"), and 258,859 pre-funded warrants (the "Pre-Funded Warrants"), each Pre-Funded Warrant entitling the holder to purchase one share of our Common Stock (and the common stock issuable from time to time upon exercise of such Pre-Funded Warrants) at (i) an offering price of $6.31 per share of common stock, and (ii) an offering price of $6.31 per Pre-funded Warrant, in each case in this offering pursuant to this prospectus supplement, the accompanying prospectus, and a securities purchase agreement entered into on June 2, 2026 (the "Purchase Agreement"), between the Company and certain accredited investors thereto (the "Purchasers"). Each Pre-Funded Warrant will have an exercise price of $0.0001, will be immediately exercisable, and is valid and exercisable until all Pre-Funded Warrants are exercised in full. This prospectus supplement also relates to the offering of the shares of Common Stock issuable upon exercise of such Pre-Funded Warrants.

Our Common Stock is listed on the Nasdaq Capital Market under the symbol "LIXT". The last sale price of our Common Stock on June 2, 2026, as reported by the Nasdaq Capital Market, was $7.04 per share. There is no established public trading market for the Pre-Funded Warrants, and we do not expect a market to develop.

Investing in any of our securities involves a high degree of risk. See "Risk Factors" beginning on page S-18 of this prospectus supplement and page 4 of the accompanying prospectus and in other documents that are incorporated by reference.

	Per Share	Per Pre-Funded Warrant	Total[(1)]
Public offering price	$ 6.31	$ 6.3099	$ 16,566,027.20
Placement agent fees	$ 0	$ 0	$ 0
Proceeds, before expenses, to us	$ 6.31	$ 6.3099	$ 16,566,027.20

(1) Includes proceeds from the assumed exercise of the Pre-Funded Warrants in cash.

Delivery of the securities offered pursuant to this prospectus supplement and the accompanying prospectus is expected to be made on or about June 4, 2026, subject to the satisfaction of certain closing conditions.

Neither the Securities and Exchange Commission nor any state securities commission has approved or disapproved of these securities or determined if this prospectus supplement is truthful or complete. Any representation to the contrary is a criminal offense.

The date of this prospectus supplement is June 4, 2026.

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Prospectus Supplement

Prospectus

You should rely only upon the information contained or incorporated by reference in this prospectus supplement, the accompanying prospectus and any related free writing prospectus required to be filed with the Securities and Exchange Commission. We have not authorized any person to provide you with different or additional information. If anyone provides you with different or additional information, you should not rely upon it. We are not making an offer to sell these securities in any jurisdiction where such offer or sale is not permitted. You should assume that the information appearing in this prospectus supplement, the accompanying prospectus, any applicable free writing prospectus and the documents incorporated by reference herein or therein is accurate only as of the respective dates of these documents or such other dates as may be specified therein. Our business, financial condition, liquidity, results of operations and prospects may have changed since those dates.

ABOUT THIS PROSPECTUS SUPPLEMENT

This prospectus supplement and the accompanying prospectus relate to the sale of our securities registered for sale under our Registration Statement on Form S-3 (File No. 333-278874) (the "Registration Statement"), which the Securities and Exchange Commission (the "Commission" or the "SEC") declared effective on May 2, 2024.

This prospectus supplement and the accompanying prospectus form part of a registration statement that we filed with the Securities and Exchange Commission, or the SEC. This document is in two parts. The first part is this prospectus supplement, which describes the specific terms of this offering and also adds to and updates information contained in the accompanying prospectus and the documents incorporated by reference herein or therein. The second part, the accompanying prospectus, provides more general information. Generally, when we refer to this prospectus, we are referring to both parts of this document combined. If the description of this offering varies between this prospectus supplement and the accompanying prospectus, you should rely on the information in this prospectus supplement, which supersedes the information in the accompanying prospectus. This prospectus supplement contains information about the securities offered in this offering and may add, update or change information in the accompanying prospectus. Before you invest in any of the securities offered under this prospectus supplement, you should carefully read both this prospectus supplement and the accompanying prospectus together with the additional information described under the headings "Where You Can Find More Information" and "Incorporation of Certain Information by Reference."

We are offering to sell, and seeking offers to buy, securities only in jurisdictions where offers and sales are permitted. The distribution of this prospectus supplement and the accompanying prospectus and the offering of the securities in certain jurisdictions may be restricted by law. Persons outside the United States who come into possession of this prospectus supplement and the accompanying prospectus must inform themselves about, and observe any restrictions relating to, the offering of the securities and the distribution of this prospectus supplement and the accompanying prospectus outside the United States. This prospectus supplement and the accompanying prospectus do not constitute, and may not be used in connection with, an offer to sell, or a solicitation of an offer to buy, any securities offered by this prospectus supplement and the accompanying prospectus by any person in any jurisdiction in which it is unlawful for such person to make such an offer or solicitation.

You should rely only on the information contained in, or incorporated by reference into, this prospectus supplement, the accompanying prospectus, the documents incorporated by reference into this prospectus supplement or the accompanying prospectus, and in any free writing prospectus that we may authorize for use in connection with this offering. We have not, and the Placement Agent has not, authorized any other person to provide you with different information. If anyone provides you with different or inconsistent information, you should not rely on it.

References in this prospectus supplement and the accompanying prospectus to the terms "we," "us," "our," "Lixte" or the "Company" or other similar terms mean Lixte Biotechnology Holdings, Inc. and its consolidated subsidiaries, unless we state otherwise or the context indicates otherwise.

CAUTIONARY NOTE REGARDING FORWARD-LOOKING STATEMENTS

This prospectus supplement, the accompanying prospectus, the documents incorporated by reference into this prospectus supplement and the accompanying prospectus and any free writing prospectus that we may authorize for use in connection with this offering contain forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, as amended (the "Securities Act"), and Section 21E of the Securities Exchange Act of 1934, as amended (the "Exchange Act"). All statements, other than statements of historical fact, that do not relate to matters of historical fact should be considered forward-looking statements, including, but not limited to, statements regarding our expectations about the trials, regulatory approval, manufacturing, distribution and commercialization of our current and future products and product candidates, and statements regarding our anticipated revenues, expenses, margins, profits and use of cash.

We have identified some of these forward-looking statements with words such as “believe”, “may”, “will”, “should”, “could”, “expect”, “intend”, “plan”, “predict”, “anticipate”, “estimate”, “continue” or other words and terms of similar meaning and the use of future dates. These forward-looking statements are based on current expectations about future events affecting us and are subject to uncertainties and factors relating to our operations and business environment, all of which are difficult to predict and many of which are beyond our control and could cause our actual results to differ materially from those matters expressed or implied by our forward-looking statements. Forward-looking statements are only predictions or statements of current plans and can be affected by inaccurate assumptions we might make or by known or unknown risks and uncertainties, including the risks described under the “Risk Factors” sections that are contained in this prospectus supplement on page S-18, in the accompanying prospectus and in our filings with the SEC that are incorporated by reference into this prospectus supplement and the accompanying prospectus, including, without limitation, the “Risk Factors” sections of our most recently filed Annual Report on Form 10-K and Quarterly Report on Form 10-Q. Such risks and uncertainties are not exclusive and further information concerning us and our business, including factors that potentially could materially affect our financial results or condition, may emerge from time to time.

Our business is subject to a number of risks of which you should be aware of before making an investment decision. Some of these risks include the following:

- We are engaged in early-stage research and as such might not be successful in our efforts to develop a portfolio of commercially viable products;
- We have incurred substantial losses since our inception and anticipate that we will continue to incur substantial and increasing losses for the foreseeable future;
- Our independent registered public accounting firm has expressed substantial doubt about our ability to continue as a going concern;
- We need significant additional financing to fund our operations and complete the development and, if approved, the commercialization of our lead product candidate, LB-100. If we are unable to raise capital when needed, we could be forced to delay, reduce or eliminate our product development programs or commercialization efforts;
- We currently have no source of revenues. We might never generate revenues or achieve profitability;
- Our ability to use net operating losses to offset future taxable income might be subject to limitations;
- Clinical-stage biopharmaceutical companies with product candidates in clinical development face a wide range of challenging activities which might entail substantial risk;
- We might find it difficult to enroll patients in our clinical trials which could delay or prevent the start of clinical trials for our product candidate;
- The results of preclinical studies or earlier clinical trials are not necessarily predictive of future results. Our lead product candidate in clinical trials, and any other product candidates that might advance into clinical trials, might not have favorable results in later clinical trials or receive regulatory approval;
- Clinical drug development involves a lengthy and expensive process with an uncertain outcome;
- There is a risk that one or more of our clinical trials could be placed on hold by regulatory authorities due to serious adverse events (SAEs) related to our drug candidate or to another company’s drug used in combination in one of our clinical trials. It is possible that the SAEs could be attributable to our drug candidate and could include, but not be limited to, unexpected severe side effects, treatment-related deaths, or long-term health complications. A dose given could result in non-tolerable adverse events defined as dose-limiting toxicity (DLT). When two DLTs occur at the same dose-level that dose-level is considered too high and unsafe. Further treatment is only allowed at lower dose-levels that have previously been found safe.
- Risks associated with operating in foreign countries could materially adversely affect our product development;
- Our current and future product candidates, the methods used to deliver them or their dosage levels may cause undesirable side effects or have other properties that could delay or prevent their regulatory approval, limit the commercial profile of an approved label or result in significant negative consequences following any regulatory approval;
- Our product development program might not uncover all possible adverse events that patients who take our lead product candidate may experience. The number of subjects exposed to our lead product candidate and the average exposure time in the clinical development program might be inadequate to detect rare adverse events or chance findings that might only be detected once the product is administered to more patients and for greater periods of time;
- Our future success is dependent on the regulatory approval of our lead product candidate;

- Our lead product candidate and future product candidates could fail to receive regulatory approval from the FDA;
- Failure to obtain regulatory approval in international jurisdictions would prevent our lead product candidate from being marketed abroad;
- Even if our current primary product candidate receives regulatory approval, it might still face future development and regulatory difficulties;
- We depend on certain key scientific personnel for our success who do not work full time for us. The loss of any such personnel could adversely affect our business, financial condition and results of operations;
- We expect to rely heavily on third parties for the conduct of clinical trials of our product candidates. If these clinical trials are not successful, or if we or our collaborators are not able to obtain the necessary regulatory approvals, we will not be able to commercialize our product candidates;
- Business interruptions could adversely affect future operations, revenues, and financial conditions, and might increase our costs and expenses;
- Our failure to find third party collaborators to assist or share in the costs of product development could materially harm our business, financial condition or results of operations;
- We might be subject to claims by third parties asserting that our employees, consultants, collaborators contractors or we have misappropriated their intellectual property, or claiming ownership of what we regard as our own intellectual property;
- We cannot be certain we will be able to obtain patent protection to protect our product candidates and technology;
- If we do not obtain patent term extension in the United States under the Hatch-Waxman Act or in foreign countries under similar legislation, our business might be materially harmed;
- If we fail to comply with our obligations in agreements under which we have licensed or, might license, intellectual property rights from third parties, or if we otherwise experience disruptions to our business relationships with our licensors, we could lose rights that are important to our business;
- We might infringe the intellectual property rights of others, which may prevent or delay our product development efforts and stop us from commercializing or increase the costs of commercializing our product candidates;
- We might be subject to claims that our employees, consultants or independent contractors have wrongfully used or disclosed alleged trade secrets of one or more third parties;
- Our intellectual property might not be sufficient to protect our intended products from competition, which might negatively affect our business as well as limit our partnership or acquisition appeal;
- If we are not able to protect and control our unpatented trade secrets, know-how and other technological innovation, we might suffer competitive harm;
- We might incur substantial costs prosecuting our patent applications, maintaining our patents and patent applications, enforcing our patents, defending against third party patent infringement suits, seeking invalidation of third party patents or in-licensing third party intellectual property, as a result of litigation or other proceedings relating to patent and other intellectual property rights;
- If we are unable to protect our intellectual property rights, our competitors might develop and market products with similar or identical features that might reduce demand for our potential products;
- Our commercial success depends upon attaining significant market acceptance of our current product candidate and future product candidates, if approved, among physicians, patients, healthcare payors and cancer treatment centers;
- Even if we are able to commercialize our lead product candidate or any future product candidates, the products might not receive coverage or adequate reimbursement from third party payors in the United States and in other countries in which we seek to commercialize our intended products, which could harm our business;
- Healthcare legislative measures aimed at reducing healthcare costs might have a material adverse effect on our business and results of operations;
- Price controls might be imposed in foreign markets, which might adversely affect our future profitability;

- Our relationships with customers and third party payors will be subject to applicable anti-kickback, fraud and abuse and other healthcare laws and regulations, which could expose us to criminal sanctions, civil penalties, contractual damages, reputational harm and diminished profits and future earnings. If we or they are unable to comply with these provisions, we might become subject to civil and criminal investigations and proceedings that could have a material adverse effect on our business, financial condition and prospects;
- Our employees might engage in misconduct or other improper activities, including noncompliance with regulatory standards and requirements, which could cause significant liability for us and harm our reputation;
- Product liability lawsuits against us could cause us to incur substantial liabilities and to limit commercialization of any products that we might develop;
- We face substantial competition, which might result in others discovering, developing or commercializing products before or more successfully than we do;
- Significant disruptions of information technology systems, computer system failures or breaches of information and cyber security could adversely affect our business;
- We might need to grow the size of our organization in the future, and we might experience difficulties in managing this growth;
- Inadequate funding for the FDA, the SEC and other government agencies could hinder their ability to hire and retain key leadership and other personnel, prevent new products and services from being developed or commercialized in a timely manner or otherwise prevent those agencies from performing normal business functions on which the operation of our business might rely, which could negatively impact our business;
- Unstable market and economic conditions and adverse developments with respect to financial institutions and associated liquidity risk may have serious adverse consequences on our business, financial condition and stock price;
- We are a "smaller reporting company" and we have elected to comply with certain reduced reporting and disclosure requirements which could make its common stock less attractive to investors;
- The price of our common stock might fluctuate substantially;
- A sale or perceived sale of a substantial number of shares of our common stock might cause the price of our common stock to decline;
- Market and economic conditions might negatively impact our business, financial condition and share price;
- If securities or industry analysts do not publish research or reports, or publish unfavorable research or reports about our business, our stock price and trading volume might decline;
- Future sales and issuances of our common stock could result in additional dilution of the percentage ownership of our stockholders and could cause our share price to fall;
- We do not intend to pay cash dividends on our shares of common stock so any returns will be limited to the value of our shares;
- We might be at risk of securities class action litigation;
- Our Certificate of Incorporation and our Amended and Restated Bylaws, and Delaware law might have anti-takeover effects that could discourage, delay or prevent a change in control, which might cause our stock price to decline;
- Financial reporting obligations of being a public company in the United States are expensive and time-consuming, and our management will be required to devote substantial time to compliance matters;
- If we fail to comply with the rules under Sarbanes-Oxley related to accounting controls and procedures in the future, or, if we discover material weaknesses and other deficiencies in our internal control and accounting procedures, our stock price could decline significantly and raising capital could be more difficult.
- We may not be able to maintain compliance with the continued listing requirements of the Nasdaq Capital Market.

Each forward-looking statement is based on information available to us as of the date of the document in which the forward-looking statement is contained. We undertake no obligation to publicly update or revise any forward-looking statement, whether as a result of new information, future events or otherwise, except as otherwise required by law.

All forward-looking statements that are made by us in this prospectus supplement, in the accompanying prospectus, in the documents incorporated by reference into this prospectus supplement and the accompanying prospectus and in any free writing prospectus that we may authorize for use in connection with this offering are qualified by these cautionary statements.

Forward-looking statements are not guarantees of future performance, and actual results may differ materially due to risks and uncertainties, including those discussed under "Risk Factors" and in our filings with the SEC.

PROSPECTUS SUPPLEMENT SUMMARY

The following summary highlights selected information about us, this offering and information contained elsewhere in or incorporated by reference into this prospectus supplement or the accompanying prospectus. This summary does not contain all the information that may be important to you. Before purchasing any of the Common Stock that we are offering, you should carefully read in their entirety this prospectus supplement and the accompanying prospectus, including the documents incorporated by reference into this prospectus supplement and the accompanying prospectus, and any free writing prospectus that we may authorize for use in this offering. In particular, you should carefully review the "Risk Factors" sections that are contained in this prospectus supplement on page S-18, in the accompanying prospectus and in our filings with the SEC that are incorporated by reference into this prospectus supplement and the accompanying prospectus, including, without limitation, the "Risk Factors" sections of our most recently filed Annual Report on Form 10-K and Quarterly Report on Form 10-Q.

Company Overview

We are a clinical-stage biopharmaceutical company focused on identifying new targets for cancer drug development and developing and commercializing cancer therapies. Our product pipeline is primarily focused on inhibitors of protein phosphatase 2A, which are used to enhance cytotoxic agents, radiation, immune checkpoint blockers and other cancer therapies. We believe that inhibitors of protein phosphatases have significant therapeutic potential for a broad range of cancers. We are focusing on the clinical development of a specific protein phosphatase inhibitor, referred to as LB-100, which has been shown to have clinical anti-cancer activity.

We believe that the mechanism by which LB-100 affects cancer cell growth is different from cancer agents currently approved for clinical use. LB-100 is currently being tested in clinical trials in Ovarian Clear Cell Carcinoma, Metastatic Micro Satellite Stable (MSS) Colon Cancer, and Advanced Soft Tissue Sarcoma. LB-100 has shown anti-cancer activity in animal models of glioblastoma multiforme, neuroblastoma, and medulloblastoma, all cancers of neural tissue. LB-100 has also been shown to enhance the effectiveness of commonly used anti-cancer drugs in animal models of melanoma, breast cancer and sarcoma. The enhancement of anti-cancer activity of these anti-cancer drugs occurs at doses of LB-100 that do not significantly increase toxicity in animals. It is therefore hoped that, when combined with standard anti-cancer regimens against many tumor types, LB-100 will improve therapeutic benefit.

As a compound moves through the FDA-approval process, it becomes an increasingly valuable property, but at a cost of additional investment at each stage. As the potential effectiveness of LB-100 has been documented at the clinical trial level, we have allocated resources to expand the breadth and depth of its patent portfolio. Our approach has been to operate with a minimum of overhead, moving compounds forward as efficiently and inexpensively as possible, and to raise funds to support each of these stages as certain milestones are reached. Our longer-term objective is to secure one or more strategic partnerships or licensing agreements with pharmaceutical companies with major programs in cancer.

Our activities are subject to significant risks and uncertainties, including the need for additional capital. We have not yet commenced any revenue-generating operations, do not have positive cash flows from operations, rely on stock-based compensation for a substantial portion of employee and consultant compensation, and are dependent on periodic access to equity capital to fund its operating requirements.

Recent Developments

On November 21, 2025, the Company entered into a share exchange agreement to acquire Liora from Orbit Capital. The acquisition was executed through multiple agreements, including (i) an initial share exchange agreement dated November 21, 2025 (the "Original SEA"); (ii) a subsequent share exchange agreement dated December 30, 2025 (the "Post-Closing SEA"); and (iii) an amended and restated agreement dated March 6, 2026 (the "A&R Agreement"). The Post-Closing SEA finalized the structure such that Lixte owned 80% of Liora and Orbit Capital owned 20% of Liora. In addition there was a royalty agreement between the Company and Orbit dated November 21, 2025, that was terminated on December 16, 2025. As of March 31, 2026 and December 31, 2025, the Company owns 80% of Liora and consolidates Liora, with the remaining 20% ownership interest presented as noncontrolling interest.

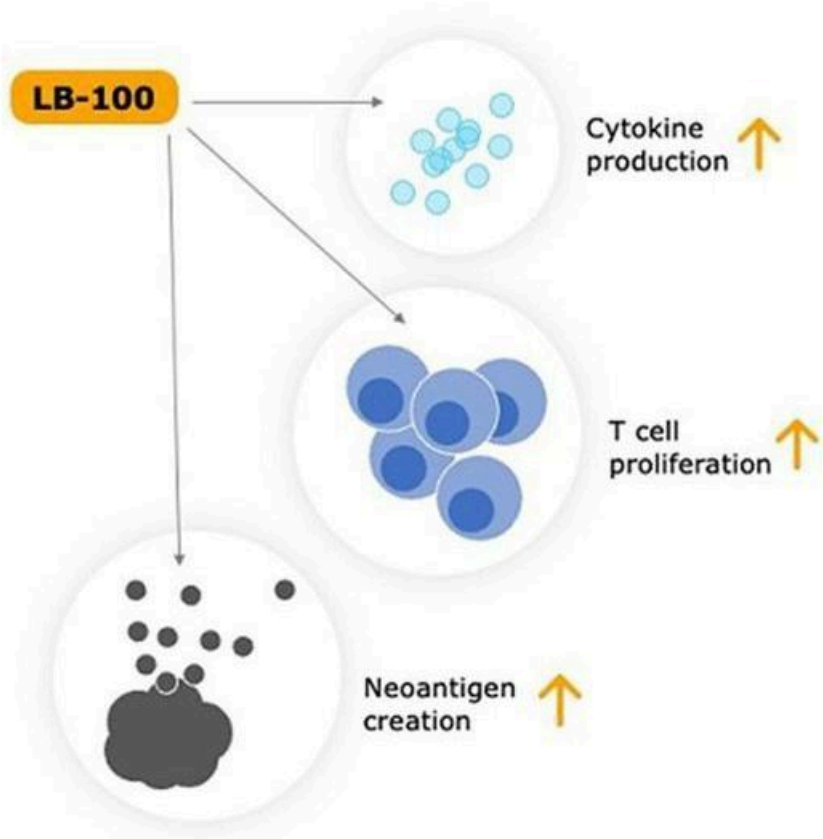
Description of Business

Most cancer patients are treated with either chemotherapy or immunotherapy or both. These therapies often have limited benefit and there is a high unmet medical need to enhance their effects. In many preclinical models we have shown that LB-100 enhances the effect of both chemotherapy and Immunotherapy

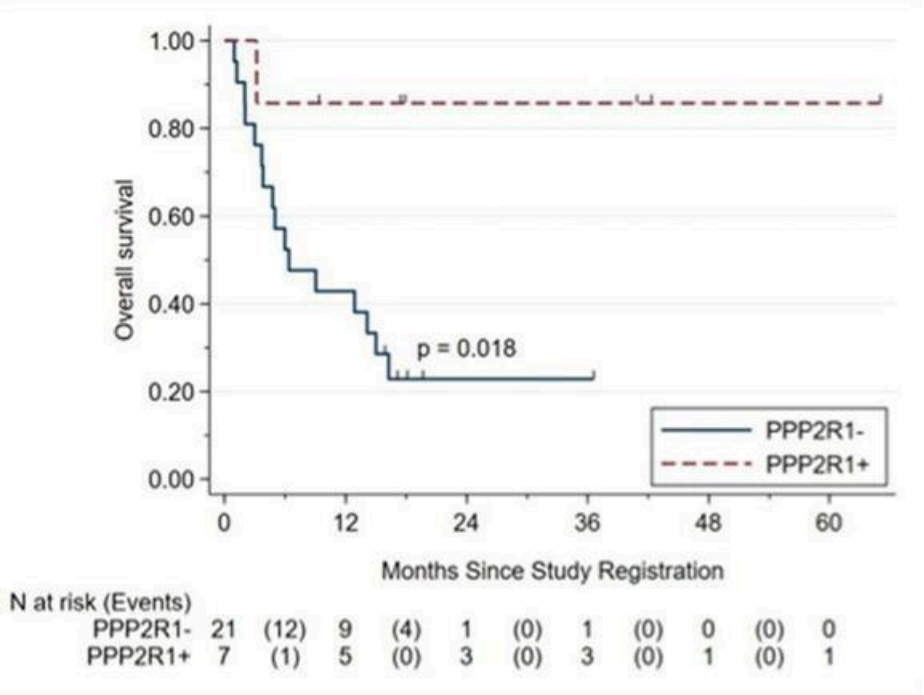
LB-100, a small molecule potent inhibitor of PP2A, was designed and developed by us. Numerous preclinical studies have documented that LB-100 potentiates most if not all anti-cancer drugs that damage DNA. LB-100 is not associated with any increase in cytotoxicity when given with cytotoxic drugs. This synergy involves transient interruption of several DNA damage repair pathways by LB-100 and an increase in cell division rate. LB-100 has FDA Investigational New Drug status in the US and Investigational Medicinal Product Dossier approval in the European Union.

In its initial Phase 1 clinical trial, LB-100 given alone daily for 3 days was non-toxic, except for a transient increase in serum creatinine believed to be caused by inhibition of PP2A in the renal tubules. In the Phase 1 clinical trial, the Maximum Tolerated Dose ("MTD") was 2.33mg/m2 daily for 3 days every 3 weeks. Of the 25 patients with heavily-treated advanced solid tumors with measurable disease, 3 patients had stable disease for 2 cycles, 3 patients had stable disease for 4 cycles, and 3 patients had stable disease for 6 cycles. One patient with pancreatic cancer had a partial response after 12 cycles lasting 534 days.

Low doses of LB-100 have now been shown to enhance immune checkpoint inhibition ("ICI") by several different mechanisms affecting the tumor compartment and immune T-cell compartment. LB-100 increases CD8+T-cell infiltration and CD8-Treg ratio, CD8+T-cell proliferation, and cytokine production induces microsatellite instability, neoantigen production and immune responsiveness, converting immunologically "cold" to "hot" cancers.



Ovarian clear cell carcinoma patients with inactivating mutations in PPP2R1A, a gene coding for a scaffold component of PP2A, and treated with immune checkpoint inhibitors, were recently found to have markedly longer survival than patients without the mutation in their cancers. Retrospective reviews of patients with a variety of cancers treated with ICI or chemotherapy show much longer survival of ICI-treated patients with a PPP2R1A mutation in their tumors.



Based on the observations in ovarian clear cell carcinoma, we have initiated a clinical trial in this disease combining LB-100 with a monoclonal antibody blocking PD-1, a protein found on T-cells (NCT06065462).

Given these preclinical and clinical observations, it is likely that LB-100 may be a general way to enhance immunotherapy responses.

		Pre-Clinical	Phase 1b	Phase 2	Phase 3	Status
LB-100 + Immunotherapy	Ovarian Clear Cell Cancer	NCT06065462				Actively Recruiting at MD Anderson And Northwestern. GSK sponsored
LB-100 + Immunotherapy	Metastatic MSI Low Colon Cancer	NCT06012734				Open at Netherlands Cancer Institute Roche sponsored.
LB-100 + Chemotherapy	Advanced Soft Tissue Sarcoma (ASTS)	NCT05809830				Completed dose escalation phase. Full report Phase 1 mid 2025

The research on the LB-100 series was initiated in 2006 under a Cooperative Research and Development Agreement ("CRADA") with the National Institute of Neurologic Disorders and Stroke or NINDS of the National Institutes of Health or NIH dated March 22, 2006 that was subsequently extended through a series of amendments until it terminated on April 1, 2013.

We have also designed and developed the LB-200 series, which consists of histone deacetylase inhibitors (HDACi). LB-200 has not advanced to the clinical stage and would require additional capital to fund further development. Accordingly, because of our focus on the clinical development of LB-100 and analogs for cancer therapy as described below in more detail, we have decided not to actively pursue the preclinical development of our LB-200 series of compounds at this time.

Clinical Trial Agreements

Spanish Sarcoma Group Collaboration Agreement

Effective July 31, 2019, we entered into a Collaboration Agreement for an Investigator-Initiated Clinical Trial with the Spanish Sarcoma Group (Grupo Español de Investigación en Sarcomas or "GEIS"), Madrid, Spain, to carry out a study entitled "Randomized phase I/II trial of LB-100 plus doxorubicin vs. doxorubicin alone in first line of advanced soft tissue sarcoma". 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 is the global standard for initial treatment of advanced soft tissue sarcomas ("ASTS"). Doxorubicin alone has been the mainstay of first line treatment of ASTS for over 40 years, with little improvement in survival from adding cytotoxic compounds to or substituting other cytotoxic compounds for doxorubicin. In animal models, LB-100 consistently enhances the anti-tumor activity of doxorubicin without apparent increases in toxicity.

GEIS has a network of referral centers in Spain and across Europe that have an impressive track record of efficiently conducting innovative studies in ASTS. We agreed to provide GEIS with a supply of LB-100 to be utilized in the conduct of this clinical trial, as well as to provide funding for the clinical trial. The goal is to enter approximately 150 to 170 patients in this clinical trial over a period of two to four years. The Phase 1 portion of the study began in the quarter ended June 30, 2023 to determine the recommended Phase 2 dose of the combination of doxorubicin and LB-100. As advanced sarcoma is a very aggressive disease, the design of the Phase 2 portion of the study assumes a median progression-free survival ("PFS"), no evidence of disease progression or death from any cause) of 4.5 months in the doxorubicin arm and an alternative median PFS of 7.5 months in the doxorubicin plus LB-100 arm to demonstrate a statistically significant decrease in relative risk of progression or death by adding LB-100. There is a planned interim analysis of the primary endpoint when approximately 50% of the 102 events required for final analysis is reached.

On October 13, 2022, we announced that the Spanish Agency for Medicines and Health Products (Agencia Española de Medicamentos y Productos Sanitarios or "AEMPS") had authorized a Phase 1b/randomized Phase 2 study of LB-100, our lead clinical compound, plus doxorubicin, versus doxorubicin alone, the global standard for initial treatment of advanced soft tissue sarcomas (ASTS). Consequently, this clinical trial commenced during the quarter ended June 30, 2023 and to be completed and a report prepared by December 31, 2026. In April 2023, GEIS completed its first site initiation visit in preparation for the clinical trial at Fundación Jiménez Díaz University Hospital (Madrid). Up to 170 patents will be entered into the clinical trial. The recruitment phase of the Phase 1b portion of the protocol was completed during the quarter ended September 30, 2024. We expect to have data on toxicity and preliminary efficacy from this portion of the clinical trial during the quarter ending December 31, 2025.

Given the focus on the combination of LB-100 with immunotherapy in ovarian clear cell carcinoma and colorectal cancer and the availability of capital resources, we entered into Amendment No. 1 to the Collaboration Agreement effective March 11, 2025 that relieved us of the financial obligation to support the randomized Phase 2 portion of the clinical trial contemplated in the Collaboration Agreement of approximately $3,095,000. As a result, it is uncertain as to whether the Phase 2 portion of this clinical trial will proceed.

Clinical Research Support Agreement Relating to Small Cell Lung Cancer

We had executed a Clinical Research Support Agreement with the City of Hope National Medical Center to carry out a Phase 1b clinical trial of LB-100 combined with an FDA-approved standard regiment for treatment of untreated extensive-stage disease small cell lung cancer. The clinical trial was initiated on March 9, 2021. However, due to the lack of patient accrual, the Company provided notice to the City of Hope National Medical Center of our intent to terminate the Clinical Research Support Agreement effective as of July 8, 2024.

MD Anderson Cancer Center Clinical Trial

On September 20, 2023, we announced an investigator-initiated Phase 1b/2 collaborative clinical trial to assess whether adding LB-100 to a human programmed death receptor-1 ("PD-1") blocking antibody of GSK plc ("GSK"), dostarlimab-gxly, may enhance the effectiveness of immunotherapy in the treatment of ovarian clear cell carcinoma ("OCCC"). The clinical trial is being sponsored by The University of Texas MD Anderson Cancer Center ("MD Anderson") and is being conducted at The University of Texas – MD Anderson Cancer Center. We are providing LB-100 and GSK is providing dostarlimab-gxly and financial support for the clinical trial. On January 29, 2024, we announced the entry of the first patient into this clinical trial. We currently expect that this clinical trial will be completed by December 31, 2027.

On February 25, 2025, we announced that we had added the Robert H. Lurie Comprehensive Cancer Center (Lurie Cancer Center) of Northwestern University as a second site in a clinical trial combining the Company's proprietary compound LB-100 with GSK's dostarlimab to treat ovarian clear cell cancer. Patient recruitment is underway, and the first patient has been dosed.

Netherlands Cancer Institute Clinical Trial

Effective June 10, 2024, we entered into a Clinical Trial Agreement with the Netherlands Cancer Institute ("NKI") to conduct a Phase 1b clinical trial of the Company's protein phosphatase inhibitor, LB-100, combined with atezolizumab, a PD-L1 inhibitor, the proprietary molecule of F. Hoffman-La Roche Ltd. ("Roche"), for patients with microsatellite stable metastatic colon cancer. Under the agreement, we will provide our lead clinical compound, LB-100, and under a separate agreement between NKI and Roche, Roche will provide atezolizumab and financial support for the clinical trial. We have no obligation to and will not provide any reimbursement of clinical trial costs. Pursuant to the agreement and the protocol set forth in the agreement, the clinical trial will be conducted by NKI at NKI's site in Amsterdam by principal investigator Neeltje Steeghs, MD, PhD, and NKI will be responsible for the recruitment of patients. The agreement provides for the protection of the respective intellectual property rights of each of Lixte, NKI and Roche.

This Phase 1b clinical trial will evaluate safety, optimal dose and preliminary efficacy of LB-100 combined with atezolizumab for the treatment of patients with metastatic microsatellite stable colorectal cancer. Immunotherapy using monoclonal antibodies like atezolizumab can enhance the body's immune response against cancer and hinder tumor growth and spread. LB-100 has been found to improve the effectiveness of anticancer drugs in killing cancer cells by inhibiting a protein called PP2A on cell surfaces. Blocking PP2A increases stress signals in tumor cells expressing the PP2A protein. Accordingly, combining atezolizumab with LB-100 may enhance treatment efficacy for metastatic colorectal cancer, as cancer cells with heightened stress signals are more vulnerable to immunotherapy.

This study comprises a dose escalation phase and a dose expansion phase. The objective of the dose escalation phase is to determine the recommended Phase 2 dose (RP2D) of LB-100 when combined with the standard dosage of atezolizumab. The dose expansion phase will further investigate the preliminary efficacy, safety, tolerability, and pharmacokinetics/dynamics of the LB-100 and atezolizumab combination. The clinical trial opened in August 2024 with the enrollment of the first patient. Patient accrual is expected to take up to 24 months, with a maximum of 37 patients with advanced colorectal cancer to be enrolled in this study.

The shelf life of the batch of LB-100 being utilized in this clinical trial was scheduled to expire on December 25, 2025, but has been extended for a final time for a period of 12 months through December 25, 2026, after which date no new patients can be recruited into this clinical trial and no patients can be treated with the current batch of LB-100. Although we do not currently intend to commission the production of a new batch of LB-100 for this clinical trial, we believe that it is likely that we will be able to recruit enough patients in sufficient time into this clinical trial to be able to reach an evaluable outcome for all end points in this clinical trial by December 25, 2026. The expiration of the shelf life of this batch of LB-100 represents an effective termination date of this clinical trial.

The principal investigator of the colorectal study testing LB-100 in combination with atezolizumab is currently investigating two Serious Adverse Events ("SAEs") observed in the clinical trial that was launched in August 2024. The Investigational Review Board (IRB) of the Netherlands Cancer Institute has requested additional information with respect to these SAEs and the study has been paused for enrollment until the IRB's questions have been, as more fully discussed below at "Risks Related to the Development and Regulatory Approval of Our Product Candidates - *A clinical trial hold due to serious adverse events could delay or halt the development of our product candidate"*.

National Cancer Institute Pharmacologic Clinical Trial

In May 2019, the National Cancer Institute (NCI) initiated a glioblastoma (GBM) pharmacologic clinical trial. This study was being conducted and funded by the NCI under a Cooperative Research and Development Agreement, with the Company being required to provide the LB-100 clinical compound.

Primary malignant brain tumors (gliomas) are very challenging to treat. Radiation combined with the chemotherapeutic drug temozolomide has been the mainstay of therapy of the most aggressive gliomas (glioblastoma multiforme or GBM) for decades, with little further benefit gained by the addition of one or more anti-cancer drugs, but without major advances in overall survival for the majority of patients. In animal models of GBM, the Company's novel protein phosphatase inhibitor, LB-100, has been found to enhance the effectiveness of radiation, temozolomide chemotherapy treatments and immunotherapy, raising the possibility that LB-100 may improve outcomes of standard GBM treatment in the clinic. Although LB-100 has proven safe in patients at doses associated with apparent anti-tumor activity against several human cancers arising outside the brain, the ability of LB-100 to penetrate tumor tissue arising in the brain was not known. Many drugs potentially useful for GBM treatment do not enter the brain in amounts necessary for anti-cancer action.

The NCI study was designed to determine the extent to which LB-100 enters recurrent malignant gliomas. Patients having surgery to remove one or more tumors received one dose of LB-100 prior to surgery and had blood and tumor tissue analyzed to determine the amount of LB-100 present and to determine whether the cells in the tumors showed the biochemical changes expected to be present if LB-100 reached its molecular target. As a result of the innovative design of the NCI study, it was believed that data from a few patients would be sufficient to provide a sound rationale for conducting a larger clinical trial to determine the effectiveness of adding LB-100 to the standard treatment regimen for GBMs. Blood and brain tumor tissue were analyzed from seven patients after intravenous infusion of a single dose of LB-100. Results of the investigation demonstrated that there was virtually no entry of LB-100 into the brain tumor tissue. Accordingly, alternative methods of drug delivery will be required to determine if LB-100 has meaningful clinical anti-cancer activity against glioblastoma multiforme and other aggressive brain tumors.

Patent and License Agreements

National Institute of Health

Effective February 23, 2024, we entered into a Patent License Agreement (the "License Agreement") with the National Institute of Neurological Disorders and Stroke ("NINDS") and the National Cancer Institute ("NCI"), each an institute or center of the National Institute of Health ("NIH"). Pursuant to the License Agreement, we have licensed exclusively NIH's intellectual property rights claimed for a Cooperative Research and Development Agreement ("CRADA") subject invention co-developed with the Company, and the licensed field of use, which focuses on promoting anti-cancer activity alone, or in combination with standard anti-cancer drugs. The scope of this clinical research extends to checkpoint inhibitors, immunotherapy, and radiation for the treatment of cancer. The License Agreement is effective, and shall extend, on a licensed product, licensed process, and country basis, until the expiration of the last-to-expire valid claim of the jointly owned licensed patent rights in each such country in the licensed territory, unless sooner terminated.

The License Agreement contemplates that we will seek to work with pharmaceutical companies and clinical trial sites (including comprehensive cancer centers) to initiate clinical trials within timeframes that will meet certain benchmarks. Data from the clinical trials will be the subject of various regulatory filings for marketing approval in applicable countries in the licensed territories. Subject to the receipt of marketing approval, we would be expected to commercialize the licensed products in markets where regulatory approval has been obtained.

Other Significant Agreements and Contracts

Netherlands Cancer Institute

On October 8, 2021, we entered into a Development Collaboration Agreement with the Netherlands Cancer Institute, Amsterdam ("NKI"), one of the world's leading comprehensive cancer centers, and Oncode Institute, Utrecht, a major independent cancer research center, for a term of three years. The Development Collaboration Agreement was subsequently modified by Amendment No. 1 thereto.

The Development Collaboration Agreement is a preclinical study intended to identify the most promising drugs to be combined with LB-100, and potentially LB-100 analogues, to be used to treat a range of cancers, as well as to identify the specific molecular mechanisms underlying the identified combinations. We agreed to fund the preclinical study, at an approximate cost of 391,000 Euros and provide a sufficient supply of LB-100 to conduct the preclinical study.

On October 3, 2023, we entered into Amendment No. 2 to the Development Collaboration Agreement with NKI, which provides for additional research activities, extends the termination date of the Development Collaboration Agreement by two years to October 8, 2026, and added 500,000 Euros to the operating budget being funded by us.

On October 4, 2024, we entered into Amendment No. 3 to the Development Collaboration Agreement with NKI, which suspended Amendment No. 2 and provided for a new study term of one year and starts upon the dosing of the first patient in the clinical trial at a project cost of 100,000 Euros.

Effective as of June 15, 2022, Dr. René Bernards was appointed to our Board of Directors as an independent director. Dr. Bernards is a leader in the field of molecular carcinogenesis and is employed by NKI.

Intellectual Property

Our intellectual property includes proprietary know-how, proprietary methodologies and extensive clinical validation data and publications. To provide legal protection of our intellectual property, we rely on a combination of patents, licenses, trade secrets, trademarks, confidentiality and non-disclosure clauses and agreements, and other forms of intellectual property protection to define and protect our rights to our products.

Our products are expected to be covered by our patents. These patents now cover sole rights to the composition and synthesis of our LB-100 series of drugs, which is the Company's lead clinical compound in development. Lixte has filed patent applications covering the treatment of cancer with LB-100. Lixte has also filed joint patent applications with the NIH and the Netherlands Cancer Institute for the treatment of cancer using LB-100 in combination with other drugs like immune checkpoint inhibitors and WEE1 inhibitors (a class of drugs that target and inhibit the WEE1 kinase enzyme that plays a crucial role in regulating cell division).

Patent applications for the LB-100 series (oxabicycloheptanes and oxabicycloheptenes) have been filed in the United States and internationally under the Patent Cooperation Treaty. Patents for composition of matter and for several uses of the LB-100 series have been issued in the United States, Mexico, Australia, Japan, China, Hong Kong, Canada, and by the European Patent Office

We strive to protect and enhance the proprietary technology, inventions, and improvements that are commercially important to the development of our business, including seeking, maintaining, and defending its patent rights, which are owned solely by our wholly-owned Delaware subsidiary, Lixte Biotechnology, Inc., except in several instances jointly with one of many of our collaborators. We also rely on trade secrets relating to its proprietary pipeline of product candidates and on know-how and continuing technological innovation to develop and strengthen its pipeline. We intend to rely on regulatory protection afforded by regulatory agencies through data exclusivity, market exclusivity, and patent term extensions, where available.

Our success will depend in large part on its ability to obtain and maintain patent and other proprietary protection for commercially important technology, inventions and know-how related to its business; defend and enforce its patents; preserve the confidentiality of its trade secrets; and operate without infringing valid and enforceable patents or proprietary rights of third parties. Our ability to stop third parties from making, using, selling, offering to sell, or importing our technology may depend on the extent to which we have rights under valid and enforceable licenses, patents, or trade secrets that cover these activities. In some cases, enforcement of these rights may depend on cooperation of the joint owners of our jointly owned patents and patent applications.

With respect to both our solely and jointly owned intellectual property, we cannot be sure that patents will be granted on any of its pending patent applications or on any patent applications filed solely or jointly by us in the future; we cannot be sure that any of our existing patents or any patents that may be granted to us in the future will be commercially useful in protecting our intended commercial products or therapeutic methods; and we cannot be sure that an agency or court would determine that the our solely or jointly owned patents are valid and enforceable.

Going Concern

We have a history of operating losses since inception. Because we are currently engaged in various early-stage clinical trials, it is expected that it will take a significant amount of time and resources to develop any product or intellectual property capable of generating sustainable revenues. Accordingly, our business is unlikely to generate any sustainable operating revenues in the next several years and may never do so. Even if we are able to generate revenues through licensing our technology, product sales or other commercial activities, there can be no assurance that we will be able to achieve and maintain positive earnings and operating cash flows. As discussed further in "Management's Discussion and Analysis of Financial Condition and Results of Operations - Liquidity and Capital Resources" included in our Annual Report on Form 10-K for the fiscal year ended December 31, 2024, which is incorporated herein by reference, our auditor has included a "going concern" explanatory paragraph in its report on our consolidated financial statements for the fiscal year ended December 31, 2024, expressing substantial doubt about our ability to continue as a going concern for the next twelve months. Our consolidated financial statements do not include any adjustments that may result from the outcome of this uncertainty. If we cannot secure the financing needed to continue as a viable business, our shareholders may lose some or all of their investment in us.

Corporate Information

We were incorporated as a Delaware Corporation on May 24, 2005, under the name SRKP7, Inc. On June 30, 2006, pursuant to a share exchange agreement, we acquired all of the outstanding shares of Lixte Biotechnology, Inc. which then became a wholly owned subsidiary. On December 7, 2006, we changed our name to Lixte Biotechnology Holdings, Inc.

Effective September 26, 2023, Bastiaan van der Baan, a director of the Company since June 17, 2022, replaced our founder, John S. Kovach, as President and Chief Executive Officer. Dr. Kovach passed away on October 5, 2023. Effective October 6, 2023, Mr. van der Baan was appointed as Chairman of the Board of Directors.

As discussed below, effective June 16, 2025, Mr. van der Baan resigned as Chairman of the Board of Directors and Chief Executive Officer, but remained as President and as a member of the Board of Directors, and was appointed as the Company's Chief Scientific Officer, and Geordan Pursglove was appointed as Chairman of the Board of Directors and Chief Executive Officer.

Our common stock and public warrants are traded on the Nasdaq Capital Market under the symbols "LIXT". On June 2, 2023, we effected a one-for-ten reverse split of our outstanding shares of common stock in order to remain in compliance with the $1.00 minimum closing bid price requirement of the Nasdaq Capital Market.

Our principal address is 433 Plaza Real, Suite 275, Boca Raton, FL 33432. Our telephone number is (631) 830-7092. We maintain a website at https://lixte.com. The information contained on our website is not, and should not be interpreted to be, incorporated into this prospectus.

Executive Management and Director Changes

Prior to and effective as of the consummation of the $5,050,000 private placement on July 2, 2025, there have been several changes with respect to our executive management and the Board of Directors as described herein.

Bastiaan van der Baan. Effective June 16, 2025, Bastiaan van der Baan resigned as Chairman of the Board of Directors and as Chief Executive Officer, but remained as President and as a member of the Board of Directors, and was appointed as Chief Scientific Officer. Mr. van der Baan's principal responsibility as President will be related to the clinical development of our LB-100 lead compound. His responsibility as Chief Scientific Officer (CSO) will be for shaping and executing the scientific vision and research and development strategy of the Company, with a focus on discovering and developing innovative cancer therapeutics. The CSO leads all research functions, oversees preclinical and translational programs, supervises the Chief Medical Officer, and ensures alignment with clinical and regulatory development goals. The CSO provides scientific leadership to internal teams and external partners, supports fundraising and business development, and serves as a key member of executive management.

In conjunction with such resignation, the stock option that Mr. van der Baan was previously granted on September 26, 2023 to acquire 250,000 shares of common stock was deemed fully vested effective with Mr. van der Baan's resignation as described herein, and the time period for Mr. van der Baan to exercise his stock option at any time in the future that he is no longer providing his services to the Company as a consultant, employee or otherwise was increased from ninety (90) days to one (1) year.

Except for the previously described changes in Mr. van der Baan's management duties and the modifications to the terms of the stock option, Mr. van der Baan's three (3) year employment agreement dated September 26, 2023 will remain in full force and effect.

If the Company does not complete a successful financing that enables it to maintain its listing on the Nasdaq Small Cap Market by July 3, 2025, the amendment to Mr. van der Baan's employment agreement as described herein will be automatically terminated retroactive to the amendment date and Mr. van der Baan will be reinstated as Chairman of the Board of Directors and Chief Executive Officer.

Geordan Pursglove. Effective June 16, 2025, Geordan Pursglove was appointed as our new Chairman of the Board of Directors and Chief Executive Officer. His responsibilities include the oversight of our business operations and strategic planning, and he will be the primary contact between our executive team and the Board of Directors. He will also be the principal spokesperson of the Company and have final say on all corporate matters, subject only to the authority of the Board of Directors.

We have entered into an employment agreement with Mr. Pursglove for a term of three (3) years effective June 16, 2025. Mr. Pursglove will receive an annual salary of $240,000, which may be increased from time to time in the sole discretion of the Board of Directors. At his election, his compensation will be payable in cash and/or restricted shares, or a combination thereof. He is also eligible to receive an annual bonus as determined in the sole discretion of the Board of Directors in the form of cash or equity, or a combination thereof. Mr. Pursglove will not receive any additional compensation for serving as the Chairman of the Board of Directors of the Company.

Effective as of the end of the first trading day for the Company's common stock immediately following the consummation of this offering, which was July 3, 2025, as an inducement for Mr. Pursglove to join our Company, as a signing bonus, he was granted a stock option to purchase 350,000 shares of our common stock at an exercise price equal to the closing price on the Nasdaq Stock Market on such date of $2.83 per share, which is exercisable for a term of five (5) years, provides for cashless exercise, and will vest 50% on the grant date, 25% on September 30, 2025, and 25% on December 31, 2025, subject to continued service.

The stock option grant was not issued under the Company's 2020 Stock Incentive Plan. The stock option agreement provided for certain registration rights (including on Form S-8) and for accelerated vesting upon the occurrence of certain events, including early termination of the employment agreement that is not the result of the voluntary termination, gross negligence or willful misconduct of Mr. Pursglove, a sale or change in control of the Company, or a sale, licensing or other disposition of all or substantially all of the assets of the Company, as defined in such stock option agreement.

If the Company does not complete a successful financing that enables it to maintain its listing on the Nasdaq Capital Market by July 3, 2025, the employment agreement with Mr. Pursglove as described herein will be deemed automatically terminated retroactively as of June 16, 2025 and the stock option grant will be cancelled, and Mr. Pursglove will promptly resign from the Board of Directors. In such event, Mr. van der Baan will be reinstated as Chairman of the Board of Directors and Chief Executive Officer.

Prior to joining the Company, Mr. Pursglove served as President, Chief Executive Officer and Chairman of the Board of Directors at Beyond Commerce, Inc. He was also President of Service 800, Inc., a leading phone and online customer satisfaction survey service that provides the most actionable customer feedback, to the most recognizable Fortune 500 companies globally, in which he led operations, scaled revenue, and oversaw the company's strategic vision. Mr. Pursglove held a board position at SemiCab Holdings, an emerging leader in the global logistics and distribution industry that was part of Algorhythm Holdings (NASDAQ: RIME). Mr. Pursglove also serves as Chief Executive Officer and a director of Powell Max Ltd. ("PMAX"). Additionally, Mr. Pursglove serves as the managing director of The 2GP Group LLC. During his time as the Managing Director of The 2GP Group, Mr. Pursglove has built multiple businesses in Sports, Sales, Marketing and Logistics. Mr. Pursglove has over a decade of experience in M&A, public markets space, capital raising, funding, growth, scaling businesses and driving innovation.

Risks Associated with Our Business

Risks Related to the Development and Regulatory Approval of Our Product Candidates

A clinical trial hold due to serious adverse events could delay or halt the development of our product candidate.

Our lead drug candidate, LB-100, is currently undergoing various clinical trials, and there is a risk that one or more of these trials could be placed on hold by regulatory authorities due to serious adverse events (SAEs) related to our drug candidate or to another company's drug used in combination in one of our clinical trials. It is possible that the SAEs could be attributable to our drug candidate and could include, but not be limited to, unexpected severe side effects, treatment-related deaths, or long-term health complications. A dose given could result in non-tolerable adverse events defined as dose-limiting toxicity (DLT). When two DLTs occur at the same dose-level that dose-level is considered too high and unsafe. Further treatment is only allowed at lower dose-levels that have previously been found safe.

If an SAE or a pattern of SAEs is observed during the course of a clinical trial involving our drug candidate, the U.S. Food and Drug Administration (FDA), European Medicines Agency (EMA), or other regulatory authorities may issue a clinical hold, requiring us to pause or discontinue further enrollment and dosing in our clinical trial. It is also possible that the clinical trial could be terminated. Any of these actions could delay or halt the development of our drug candidate, increase development costs, and negatively impact our ability to ultimately achieve regulatory approval. Additionally, if an SAE is confirmed to be drug-related, we may be required to conduct additional studies, modify the study design, or abandon further development of the drug candidate altogether, which could materially impact our business, financial condition, and prospects.

The occurrence of an SAE and any resulting clinical hold could also harm our reputation with patients, physicians, health institutions, and investors, diminish our ability to attract clinical trial participants, and damage our ability to interest investors and obtain financing in the future. There can be no assurances that we will not experience such SAEs in the future or that any related clinical hold will be lifted in a timely manner, or at all.

The principal investigator of the colorectal study testing LB-100 in combination with atezolizumab (Roche PD-L1 inhibitor) is currently investigating two SAEs observed in the clinical trial that was launched in August 2024. The Institutional Review Board (the "IRB") of the Netherlands Cancer Institute ("NKI") has put the colorectal cancer study on hold. The adverse reactions that developed in the two patients were dyspnea (shortness of breath) due to lung toxicity possibly or probably related to the combination of LB-100 and atezolizumab in one patient and fever and aphasia possibly or probably related to the combination of LB-100 and atezolizumab in the second patient. The patient who developed lung toxicity deceased due to the combination of lung metastases of colorectal cancer and dyspnea. The patient with fever and aphasia fully recovered from the adverse events with supportive medication.

Given the identified adverse events in the two patients in the clinical trial, the IRB requested from the principal investigator of the study at the NKI information as to whether the adverse events could have been caused by the combination of LB-100 and atezolizumab and information about the mode of action of the combination of LB-100 and atezolizumab. The principal investigator prepared a response to the IRB detailing the safety experience with LB-100 given alone and in combination with other cancer drugs, especially doxorubicin and dostarlimab. Doxorubicin is a well-known chemotherapy, and dostarlimab is a well-known immunotherapy of which the mode of action is closely related to that of atezolizumab.

The reported adverse events in the colorectal cancer study have not been seen in any other patients thus far treated with LB-100 alone or in combination with other cancer drugs. Through early July 2025, the Company has been informed that a total of 82 patients had received or were receiving experimental treatment with LB-100.

In May 2025, the Company updated the safety overview of LB-100 and delivered the updated version 5.0 of the Investigator's Brochure (the "IB"), which contains all of the relevant preclinical, clinical and pharmacologic data with respect to the study of the LB-100 clinical compound in humans, to the investigators of all ongoing clinical trials. The investigators of the study in colorectal cancer (NCT06012734) submitted a detailed response to the IRB, including the updated IB. The Company is currently awaiting the outcome of the IRB review.

Our business is subject to a number of risks of which you should be aware of before making an investment decision. Some of these risks include the following:

- We have incurred substantial losses since our inception and anticipate that we will continue to incur substantial and increasing losses for the foreseeable future.
- We will require substantial additional financing to achieve our goals, and a failure to obtain this necessary capital when needed could force us to delay, limit, reduce or terminate our product development or commercialization efforts.
- We currently have no source of revenues. We may never generate revenues or achieve profitability.
- We expect to continue to incur significant operating and non-operating expenses, which may make it difficult for us to secure sufficient financing and may lead to uncertainty about our ability to continue as a going concern.
- We are dependent in part on technologies we license, and if we lose the right to license such technologies or we fail to license new technologies in the future, our ability to develop new products would be harmed, and if we fail to meet our obligations under our current or future license agreements, we may lose the ability to develop our product candidate.
- We expect to face substantial competition, which may result in others discovering, developing or commercializing products before or more successfully than we do.
- We are currently a clinical-stage biopharmaceutical company with a product candidate in clinical development. If we are unable to successfully develop and commercialize our product candidate or experience significant delays in doing so, our business may be materially harmed.
- Our success relies on third-party suppliers and manufacturers. Any failure by such third parties, including, but not limited to, failure to successfully perform and comply with regulatory requirements, could negatively impact our business and our ability to develop and market our product candidate, and our business could be substantially harmed.
- Our future success is dependent on the regulatory approval of our product candidate.
- Our business may be adversely affected by the ongoing coronavirus pandemic.
- Business interruptions could adversely affect future operations, revenues, and financial conditions, and may increase our cost of expenses.
- Our failure to find third party collaborators to assist or share in the costs of product development could materially harm our business, financial condition, and results of operations.
- If we fail to comply with our obligations under our license agreement with licensors, we could lose rights that are important to our business.
- We may infringe the intellectual property rights of others, which may prevent or delay our product development efforts.
- Our intellectual property may not be sufficient to protect our products from competition.

THE OFFERING

Issuer	Lixte Biotechnology Holdings, Inc.
Common Stock offered by us	2,366,503 shares of Common Stock.
Pre-Funded Warrants offered by us	We are also offering Pre-Funded Warrants to purchase up to 258,859 shares of Common Stock in lieu of shares of Common Stock to the Purchaser whose purchase of shares of Common Stock in this offering would otherwise result in the Purchaser, together with its affiliates and certain related parties, beneficially owning more than 4.99% of our outstanding Common Stock immediately following the consummation of this offering. Each Pre-Funded Warrant is exercisable for one share of our Common Stock. The purchase price of each Pre-Funded Warrant is equal to the price at which the share of Common Stock is being sold to the public, minus $0.0001 per share. The Pre-Funded Warrants are exercisable immediately, at an exercise price of $0.0001 per share, and may be exercised at any time until all of the Pre-Funded Warrants are exercised in full. This offering also relates to the shares of Common Stock issuable upon exercise of the Pre-Funded Warrants sold in this offering.
Common Stock to be outstanding after the offering	15,278,806 shares (as of June 2, 2026), assuming the issuance of 258,859 shares of Common Stock upon the exercise of the Pre-Funded Warrants.
Use of proceeds	We estimate the net proceeds to us from this offering will be approximately $16,566,027.20. We intend to use the net proceeds from this offering for working capital and general corporate purposes, including for further clinical development of our lead compound LB-100. See “Use of Proceeds”.
Risk factors	An investment in our securities involves a high degree of risk. See “Risk Factors” beginning on page S-18 for a discussion of certain factors that you should consider when evaluating an investment in our securities.
NASDAQ symbols	Our Common Stock is listed on the Nasdaq Capital Market under the symbol “LIXT”.

The number of shares of our Common Stock to be outstanding after this offering as shown above is based on 15,019,947 shares of Common Stock outstanding at June 2, 2026, and excludes any outstanding options and warrants.

Unless otherwise indicated, all information in this prospectus supplement assumes the exercises of the Pre-Funded Warrants offered and sold in this offering and no exercise of outstanding options or warrants.

RISK FACTORS

The following risk factors, together with the other information presented in this document or included by reference, should be considered by investors.

The price of our common stock might fluctuate substantially.

You should consider an investment in our common stock to be risky. Some factors that might cause the market price of our common stock to fluctuate, in addition to the other risks mentioned in this "Risk Factors," are:

- sale of our common stock by our stockholders, executives, and directors and our stockholders;
- volatility and limitations in trading volumes of our shares of common stock;
- our ability to obtain financings to conduct and complete research and development activities including, but not limited to, our clinical trials, and other business activities;
- the timing and success of introductions of new products by us or our competitors or any other change in the competitive dynamics of our industry, including consolidation among competitors, customers or strategic partners;
- network outages or security breaches;
- our ability to secure resources and the necessary personnel to conduct clinical trials on our desired schedule;
- commencement, enrollment or results of our clinical trials for our lead product candidate or any future clinical trials we might conduct;
- changes in the development status of our lead product candidate;
- any delays or adverse developments or perceived adverse developments with respect to the FDA's review of our planned preclinical and clinical trials;
- any delay in our submission for studies or product approvals or adverse regulatory decisions, including failure to receive regulatory approval for our lead product candidate;
- unanticipated safety concerns related to the use of our lead product candidate;
- failures to meet external expectations or management guidance;
- changes in our capital structure or dividend policy, future issuances of securities, sales of large blocks of common stock by our stockholders;
- our cash position;

- announcements and events surrounding financing efforts, including debt and equity securities;
- our inability to enter into new markets or develop new products;
- reputational issues;
- competition from existing technologies and products or new technologies and products that might emerge;
- announcements of acquisitions, partnerships, collaborations, joint ventures, new products, capital commitments, or other events by us or our competitors;
- changes in general economic, political and market conditions in or any of the regions in which we conduct our business;
- changes in industry conditions or perceptions;
- changes in valuations of similar companies or groups of companies;
- analyst research reports, recommendation and changes in recommendations, price targets, and withdrawals of coverage;
- departures and additions of key personnel;
- disputes and litigations related to intellectual properties, proprietary rights, and contractual obligations;
- changes in applicable laws, rules, regulations, or accounting practices and other dynamics; and
- other events or factors, many of which might be out of our control.

In addition, if the market for stocks in our industry or industries related to our industry, or the stock market in general, experiences a loss of investor confidence, the trading price of our common stock could decline for reasons unrelated to our business, financial condition and results of operations. If any of the foregoing occurs, it could cause our stock price to fall and might expose us to lawsuits that, even if unsuccessful, could be costly to defend and a distraction to management.

Risks Related to this Offering and our Common Stock

You may experience dilution of your ownership interests because of the future issuance of additional shares of Common Stock.

In the future, we will need to issue additional authorized but previously unissued equity securities, resulting in the dilution of the ownership interests of our stockholders. We may also issue additional Common Stock, warrants or other securities that are convertible into or exercisable for Common Stock in connection with hiring or retaining employees, future acquisitions, future sales of securities for capital raising purposes, or for other business purposes. The future issuance of any such additional shares of Common Stock may create downward pressure on the trading price of the Common Stock. There can be no assurance that we will not be required to issue additional shares, warrants or other convertible securities in the future in conjunction with any capital raising efforts, including at a price (or exercise prices) below the offering price of the shares of Common Stock in this offering.

Our management will have broad discretion over the use of the proceeds to us from this offering and may apply it to uses that do not improve our operating results or the value of our securities.

Our management will have broad discretion in the application of the net proceeds from this offering, and investors will be relying solely on such judgment of our management regarding the application of these proceeds. Although we expect to use the net proceeds from this offering for working capital and general corporate purposes, including the ongoing clinical development of our lead compound LB-100, we have not allocated these net proceeds for specific purposes. Investors will not have the opportunity, as part of their investment decision, to assess whether the proceeds are being used appropriately. Our use of the proceeds may not improve our business prospects or increase the value of the securities being offered hereby.

There is no public market for the Warrants being offered in this offering.

There is no established public trading market for the Pre-Funded Warrants being offered in this offering, and we do not expect a market to develop. In addition, we do not intend to apply to list the Pre-Funded Warrants on any securities exchange or nationally recognized trading system. Without an active market, the liquidity of the Pre-Funded Warrants will be limited.

Holders of our Warrants will have no rights as holders of Common Stock until such warrants are exercised.

Until you acquire shares of Common Stock upon exercise of your Pre-Funded Warrants, you will have no rights with respect to Common Stock issuable upon exercise of your warrants. Upon exercise of your Warrants, you will be entitled to exercise the rights of a holder of Common Stock only as to matters for which the record date occurs after the exercise date.

The Warrants are speculative in nature.

The Pre-Funded Warrants offered hereby do not confer any rights of ownership of our Common Stock on their holders, such as voting rights or the right to receive dividends, but rather merely represent the right to acquire Common Stock at a fixed price. Specifically, commencing on the date of issuance, holders of the Pre-Funded Warrants may acquire Common Stock issuable upon exercise of such warrants at an exercise price of $0.0001 per common share. Moreover, following this offering, the market value of the Pre-Funded Warrants is uncertain, and there can be no assurances that the market value of the Pre-Funded Warrants will equal or exceed their public offering price.

DIVIDEND POLICY

The Company's dividend policy is determined by its Board of Directors and will depend upon a number of factors, including the Company's financial condition and performance, its cash needs and expansion plans, income tax consequences, and the restrictions that applicable laws and any credit or other contractual arrangements may then impose. The Company has not paid any cash dividends on its common stock to date and at the current time the Company does not anticipate paying a cash dividend on its common stock in the foreseeable future. Rather, the Company anticipates that it will retain earnings, if any, for use in the development of its business.

DILUTION

The sale of our securities in this offering will have a dilutive impact on our stockholders. As a result, our net income/(loss) per share would decrease in future periods and the market price of our Common Stock could decline.

If you invest in our securities in this offering, your ownership interest will be diluted to the extent of the difference between the offering price per share of our Common Stock and accompanying Pre-Funded Warrant in this offering and the as adjusted net tangible book value per share of our Common Stock immediately after this offering. Our net tangible book value as of March 31, 2026, before this offering, was $9,178,592 or $0.79 per share of Common Stock. Net tangible book value per share represents the amount of total tangible assets (total assets less intangible assets) less total liabilities, divided by the number of shares of our common stock outstanding as of March 31, 2026.

As-adjusted net tangible book value per share represents our net tangible book value per share after giving effect to the issuance and sale of all Common Shares and Pre-Funded Warrants offered hereby (and assuming the exercise of the Pre-Funded Warrants), and after deducting estimated offering expenses payable by us in connection with this offering. The as-adjusted net tangible book value was calculated on a cash basis and does not consider the potential accounting classifications of the Pre-Funded Warrants.

The following table illustrates this per share dilution:

Offering price per share		$ 6.31
Historical net tangible book value per share as of March 31, 2026	$ 0.79	
Increase in net tangible book value per share attributable to this offering	$ 1.01	
As adjusted net tangible book value per share after this offering		$ 1.80
Dilution per share to new investors participating in this offering		$ 4.51

The table and calculations set forth above are based on 11,632,944 shares of Common Stock outstanding as of March 31, 2026, and assumes no exercise of any outstanding stock options or warrants or conversion of the Series B Preferred Stock. To the extent that the Series B Preferred Stock is converted into common stock, outstanding options or warrants are exercised, new options or other equity grants are issued under or outside of our equity incentive plans or we otherwise issue additional shares of Common Stock in the future, there will be further dilution to new investors participating in this offering.

USE OF PROCEEDS

Assuming all of the shares offered in this offering are sold, we estimate that our net proceeds from this offering will be approximately $16,566,027.20.

We intend to use the net proceeds from this offering for working capital and general corporate purposes, including for further clinical development of our lead compound LB-100.

As of the date of this prospectus supplement, the Company cannot specify with certainty all of the particular uses for the net proceeds to be received upon the completion of this offering. The amounts and timing of its actual expenditures will depend on numerous factors, including the status of the Company's drug development activities, clinical trial programs, patent expenditures, regulatory and compliance issues, research and development activities, and other operating expenditures. Accordingly, the Company's management will have broad discretion in the application of the net proceeds and investors will be relying on the judgment of its management regarding the application of the proceeds of this offering.

DESCRIPTION OF SECURITIES

Common Stock

We are authorized to issue 100,000,000 shares of Common Stock, par value $0.0001 per share, and 10,000,000 shares of preferred stock, par value $0.0001 per share. As of June 2, 2026, we had 12,653,444 shares of common stock outstanding. A description of the common stock we are offering pursuant to this prospectus supplement is set forth under the heading "Description of Capital Stock – Common Stock", beginning on page S-23 of the accompanying prospectus.

On June 2, 2023, the Company effected a 1-for-10 reverse split of its issued and outstanding shares of Common Stock. While the Certificate of Amendment reduced the number of outstanding shares of Common Stock, it did not reduce the number of authorized shares of Common Stock or preferred stock.

Holders of shares of Common Stock will be entitled to receive dividends if and when declared by the board of directors from funds legally available therefore, and, upon liquidation, dissolution or winding-up of our Company, will be entitled to share ratably in all assets remaining after payment of liabilities. The holders of shares of Common Stock will not have any preemptive rights, but will be entitled to one vote for each share of Common Stock held of record. Stockholders will not have the right to cumulate their votes for the election of directors.

Pre-Funded Warrants

The term "pre-funded" refers to the fact that the purchase price of our Common Stock in this offering includes almost the entire exercise price that will be paid under the Pre-Funded Warrants, except for a nominal remaining exercise price of $0.0001. The purpose of the Pre-Funded Warrants is to enable the investor that may have restrictions on its ability to beneficially own more than 4.99% of our outstanding Common Stock following the consummation of this offering the opportunity to make an investment in the Company without triggering its ownership restrictions, by receiving Pre-Funded Warrants in lieu of our Common Stock which would result in such ownership of more than 9.99% and receive the ability to exercise its option to purchase the shares underlying the Pre-Funded Warrants at such nominal price at a later date.

Exercisability. The holder may exercise the Pre-Funded Warrants immediately and at any time until the Pre-Funded Warrants are exercised in full. The Pre-Funded Warrants are exercisable, at the option of the holder, in whole or in part, by delivering to us a written exercise notice accompanied, within one trading day, by payment in full for the number of shares of our Common Stock purchased upon such exercise. The holder of Pre-Funded Warrants does not have the right to exercise any portion of the Pre-Funded Warrant if the holder would have beneficially owned in excess of 4.99% of the shares of our Common Stock outstanding immediately after giving effect to such purchase.

Cashless Exercise. The holder may exercise its Pre-Funded Warrants on a cashless basis. When exercised on a cashless basis, a portion of the Pre-Funded Warrants are cancelled in payment of the purchase price payable in respect of the number of shares of our Common Stock purchasable upon such exercise.

Exercise Price. The exercise price of Common Stock purchasable upon exercise of the Pre-Funded Warrants is $0.0001 per share. The exercise price and the number of shares issuable upon exercise of the Pre-Funded Warrants is subject to appropriate adjustment in the event of recapitalization events, stock dividends, stock splits, stock combinations or similar events affecting our Common Stock.

Transferability. The Pre-Funded Warrants may be transferred at the option of the holder without obtaining our consent.

Exchange Listing. We do not plan on making an application to quote the Pre-Funded Warrants on The Nasdaq Capital Market, or any other national securities exchange or any other trading system. Our Common Stock underlying the Pre-Funded Warrants is quoted on the Nasdaq Capital Market.

Rights as a Stockholder. Except as otherwise provided in the Pre-Funded Warrants, including the right for Pre-Funded Warrant holders to receive the same dividends and distributions as holders of Common Stock, or by virtue of such holder's ownership of our Common Stock, the holders of the Pre-Funded Warrants do not have the rights or privileges of holders of our Common Stock, including any voting rights, until they exercise their Pre-Funded Warrants.

PLAN OF DISTRIBUTION

We have entered into Purchase Agreements directly with the Purchasers in connection with this offering. We will only sell to such investors who have entered into the Purchase Agreement with us. The Purchase Agreements contain customary representations, warranties and covenants. The offering is expected to close on or about June 4, 2026, subject to satisfaction of customary closing conditions.

Fees and Expenses

The following table shows the per share price and total cash fees we will pay in connection with the sale of the securities pursuant to this prospectus supplement.:

	Per Share	Per Pre-Funded Warrant	Total[(1)]
Public offering price	$ 6.31	$ 6.3099	$ 16,566,027.20
Placement agent fees	$ 0	$ 0	$ 0
Proceeds, before expenses, to us	$ 6.31	$ 6.3099	$ 16,566,027.20

(1) Includes proceeds from the assumed exercise of the Pre-Funded Warrants in cash.

We estimate the total expenses payable by us for this offering, including registration, filing and listing fees, printing fees and legal and accounting expenses to be approximately $0.

Regulation M

The Placement Agent may be deemed to be an underwriter within the meaning of Section 2(a)(11) of the Securities Act, and any commissions received by it and any profit realized on the resale of the securities sold by it while acting as principal might be deemed to be underwriting discounts or commissions under the Securities Act. As an underwriter, the Placement Agent would be required to comply with the requirements of the Securities Act and the Exchange Act, including, without limitation, Rule 415(a)(4) under the Securities Act and Rule 10b-5 and Regulation M under the Exchange Act. These rules and regulations may limit the timing of purchases and sales of our securities by the Placement Agent acting as principal. Under these rules and regulations, the Placement Agent:

- may not engage in any stabilization activity in connection with our securities; and
- may not bid for or purchase any of our securities or attempt to induce any person to purchase any of our securities, other than as permitted under the Exchange Act, until it has completed its participation in the distribution.

Determination of Offering Price

The public offering price of the securities we are offering was negotiated between us and the investors, based on the trading of our Common Stock prior to the offering, among other things. Other factors considered in determining the public offering price of the securities we are offering include our history and prospects, the stage of development of our business, our business plans for the future and the extent to which they have been implemented, an assessment of our management, general conditions of the securities markets at the time of the offering and such other factors as were deemed relevant.

Listing

Our common stock is listed on the Nasdaq Capital Market under the symbols “LIXT”.

Transfer Agent and Registrar

The transfer agent and registrar for our common stock is Vstock Transfer.

Electronic Distribution

This prospectus may be made available in electronic format on websites or through other online services maintained by the investor or by an affiliate. Other than this prospectus, the information on the investor’s website and any information contained in any other website maintained by the investor is not part of this prospectus or the registration statement of which this prospectus forms a part, has not been approved and/or endorsed by us or the investor, and should not be relied upon by investors.

Offer Restrictions Outside the United States

Other than in the United States, no action has been taken by us that would permit a public offering of the securities offered by this prospectus in any jurisdiction where action for that purpose is required. The securities offered by this prospectus may not be offered or sold, directly or indirectly, nor may this prospectus or any other offering material or advertisements in connection with the offer and sale of any such securities be distributed or published in any jurisdiction, except under circumstances that will result in compliance with the applicable rules and regulations of that jurisdiction. Persons who come into possession of this prospectus are advised to inform themselves about and to observe any restrictions relating to the offering and the distribution of this prospectus. This prospectus does not constitute an offer to sell or a solicitation of an offer to buy any securities offered by this prospectus in any jurisdiction in which such an offer or a solicitation is unlawful

LEGAL MATTERS

The validity of the shares of common stock offered hereby will be passed upon for us by Sichenzia Ross Ference Carmel LLP, New York, NY.

EXPERTS

Weinberg & Company, P.A., our independent, registered public accounting firm, has audited our consolidated financial statements as of December 31, 2025 and 2024 and for the years then ended included in our Annual Report on Form 10-K for the fiscal year ended December 31, 2025, which is incorporated by reference into this prospectus and elsewhere in the registration statement of which this prospectus is a part. Our consolidated financial statements are incorporated by reference in reliance on Weinberg & Company P.A.'s report, which includes an explanatory paragraph regarding substantial doubt about the Company's ability to continue as a going concern, given on their authority as experts in accounting and auditing.

WHERE YOU CAN FIND MORE INFORMATION

We file annual, quarterly and current reports, proxy statements and other information with the SEC, which are available at the SEC's website at http://www.sec.gov. In addition, we maintain a website that contains information about us at http://www.lixte.com. The information found on, or otherwise accessible through, our website is not incorporated into, and does not form a part of, this prospectus supplement or any other report or document we file with or furnish to the SEC.

We have filed with the SEC a registration statement on Form S-3 (File No. 333-278874) under the Securities Act with respect to the shares of common stock offered by this prospectus supplement. When used in this prospectus supplement, the term "registration statement" includes amendments to the registration statement as well as the exhibits, schedules, financial statements and notes filed as part of the registration statement or incorporated by reference therein. This prospectus supplement, which constitutes a part of the registration statement, omits some information contained in the registration statement in accordance with SEC rules and regulations. You should review the information and exhibits in the registration statement for further information on us and our consolidated subsidiaries and the common stock we are offering by this prospectus supplement. Statements herein concerning any document we filed as an exhibit to the registration statement or that we otherwise filed with the SEC are not intended to be comprehensive and are qualified by reference to these filings. You should review the complete document to evaluate these statements. You can obtain a copy of the registration statement from the SEC at the address listed above or from the SEC's website.

INCORPORATION OF DOCUMENTS BY REFERENCE

This prospectus supplement is part of the registration statement but the registration statement includes and incorporates by reference additional information and exhibits. The SEC permits us to "incorporate by reference" the information contained in documents we file with the SEC, which means that we can disclose important information to you by referring you to those documents rather than by including them in this prospectus supplement. Information that is incorporated by reference is considered to be part of this prospectus supplement and you should read it with the same care that you read this prospectus supplement. Information that we file later with the SEC will automatically update and supersede the information that is either contained, or incorporated by reference, in this prospectus supplement, and will be considered to be a part of this prospectus supplement from the date those documents are filed. We have filed with the SEC, and incorporate by reference in this prospectus supplement:

- our Current Reports on Form 8-K, filed with the SEC on February 18, 2026, March 10, 2026, March 20, 2026, April 17, 2026, and June 1, 2026;
- our Quarterly Report on Form 10-Q for the quarterly period ended March 31, 2026, filed with the SEC on May 14, 2026, and
- our Annual Report on Form 10-K for the fiscal year ended December 31, 2025, filed with the SEC on March 31, 2026.

In addition, all documents subsequently filed by us pursuant to Sections 13(a), 13(c), 14 or 15(d) of the Securities Exchange Act of 1934, as amended, prior to the termination of the offering (excluding any information furnished rather than filed) shall be deemed to be incorporated by reference into this prospectus supplement.

Notwithstanding the statements in the preceding paragraphs, no document, report or exhibit (or portion of any of the foregoing) or any other information that we have "furnished" to the SEC pursuant to the Securities Exchange Act of 1934, as amended, shall be incorporated by reference into this prospectus supplement.

We will furnish without charge to you, on written or oral request, a copy of any or all of the documents incorporated by reference in this prospectus supplement, including exhibits to these documents. You should direct any requests for documents to:

Lixte Biotechnology Holdings, Inc.
433 Plaza Real, Suite 275
Boca Raton, FL 33432
Phone: (631) 830-7092

You also may access these filings on our website at http://www.lixte.com. We do not incorporate the information on our website into this prospectus supplement or any supplement to this prospectus and you should not consider any information on, or that can be accessed through, our website as part of this prospectus supplement or any supplement to this prospectus (other than those filings with the SEC that we specifically incorporate by reference into this prospectus supplement or any supplement to this prospectus).

Any statement contained in a document incorporated or deemed to be incorporated by reference in this prospectus supplement will be deemed modified, superseded or replaced for purposes of this prospectus supplement to the extent that a statement contained in this prospectus supplement modifies, supersedes or replaces such statement. Any statement contained herein or in any document incorporated or deemed to be incorporated by reference shall be deemed to be modified or superseded for purposes of the registration statement of which this prospectus supplement forms a part to the extent that a statement contained in any other subsequently filed document which also is or is deemed to be incorporated by reference modifies or supersedes such statement. Any such statement so modified or superseded shall not be deemed to constitute a part of the registration statement of which this prospectus supplement forms a part, except as so modified or superseded.

Dated May 3, 2024

PROSPECTUS

LIXTE BIOTECHNOLOGY HOLDINGS, INC.

$50,000,000
Common Stock
Preferred Stock
Debt Securities
Warrants
Rights
Units

From time to time, we may offer and sell up to an aggregate amount of $50,000,000 of any combination of the securities described in this prospectus in one or more offerings. We may also offer securities as may be issuable upon conversion, redemption, repurchase, exchange or exercise of any securities registered hereunder, including any applicable antidilution provisions. We may sell the securities to or through underwriters and also to other purchasers or through agents. The names of any underwriters or agents, and any fees, discounts or other compensation payable to them will be set forth in the applicable prospectus supplement accompanying this prospectus.

We will provide the specific terms of these offerings in one or more supplements to this prospectus. We may also authorize one or more free writing prospectuses to be provided to you in connection with these offerings. The prospectus supplement and any related free writing prospectus may also update or change information contained in this prospectus. You should carefully read this prospectus, the applicable prospectus supplement and any related free writing prospectus, as well as any documents incorporated by reference, before buying any of the securities being offered.

Our common stock is listed on The Nasdaq Capital Market under the symbol "LIXT". On April 30, 2024, the last reported sale price of our common stock on The Nasdaq Capital Market was $2.76 per share. As of April 30, 2024, the aggregate market value of our outstanding shares of Common Stock held by non-affiliates was $6,049,771 based on 2,249,290 shares of common stock outstanding, of which 2,191,946 shares were held by non-affiliates on such date, and based on a closing sale price of our common stock of $2.76 per share on that date. Pursuant to General Instruction I.B.6 of Form S-3, in no event will we sell securities in a public primary offering with a value exceeding 1/3 of our public float in any 12-month period so long as our public float remains below $75,000,000.

These securities may be sold directly by us, through dealers or agents designated from time to time, to or through underwriters, dealers, or through a combination of these methods on a continuous or delayed basis. See "Plan of Distribution" in this prospectus. We may also describe the plan of distribution for any particular offering of our securities in a prospectus supplement. If any agents, underwriters or dealers are involved in the sale of any securities in respect of which this prospectus is being delivered, we will disclose their names and the nature of our arrangements with them in a prospectus supplement. The price to the public of such securities and the net proceeds we expect to receive from any such sale by us will also be included in a prospectus supplement.

Investing in our securities involves significant risks. You should review carefully the risks and uncertainties described under the heading "Risk Factors" beginning on page 4 of this prospectus and in any applicable prospectus supplement and free writing prospectuses we have authorized for use in connection with a specific offering, and under similar headings in the other documents that are incorporated by reference into this prospectus or any prospectus supplement or free writing prospectuses.

Neither the Securities and Exchange Commission nor any state securities commission has approved or disapproved of these securities or passed upon the adequacy or accuracy of this prospectus. Any representation to the contrary is a criminal offense.

The date of this prospectus is May 3, 2024.

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ABOUT THIS PROSPECTUS

This prospectus is part of a registration statement that we filed with the Securities and Exchange Commission (the "SEC") using a "shelf" registration process. Under this shelf registration process, we may, from time to time, offer and sell, either individually or in combination, in one or more offerings, up to a total dollar amount of $50,000,000 of shares of our common stock ("Common Stock"), preferred stock ("Preferred Stock"), various series of debt securities, rights to purchase shares of our Common Stock or Preferred Stock, and/or warrants to purchase any such securities, either individually or as units comprised of a combination of one or more of the other securities.

This prospectus provides you with a general description of the securities we may offer. Each time we offer securities under this prospectus, we will provide a prospectus supplement that will contain more specific information about the terms of that offering. We may also authorize one or more free writing prospectuses to be provided to you that may contain material information relating to these offerings. The prospectus supplement and any related free writing prospectus that we may authorize to be provided to you may also update or change any of the information contained in this prospectus or in the documents that we have incorporated by reference into this prospectus. We urge you to read carefully this prospectus, any applicable prospectus supplement and any related free writing prospectuses we have authorized for use in connection with a specific offering, together with the information incorporated herein by reference as described under the heading "Information Incorporated by Reference", before buying any of the securities being offered.

You should rely only on the information contained in, or incorporated by reference into, this prospectus and any applicable prospectus supplement, along with the information contained in any free writing prospectuses we have authorized for use in connection with a specific offering. We have not authorized anyone to provide you with information in addition to or different from that contained in this prospectus, any applicable prospectus supplement and any related free writing prospectus. We take no responsibility for and can provide no assurances as to the reliability of, any information not contained in this prospectus, any applicable prospectus supplement or any related free writing prospectus that we may authorize to be provided to you. This prospectus is an offer to sell only the securities offered hereby, but only under circumstances and in jurisdictions where it is lawful to do so. You should assume that the information in this prospectus, any applicable prospectus supplement or any related free writing prospectus is accurate only as of the date on the front of the document and that any information incorporated by reference is accurate only as of the date of the document incorporated by reference, regardless of the time of delivery of this prospectus, any applicable prospectus supplement or any related free writing prospectus, or any sale of a security. Our business, financial condition, results of operations and prospects may have changed since those dates.

References in this prospectus to the terms "Lixte", "we", "us", "our" or the "Company" or other similar terms refer, collectively, to Lixte Biotechnology Holdings, Inc. and its consolidated subsidiary, unless we state otherwise or the context indicates otherwise.

When we refer to "you", we mean the potential holders of the applicable series of securities.

NOTE ABOUT FORWARD-LOOKING STATEMENTS

This prospectus and the information incorporated herein by reference includes forward-looking statements within the meaning of Section 27A of the Securities Act, as amended (the "Securities Act"), and Section 21E of the Securities Exchange Act of 1934, as amended (the "Exchange Act"). For this purpose, any statements contained herein, other than statements of historical fact, may be forward-looking statements under the provisions of the Private Securities Litigation Reform Act of 1995, including any statements about our future performance, business, financial condition, strategic transactions (including mergers, acquisitions and management services agreements), sources of revenue, operating results, plans, objectives, expectations and intentions; any statements regarding future economic conditions; and any statements of belief or assumptions including underlying any of the foregoing. In this prospectus and the information incorporated herein by reference, words such as "anticipate", "believe", "estimate", and variations of such words or similar expressions are used to identify these forward-looking statements. Actual results may differ materially from those indicated by such forward-looking statements as a result of various important factors. These risks are described in greater detail in the section entitled "Risk Factors" of this prospectus. Many of these factors that will determine actual results are beyond our ability to control or predict. If one or more of these factors materialize, or if any underlying assumptions prove incorrect, actual results, performance or achievements may vary materially from any future results, performance or achievements expressed or implied by these forward-looking statements. In addition, any forward-looking statements in this prospectus represent our views only as of the date of this prospectus and should not be relied upon as representing our views as of any subsequent date. We anticipate that subsequent events and developments will cause its views to change. However, while we may elect to update these forward-looking statements publicly at some point in the future, we specifically disclaim any obligation to do so, except as may be required by law, whether as a result of new information, future events or otherwise. Our forward-looking statements generally do not reflect the potential impact of any future acquisitions, mergers, dispositions, joint ventures or investments we may make.

Refer to the section entitled "Risk Factors" of this prospectus, and any other risk factors set forth in any accompanying prospectus supplement and in any information incorporated by reference in this prospectus or any accompanying prospectus supplement to better understand the risks and uncertainties inherent in our business and underlying any forward-looking statements, as well as any other risk factors and cautionary statements described in the documents we file from time to time with the SEC, specifically our most recent Annual Report on Form 10-K, Quarterly Reports on Form 10-Q, Definitive Proxy Statements on Schedule 14A and Current Reports on Form 8-K, including sections therein titled "Risk Factors" and "Note About Forward-Looking Statements", respectively. See "Information Incorporated by Reference" in this prospectus.

PROSPECTUS SUMMARY

This summary highlights selected information contained elsewhere in this prospectus. This summary is not complete and does not contain all the information that you should consider before making a decision to invest in our securities. We urge you to carefully read this entire prospectus and all applicable prospectus supplements, including the more detailed information regarding our Company, the securities being registered hereby, as well as our consolidated financial statements, the notes to the consolidated financial statements and other information incorporated by reference from our other filings with the SEC. Investing in our securities involves a high degree of risks. Therefore, carefully consider the risk factors set forth in Lixte's most recent annual and quarterly filings with the SEC, as well as other information in this prospectus, all applicable prospectus supplements and the documents incorporated by reference herein or therein, before purchasing our securities. Each of the risk factors could adversely affect our business, operating results and financial condition, as well as adversely affect the value of an investment in our securities.

The Company

Company Overview

We are a clinical-stage biopharmaceutical company dedicated to improving patients' lives by developing a drug class called Protein Phosphatase 2A inhibitors. Our corporate office is located in Pasadena, California.

Our product pipeline is primarily focused on inhibitors of protein phosphatase 2A, used in combination with cytotoxic agents and/or x-ray, immune checkpoint blockers and other cancer therapies. We believe that inhibitors of protein phosphatases have significant therapeutic potential for a broad range of cancers. We are focusing on the clinical development of a specific protein phosphatase inhibitor, referred to as LB-100, which has been shown to have clinical anti-cancer activity at doses that produce little or no toxicity.

Our activities are subject to significant risks and uncertainties, including the need for additional capital. We have not yet commenced any revenue-generating operations, do not have positive cash flows from operations, rely on stock-based compensation for a substantial portion of employee and consultant compensation, and are dependent on periodic infusions of equity capital to fund its operating requirements.

Risks Associated with Our Business

Our business is subject to a number of risks of which you should be aware of before making an investment decision. Some of these risks include the following:

- We are engaged in early-stage research and as such might not be successful in our efforts to develop a portfolio of commercially viable products.
- We have incurred substantial losses since our inception and anticipate that we will continue to incur substantial and increasing losses for the foreseeable future.
- We need significant additional financing to fund our operations and complete the development and, if approved, the commercialization of our lead product candidate, LB-100. If we are unable to raise capital when needed, we could be forced to delay, reduce or eliminate our product development programs or commercialization efforts.
- We currently have no source of revenues. We might never generate revenues or achieve profitability.
- Clinical-stage biopharmaceutical companies with product candidates in clinical development face a wide range of challenging activities which might entail substantial risk.

- We might find it difficult to enroll patients in our clinical trials which could delay or prevent the start of clinical trials for our product candidate.
- Clinical drug development involves a lengthy and expensive process with an uncertain outcome.
- Risks associated with operating in foreign countries could materially adversely affect our product development.
- Our current and future product candidates, the methods used to deliver them or their dosage levels may cause undesirable side effects or have other properties that could delay or prevent their regulatory approval, limit the commercial profile of an approved label or result in significant negative consequences following any regulatory approval.
- Our product development program might not uncover all possible adverse events that patients who take our lead product candidate may experience. The number of subjects exposed to our lead product candidate and the average exposure time in the clinical development program might be inadequate to detect rare adverse events or chance findings that might only be detected once the product is administered to more patients and for greater periods of time.
- Our future success is dependent on the regulatory approval of our lead product candidate.
- Our lead product candidate and future product candidates could fail to receive regulatory approval from the FDA.
- Failure to obtain regulatory approval in international jurisdictions would prevent our lead product candidate from being marketed abroad.
- Even if our current primary product candidate received regulatory approval, it might still face future development and regulatory difficulties.
- We depend on certain key scientific personnel for our success who do not work full time for us. The loss of any such personnel could adversely affect our business, financial condition and results of operations.
- We expect to rely heavily on third parties for the conduct of clinical trials of our product candidates. If these clinical trials are not successful, or if we or our collaborators are not able to obtain the necessary regulatory approvals, we will not be able to commercialize our product candidates.
- Our failure to find third party collaborators to assist or share in the costs of product development could materially harm our business, financial condition or results of operations.
- We might be subject to claims by third parties asserting that our employees, consultants, collaborators contractors or we have misappropriated their intellectual property, or claiming ownership of what we regard as our own intellectual property.
- We cannot be certain we will be able to obtain patent protection to protect our product candidates and technology.
- If we do not obtain patent term extension in the United States under the Hatch-Waxman Act or in foreign countries under similar legislation, our business might be materially harmed.

- If we fail to comply with our obligations in agreements under which we have licensed or, might license, intellectual property rights from third parties, or if we otherwise experience disruptions to our business relationships with our licensors, we could lose rights that are important to our business.

- We might infringe the intellectual property rights of others, which may prevent or delay our product development efforts and stop us from commercializing or increase the costs of commercializing our product candidates.

- We might be subject to claims that our employees, consultants or independent contractors have wrongfully used or disclosed alleged trade secrets of one or more third parties.

- Our intellectual property might not be sufficient to protect our intended products from competition, which might negatively affect our business as well as limit our partnership or acquisition appeal.

- If we are not able to protect and control our unpatented trade secrets, know-how and other technological innovation, we might suffer competitive harm.

- We might incur substantial costs prosecuting our patent applications, maintaining our patents and patent applications, enforcing our patents, defending against third party patent infringement suits, seeking invalidation of third party patents or in-licensing third party intellectual property, as a result of litigation or other proceedings relating to patent and other intellectual property rights.

- Our commercial success depends upon attaining significant market acceptance of our current product candidate and future product candidates, if approved, among physicians, patients, healthcare payors and cancer treatment centers.

- Even if we are able to commercialize our lead product candidate or any future product candidates, the products might not receive coverage or adequate reimbursement from third party payors in the United States and in other countries in which we seek to commercialize our intended products, which could harm our business.

- We face substantial competition, which might result in others discovering, developing or commercializing products before or more successfully than we do.

- Our business might be adversely affected by a recurrence of the Coronavirus pandemic or a pandemic due to the emergence of another virus.

- Significant disruptions of information technology systems, computer system failures or breaches of information and cyber security could adversely affect our business.

- We might need to grow the size of our organization in the future, and we might experience difficulties in managing this growth.

RISK FACTORS

Investing in our securities involves significant risks. Before making an investment decision, with respect to any of our securities, you should carefully consider the information set forth in this prospectus, including under the heading "Risks Associated with our Business" and in any applicable prospectus supplement and in the documents incorporated by reference into this prospectus, including our most recent Annual Report on Form 10-K, as revised or supplemented by our subsequent Quarterly Reports on Form 10-Q or Current Reports on Form 8-K on file with the SEC, all of which are incorporated herein by reference, and which may be amended, supplemented or superseded from time to time by other reports we file with the SEC in the future

The risks included in this prospectus, the applicable prospectus supplement and the documents we have incorporated by reference are not the only ones we face. There may be other unknown or unpredictable economic, business, competitive, regulatory or other factors that could have material adverse effects on our future results. The occurrence of any of these risks could materially adversely affect our business, financial condition, results of operations and prospects. As a result, the value of our securities could decline and you could lose part or all of your investment therein. Past financial performance may not be a reliable indicator of future performance and historical trends should not be used to anticipate results or trends in future periods. Conditions that we currently deem to be immaterial may also materially and adversely affect our business, financial condition, cash flows and results of operation. For more information, see "Information Incorporated by Reference" in this prospectus.

THE SECURITIES WE MAY OFFER

We may offer shares of Common Stock and Preferred Stock, various series of debt securities, rights to purchase shares of Common Stock and Preferred Stock, and/or warrants to purchase any such securities, either individually or in combination, up to a total dollar amount of $50,000,000 from time to time under this prospectus, together with any applicable prospectus supplement and any related free writing prospectuses, at prices and on terms to be determined by market conditions at the time of any offering. This prospectus provides you with a general description of the securities we may offer. Each time we offer a type or series of securities under this prospectus, we will provide a prospectus supplement that will describe the specific amounts, prices and other important terms of the securities, including, to the extent applicable:

- designation or classification;
- aggregate principal amount or aggregate offering price;
- maturity;
- original issue discount, if any;
- rates and times of payment of interest or dividends, if any;
- redemption, conversion, exchange or sinking fund terms, if any;
- conversion or exchange prices or rates, if any, and, if applicable, any provisions for changes to or adjustments in the conversion or exchange prices or rates and in the securities or other property receivable upon conversion or exchange;
- ranking;
- restrictive covenants, if any;
- voting or other rights, if any; and
- important U.S. federal income tax considerations.

Any applicable prospectus supplement and any related free writing prospectus that we may authorize to be provided to you may add, update or change any of the information contained in this prospectus or in the documents we have incorporated by reference. However, no prospectus supplement or free writing prospectus will offer a security that is not registered and described in this prospectus at the time of the effectiveness of the registration statement of which this prospectus is a part.

THIS PROSPECTUS MAY NOT BE USED TO CONSUMMATE A SALE BY US OF OUR SECURITIES UNLESS IT IS ACCOMPANIED BY A PROSPECTUS SUPPLEMENT.

We may sell the securities directly to investors or to or through agents, underwriters or dealers. We and our agents or underwriters, reserve the right to accept or reject all or part of any proposed purchase of securities. If we do offer securities to or through agents or underwriters, we will include in the applicable prospectus supplement:

- the names of those agents or underwriters;
- applicable fees, discounts and commissions to be paid to them;
- details regarding over-allotment or other options, if any; and
- the net proceeds to us.

USE OF PROCEEDS

Except as described in any applicable prospectus supplement or in any related free writing prospectuses we have authorized for use in connection with a specific offering, we currently intend to use the net proceeds from the sale of the securities offered by us hereunder, if any, for working capital, research and development costs, capital expenditures, and general corporate purposes, funding future acquisition of other companies, purchasing other assets or lines of business, repurchasing Common Stock, or for any other purpose we describe in the applicable prospectus supplement. We have not determined the amounts we plan to spend on any of these areas or the timing of these expenditures. As a result, our management will have broad discretion regarding the application of the net proceeds from the sale of securities described in this prospectus.

DESCRIPTION OF CAPITAL STOCK

The following is a summary description of the Common Stock, which does not purport to be complete and is summarized from, and is qualified in its entirety by reference to, our Certificate of Incorporation, as amended, and Amended and Restated Bylaws, and Certificate of Designation, to which you should refer and copies of which are incorporated herein by reference as Exhibits 3.1 - 3.5 and 4.1, respectively, and to the registration statement on Form S-3 of which this prospectus forms a part. The summary below is also qualified by provisions of applicable law, including the Delaware General Corporation Law.

Common Stock

We are authorized to issue up to a total of 100,000,000 shares of common stock, par value $0.0001 per share. Holders of our common stock are entitled to one vote for each share held on all matters submitted to a vote of our stockholders. Holders of our common stock have no cumulative voting rights.

Further, holders of our common stock have no pre-emptive or conversion rights or other subscription rights. Upon our liquidation, dissolution or winding-up, holders of our common stock are entitled to share in all assets remaining after payment of all liabilities and the liquidation preferences of any of our outstanding shares of preferred stock. Subject to preferences that may be applicable to any outstanding shares of preferred stock, holders of our common stock are entitled to receive dividends, if any, as may be declared from time to time by our board of directors out of our assets which are legally available. Each outstanding share of our common stock is, and all shares of common stock to be issued in this offering when they are paid for, will be fully paid and non-assessable.

The holders of 33-1/3% of the shares of our common stock outstanding, represented in person or by proxy, are necessary to constitute a quorum for the transaction of business at any meeting. Except in regards to proposals that require the approval of a majority of the issued and outstanding shares, if a quorum is present, an action by stockholders entitled to vote on a matter is approved if the number of votes cast in favor of the action exceeds the number of votes cast in opposition to the action, with the exception of the election of directors, which requires a plurality of the votes cast.

Preferred Stock

Our board of directors has the authority, without further action by the stockholders, to issue up to 10,000,000 shares of preferred stock in one or more series and to fix the designations, powers, preferences, privileges, and relative participating, optional, or special rights as well as the qualifications, limitations, or restrictions of the preferred stock, including dividend rights, conversion rights, voting rights, terms of redemption, and liquidation preferences, any or all of which may be greater than the rights of the common stock. Our board of directors, without stockholder approval, will be able to issue convertible preferred stock with voting, conversion, or other rights that could adversely affect the voting power and other rights of the holders of common stock. Preferred stock could be issued quickly with terms calculated to delay or prevent a change of control or make removal of management more difficult. Additionally, the issuance of preferred stock may have the effect of decreasing the market price of our common stock, and may adversely affect the voting and other rights of the holders of common stock. At present, we have no plans to issue any shares of preferred stock following this offering.

We have designated a total of 350,000 shares as our Series A Convertible Preferred Stock, which are non-voting and not subject to increase without the written consent of a majority of the holders of such series. The holders of each tranche of 175,000 shares are entitled to receive a per share dividend equal to 1% of our annual net revenue divided by 175,000, until converted or redeemed. Each share of Series A Convertible Preferred Stock may be converted, at the option of the holder, into 2.083 shares of common stock (subject to customary anti-dilution provisions), and are subject to mandatory conversion at the conversion rate in the event of a merger or sale transaction resulting in gross proceeds to us of at least $21,875,000. Each share has a liquidation preference based on its assumed conversion into shares of common stock.

Our board of directors will fix the designations, voting powers, rights, preferences and privileges of each series, as well as the qualifications, limitations or restrictions thereof, of the Preferred Stock of each series that we offer under this prospectus and applicable prospectus supplements in the certificate of designation relating to that series. We will file as an exhibit to the registration statement of which this prospectus is a part, or will incorporate by reference from reports that we file with the SEC, the form of any certificate of designation that describes the terms of the series of Preferred Stock we are offering before the issuance of that series of Preferred Stock. This description will include:

- the title and stated value;
- the number of shares being offered;
- the liquidation preference per share;
- the purchase price per share;
- the dividend rate per share, dividend period and payment dates and method of calculation for dividends;
- whether dividends will be cumulative or non-cumulative and, if cumulative, the date from which dividends will accumulate;

- our right, if any, to defer payment of dividends and the maximum length of any such deferral period;
- the procedures for any auction and remarketing, if any;
- the provisions for a sinking fund, if any;
- the provisions for redemption or repurchase, if applicable, and any restrictions on our ability to exercise those redemption and repurchase rights;
- any listing of the Preferred Stock on any securities exchange or market;
- whether the Preferred Stock will be convertible into Common Stock, and the conversion rate or conversion price, or how they will be calculated, and the exchange period;
- voting rights, if any, of the Preferred Stock;
- preemption rights, if any;
- restrictions on transfer, sale or other assignment, if any;
- a discussion of any material or special United States federal income tax considerations applicable to the Preferred Stock;
- the relative ranking and preferences of the Preferred Stock as to dividend rights and rights if we liquidate, dissolve or wind up our affairs;
- the limitations on issuances of any class or series of Preferred Stock ranking senior to or on a parity with the series of Preferred Stock being issued as to dividend rights and rights if we liquidate, dissolve or wind up our affairs; and
- any other specific terms, rights, preferences, privileges, qualifications or restrictions of the Preferred Stock.

Upon issuance, the shares of Preferred Stock will be fully paid and non-assessable.

Anti-Takeover Provisions of Delaware Law, our Certificate of Incorporation and our Amended and Restated Bylaws

Delaware Law

We are governed by the provisions of Section 203 of the Delaware General Corporation Law. In general, Section 203 prohibits a publicly traded Delaware corporation from engaging in a business combination with an interested stockholder for a period of three years after the date of the transaction in which the person became an interested stockholder, unless the business combination is approved in a prescribed manner. A business combination includes mergers, asset sales or other transactions resulting in a financial benefit to the stockholder. An interested stockholder is a person who, together with affiliates and associates, owns (or within three years, did own) 15% or more of the corporation's voting stock, subject to certain exceptions. The statute could have the effect of delaying, deferring or preventing a change in control of our Company.

Board of Directors Vacancies

Our Certificate of Incorporation and Amended and Restated Bylaws authorize only our board of directors to fill vacant directorships. In addition, the number of directors constituting our board of directors may be set only by resolution of the majority of the incumbent directors.

Stockholder Action; Special Meeting of Stockholders

Our Certificate of Incorporation and Amended and Restated Bylaws provide that our stockholders may take action by written consent. Our Certificate of Incorporation and Amended and Restated Bylaws further provide that special meetings of our stockholders may be called by a majority of the board of directors, the Chief Executive Officer, or the Chairman of the board of directors.

Advance Notice Requirements for Stockholder Proposals and Director Nominations

Our Amended and Restated Bylaws provide that stockholders seeking to bring business before our annual meeting of stockholders, or to nominate candidates for election as directors at our annual meeting of stockholders, must provide timely notice of their intent in writing. To be timely, a stockholder's notice must be delivered to the secretary at our principal executive offices not later than the close of business on the 90^{th} day nor earlier than the close of business on the 120^{th} day prior to the first anniversary of the preceding year's annual meeting; provided, however, that in the event the date of the annual meeting is more than 30 days before or more than 60 days after such anniversary date, or if no annual meeting was held in the preceding year, notice by the stockholder to be timely must be so delivered not earlier than the close of business on the 120^{th} day prior to such annual meeting and not later than the close of business on the later of the 90^{th} day prior to such annual meeting or the 10^{th} day following the day on which a public announcement of the date of such meeting is first made by us. These provisions may preclude our stockholders from bringing matters before our annual meeting of stockholders or from making nominations for directors at our annual meeting of stockholders.

These provisions could discourage a potential acquirer from acquiring Lixte Biotechnology Holdings, Inc. or otherwise attempting to obtain control and increase the likelihood that its incumbent directors and officers will retain their positions.

Transfer Agent and Registrar

The transfer agent and registrar for our common stock is Computershare Inc.

The Nasdaq Capital Market

Our common stock is listed on The Nasdaq Capital Market under the symbol "LIXT".

DESCRIPTION OF DEBT SECURITIES

The following description, together with the additional information we include in any applicable prospectus supplement or free writing prospectus, summarizes certain general terms and provisions of the debt securities that we may offer under this prospectus. When we offer to sell a particular series of debt securities, we will describe the specific terms of the series in a prospectus supplement. We will also indicate in the prospectus supplement to what extent the general terms and provisions described in this prospectus apply to a particular series of debt securities. To the extent the information contained in the prospectus supplement differs from this summary description, you should rely on the information in the prospectus supplement.

We may issue debt securities either separately, or together with, or upon the conversion or exercise of or in exchange for, other securities described in this prospectus. Debt securities may be our senior, senior subordinated or subordinated obligations and, unless otherwise specified in the prospectus supplement, the debt securities will be our direct, unsecured obligations and may be issued in one or more series.

The debt securities will be issued under an indenture between us and a trustee named in the prospectus supplement. We have summarized select portions of the indenture below. The summary is not complete. The form of the indenture has been filed as an exhibit to the registration statement of which this prospectus is a part, and you should read the indenture for provisions that may be important to you. Capitalized terms used in the summary and not defined in this prospectus have the meanings specified in the indenture.

General

The terms of each series of debt securities will be established by or pursuant to a resolution of our board of directors and set forth or determined in the manner provided in a resolution of our board of directors, in an officer's certificate or by a supplemental indenture. The particular terms of each series of debt securities will be described in a prospectus supplement relating to such series (including any pricing supplement or term sheet).

The indenture would not limit the amount of debt securities that we may issue under it. Debt securities issued under the indenture may be in one or more series with the same or various maturities, at par, at a premium, or at a discount. We will set forth in a prospectus supplement (including any pricing supplement or term sheet) relating to any series of debt securities being offered, the aggregate principal amount and the following terms of the debt securities, if applicable:

- the title and ranking of the debt securities (including the terms of any subordination provisions);
- the price or prices (expressed as a percentage of the principal amount) at which we will sell the debt securities;
- any limit on the aggregate principal amount of the debt securities;
- the date or dates on which the principal on a particular series of debt securities is payable;
- the rate or rates (which may be fixed or variable) per annum or the method used to determine the rate or rates (including any commodity, commodity index, stock exchange index or financial index) at which the debt securities will bear interest, the date or dates from which interest will accrue, the date or dates on which interest will commence and be payable and any regular record date for the interest payable on any interest payment date;
- the place or places where principal of, and interest, if any, on the debt securities will be payable (and the method of such payment), where the debt securities of such series may be surrendered for registration of transfer or exchange, and where notices and demands to us in respect of the debt securities may be delivered;
- the period or periods within which, the price or prices at which and the terms and conditions upon which we may redeem the debt securities;
- any obligation we have to redeem or purchase the debt securities pursuant to any sinking fund or analogous provisions or at the option of a holder of debt securities and the period or periods within which, the price or prices at which and the terms and conditions upon which the debt securities of a particular series shall be redeemed or purchased, in whole or in part, pursuant to such obligation;
- the dates on which and the price or prices at which we will repurchase debt securities at the option of the holders of debt securities and other detailed terms and provisions of these repurchase obligations;
- the denominations in which the debt securities will be issued, if other than denominations of $1,000 and any integral multiple thereof;
- whether the debt securities will be issued in the form of certificated debt securities or global debt securities;
- the portion of principal amount of the debt securities payable upon declaration of acceleration of the maturity date, if other than the principal amount;

- the currency of denomination of the debt securities, which may be U.S. dollars or any foreign currency, and if such currency of denomination is a composite currency, the agency or organization, if any, responsible for overseeing such composite currency;
- the designation of the currency, currencies or currency units in which payment of principal of, and premium and interest on, the debt securities will be made;
- if payments of principal of, or premium or interest on, the debt securities will be made in one or more currencies or currency units other than that or those in which the debt securities are denominated, the manner in which the exchange rate with respect to these payments will be determined;
- the manner in which the amounts of payment of principal of, and premium, if any, and interest on, the debt securities will be determined, if these amounts may be determined by reference to an index based on a currency or currencies or by reference to a commodity, commodity index, stock exchange index or financial index;
- any provisions relating to any security provided for the debt securities;
- any addition to, deletion of or change in the events of default described in this prospectus or in the indenture with respect to the debt securities and any change in the acceleration provisions described in this prospectus or in the indenture with respect to the debt securities;
- any addition to, deletion of or change in the covenants described in this prospectus or in the indenture with respect to the debt securities;
- any depositaries, interest rate calculation agents, exchange rate calculation agents or other agents with respect to the debt securities;
- the provisions, if any, relating to conversion or exchange of any debt securities of such series, including if applicable, the conversion or exchange price and period, provisions as to whether conversion or exchange will be mandatory, the events requiring an adjustment of the conversion or exchange price and provisions affecting conversion or exchange;
- any other terms of the debt securities, which may supplement, modify or delete any provision of the indenture as it applies to that series, including any terms that may be required under applicable law or regulations or advisable in connection with the marketing of the securities; and
- whether any of our direct or indirect subsidiaries will guarantee the debt securities of that series, including the terms of subordination, if any, of such guarantees.

We may issue debt securities that provide for an amount less than their stated principal amount to be due and payable upon declaration of acceleration of their maturity pursuant to the terms of the indenture. We will provide you with information on the material U.S. federal income tax considerations applicable to any of these debt securities in the applicable prospectus supplement.

If we denominate the purchase price of any of the debt securities in a foreign currency or currencies or a foreign currency unit or units, or if the principal of, and premium, if any, and interest on, any series of debt securities is payable in a foreign currency or currencies or a foreign currency unit or units, we will provide you with information on the restrictions, elections, general tax considerations, specific terms and other information with respect to that issue of debt securities and such foreign currency or currencies or foreign currency unit or units in the applicable prospectus supplement.

Transfer and Exchange

Each debt security will be represented by either one or more global securities registered in the name of The Depository Trust Company ("DTC" or the "Depositary") or a nominee of the Depositary (we will refer to any debt security represented by a global debt security as a "book-entry debt security"), or a certificate issued in definitive registered form (we will refer to any debt security represented by a certificated security as a "certificated debt security") as set forth in the applicable prospectus supplement. Except as set forth under the heading "Legal Ownership of Securities" below, book-entry debt securities will not be issuable in certificated form.

Certificated Debt Securities

You may transfer or exchange certificated debt securities at any office we maintain for this purpose in accordance with the terms of the indenture. No service charge will be made for any transfer or exchange of certificated debt securities, but we may require payment of a sum sufficient to cover any tax or other governmental charge payable in connection with a transfer or exchange.

You may effect the transfer of certificated debt securities and the right to receive the principal of, premium and interest on certificated debt securities only by surrendering the certificate representing those certificated debt securities and either reissuance by us or the trustee of the certificate to the new holder or the issuance by us or the trustee of a new certificate to the new holder.

Global Debt Securities and Book-Entry System

Each global debt security representing book-entry debt securities will be deposited with, or on behalf of, the Depositary, and registered in the name of the Depositary or a nominee of the Depositary. See the section of this prospectus entitled "Legal Ownership of Securities" for more information.

Covenants

We will set forth in the applicable prospectus supplement any restrictive covenants applicable to any issue of debt securities.

No Protection in the Event of a Change of Control

Unless we state otherwise in the applicable prospectus supplement, the debt securities will not contain any provisions that may afford holders of the debt securities protection in the event we have a change in control or in the event of a highly leveraged transaction (whether or not such transaction results in a change in control) that could adversely affect holders of debt securities.

Consolidation, Merger and Sale of Assets

We may not consolidate with or merge with or into, or convey, transfer or lease all or substantially all of our properties and assets to, any person (a "successor person") unless:

- we are the surviving corporation or the successor person (if other than Lixte Biotechnology Holdings, Inc.) is a corporation organized and validly existing under the laws of any U.S. domestic jurisdiction and expressly assumes our obligations on the debt securities and under the indenture;
- immediately after giving effect to the transaction, no default or event of default, shall have occurred and be continuing; and
- certain other conditions are met.

Notwithstanding the above, any of our subsidiaries may consolidate with, merge into or transfer all or part of its properties to us.

Events of Default

An "event of default" means with respect to any series of debt securities, any of the following:

- default in the payment of any interest upon any debt security of that series when it becomes due and payable, and continuance of such default for a period of 30 days (unless the entire amount of the payment is deposited by us with the trustee or with a paying agent prior to the expiration of the 30-day period);
- default in the payment of principal of any debt security of that series at its maturity;
- default in the performance or breach of any other covenant or warranty by us in the indenture or any debt security (other than a covenant or warranty that has been included in the indenture solely for the benefit of a series of debt securities other than that series), which default continues uncured for a period of 60 days after we receive written notice from the trustee or Lixte Biotechnology Holdings, Inc. and the trustee receive written notice from the holders of not less than 25% in principal amount of the outstanding debt securities of that series as provided in the indenture;
- certain voluntary or involuntary events of bankruptcy, insolvency or reorganization of Lixte Biotechnology Holdings, Inc.; or
- any other event of default provided with respect to debt securities of that series that is described in the applicable prospectus supplement.

No event of default with respect to a particular series of debt securities (except as to certain events of bankruptcy, insolvency or reorganization) necessarily constitutes an event of default with respect to any other series of debt securities. The occurrence of certain events of default or an acceleration under the indenture may constitute an event of default under certain indebtedness of ours or our subsidiaries outstanding from time to time.

We will provide the trustee written notice of any default or event of default within 30 days of becoming aware of the occurrence of such default or event of default, which notice will describe in reasonable detail the status of such default or event of default and what action we are taking or propose to take in respect thereof.

If an event of default with respect to debt securities of any series at the time outstanding occurs and is continuing, then the trustee or the holders of not less than 25% in principal amount of the outstanding debt securities of that series may, by a notice in writing to us (and to the trustee if given by the holders), declare to be due and payable immediately the principal of (or, if the debt securities of that series are discount securities, that portion of the principal amount as may be specified in the terms of that series) and accrued and unpaid interest, if any, on all debt securities of that series. In the case of an event of default resulting from certain events of bankruptcy, insolvency or reorganization, the principal (or such specified amount) of and accrued and unpaid interest, if any, on all outstanding debt securities will become and be immediately due and payable without any declaration or other act on the part of the trustee or any holder of outstanding debt securities. At any time after a declaration of acceleration with respect to debt securities of any series has been made, but before a judgment or decree for payment of the money due has been obtained by the trustee, the holders of a majority in principal amount of the outstanding debt securities of that series may rescind and annul the acceleration if all events of default, other than the non-payment of accelerated principal and interest, if any, with respect to debt securities of that series, have been cured or waived as provided in the indenture. We refer you to the prospectus supplement relating to any series of debt securities that are discount securities for the particular provisions relating to acceleration of a portion of the principal amount of such discount securities upon the occurrence of an event of default.

The indenture provides that the trustee may refuse to perform any duty or exercise any of its rights or powers under the indenture unless the trustee receives indemnity satisfactory to it against any cost, liability or expense that might be incurred by it in performing such duty or exercising such right or power. Subject to certain rights of the trustee, the holders of a majority in principal amount of the outstanding debt securities of any series will have the right to direct the time, method and place of conducting any proceeding for any remedy available to the trustee or exercising any trust or power conferred on the trustee with respect to the debt securities of that series.

No holder of any debt security of any series will have any right to institute any proceeding, judicial or otherwise, with respect to the indenture or for the appointment of a receiver or trustee, or for any remedy under the indenture, unless:

- that holder has previously given to the trustee written notice of a continuing event of default with respect to debt securities of that series; and
- the holders of not less than 25% in principal amount of the outstanding debt securities of that series have made written request, and offered indemnity or security satisfactory to the trustee, to the trustee to institute the proceeding as trustee, and the trustee has not received from the holders of not less than a majority in principal amount of the outstanding debt securities of that series a direction inconsistent with that request and has failed to institute the proceeding within 60 days.

Notwithstanding any other provision in the indenture, the holder of any debt security will have an absolute and unconditional right to receive payment of the principal of, and premium and any interest on, that debt security on or after the due dates expressed in that debt security and to institute suit for the enforcement of payment.

The indenture requires us, within 120 days after the end of our fiscal year, to furnish to the trustee a statement as to compliance with the indenture. If a default or event of default occurs and is continuing with respect to the securities of any series and if it is known to a responsible officer of the trustee, the trustee shall mail to each holder of the securities of that series notice of a default or event of default within 90 days after it occurs or, if later, after a responsible officer of the trustee has knowledge of such default or event of default. The indenture provides that the trustee may withhold notice to the holders of debt securities of any series of any default or event of default (except in payment on any debt securities of that series) with respect to debt securities of that series if the trustee determines in good faith that withholding notice is in the interest of the holders of those debt securities.

Modification and Waiver

We and the trustee may modify, amend or supplement the indenture or the debt securities of any series without the consent of any holder of any debt security:

- to cure any ambiguity, defect or inconsistency;
- to comply with covenants in the indenture described above under the heading “Consolidation, Merger and Sale of Assets”;
- to provide for uncertificated securities in addition to or in place of certificated securities;
- to add guarantees with respect to debt securities of any series or secure debt securities of any series;
- to surrender any of our rights or powers under the indenture;
- to add covenants or events of default for the benefit of the holders of debt securities of any series;
- to comply with the applicable procedures of the Depositary;
- to make any change that does not adversely affect the rights of any holder of debt securities;
- to provide for the issuance of and establish the form and terms and conditions of debt securities of any series as permitted by the indenture;

- to effect the appointment of a successor trustee with respect to the debt securities of any series and to add to or change any of the provisions of the indenture to provide for or facilitate administration by more than one trustee; or

- to comply with requirements of the SEC in order to effect or maintain the qualification of the indenture under the Trust Indenture Act of 1939.

We may also modify and amend the indenture with the consent of the holders of at least a majority in principal amount of the outstanding debt securities of each series affected by the modification or amendment. We may not make any modification or amendment without the consent of the holders of each affected debt security then outstanding if that amendment would:

- reduce the amount of debt securities whose holders must consent to an amendment, supplement or waiver;

- reduce the rate of or extend the time for payment of interest (including default interest) on any debt security;

- reduce the principal of or premium on or change the fixed maturity of any debt security or reduce the amount of, or postpone the date fixed for, the payment of any sinking fund or analogous obligation with respect to any series of debt securities;

- reduce the principal amount of discount securities payable upon acceleration of maturity;

- waive a default or event of default in the payment of the principal of, or premium or interest on, any debt security (except a rescission of acceleration of the debt securities of any series by the holders of at least a majority in aggregate principal amount of the outstanding debt securities of that series and a waiver of the payment default that resulted from such acceleration);

- make the principal of, or premium or interest on, any debt security payable in a currency other than that stated in the debt security;

- make any change to certain provisions of the indenture relating to, among other things, the right of the holders of debt securities to receive payment of the principal of, and premium and interest on, those debt securities and to institute suit for the enforcement of any such payment and to waivers or amendments; or

- waive a redemption payment with respect to any debt security.

Except for certain specified provisions, the holders of at least a majority in principal amount of the outstanding debt securities of any series may on behalf of the holders of all debt securities of that series waive our compliance with provisions of the indenture. The holders of a majority in principal amount of the outstanding debt securities of any series may on behalf of the holders of all of the debt securities of such series waive any past default under the indenture with respect to that series and its consequences, except a default in the payment of the principal of, or any interest on, any debt security of that series; provided, however, that the holders of a majority in principal amount of the outstanding debt securities of any series may rescind an acceleration and its consequences, including any related payment default that resulted from the acceleration.

Defeasance of the Debt Securities and Certain Covenants in Certain Circumstances

Legal Defeasance

The indenture provides that, unless otherwise provided by the terms of the applicable series of debt securities, we may be discharged from any and all obligations in respect of the debt securities of any series (subject to certain exceptions). We will be so discharged upon the deposit with the trustee, in trust, of cash and/or U.S. government obligations or, in the case of debt securities denominated in a single currency other than U.S. dollars, cash and/or government obligations of the government that issued or caused to be issued such currency, that, through the payment of interest and principal in accordance with their terms, will provide cash in an amount sufficient in the opinion of a nationally recognized firm of independent public accountants or investment bank to pay and discharge each installment of principal of, premium and interest on, and any mandatory sinking fund payments in respect of, the debt securities of that series on the stated maturity of those payments in accordance with the terms of the indenture and those debt securities.

This discharge may occur only if, among other things, we have delivered to the trustee an opinion of counsel stating that we have received from, or there has been published by, the U.S. Internal Revenue Service a ruling or, since the date of execution of the indenture, there has been a change in the applicable U.S. federal income tax law, in either case to the effect that, and based thereon such opinion shall confirm that, the holders of the debt securities of that series will not recognize income, gain or loss for U.S. federal income tax purposes as a result of the deposit, defeasance and discharge and will be subject to U.S. federal income tax on the same amounts and in the same manner and at the same times as would have been the case if the deposit, defeasance and discharge had not occurred.

Defeasance of Certain Covenants

The indenture provides that, unless otherwise provided by the terms of the applicable series of debt securities, upon compliance with certain conditions:

- we may omit to comply with the covenant described under the heading "Consolidation, Merger and Sale of Assets" and certain other covenants set forth in the indenture, as well as any additional covenants that may be set forth in the applicable prospectus supplement; and

- any omission to comply with those covenants will not constitute a default or an event of default with respect to the debt securities of that series (a "covenant defeasance").

The conditions include:

- depositing with the trustee cash and/or U.S. government obligations or, in the case of debt securities denominated in a single currency other than U.S. dollars, cash and/or government obligations of the government that issued or caused to be issued such currency, that, through the payment of interest and principal in accordance with their terms, will provide cash in an amount sufficient in the opinion of a nationally recognized firm of independent public accountants or investment bank to pay and discharge each installment of principal of, premium and interest on, and any mandatory sinking fund payments in respect of, the debt securities of that series on the stated maturity of those payments in accordance with the terms of the indenture and those debt securities; and

- delivering to the trustee an opinion of counsel to the effect that we have received from, or there has been published by, the U.S. Internal Revenue Service a ruling or, since the date of execution of the indenture, there has been a change in the applicable U.S. federal income tax law, in either case to the effect that, and based thereon such opinion shall confirm that, the holders of the debt securities of that series will not recognize income, gain or loss for U.S. federal income tax purposes as a result of the deposit and related covenant defeasance and will be subject to U.S. federal income tax on the same amounts and in the same manner and at the same times as would have been the case if the deposit and related covenant defeasance had not occurred.

No Personal Liability of Directors, Officers, Employees or Stockholders

None of our past, present or future directors, officers, employees or stockholders, as such, will have any liability for any of our obligations under the debt securities or the indenture or for any claim based on, or in respect or by reason of, such obligations or their creation. By accepting a debt security, each holder waives and releases all such liability. This waiver and release is part of the consideration for the issue of the debt securities. However, this waiver and release may not be effective to waive liabilities under U.S. federal securities laws, and it is the view of the SEC that such a waiver is against public policy.

Governing Law

The indenture and the debt securities, including any claim or controversy arising out of or relating to the indenture or the debt securities, will be governed by the laws of the State of New York.

The indenture provides that we, the trustee and the holders of the debt securities (by their acceptance of the debt securities) irrevocably waive, to the fullest extent permitted by applicable law, any and all right to trial by jury in any legal proceeding arising out of or relating to the indenture, the debt securities or the transactions contemplated thereby.

The indenture provides that any legal suit, action or proceeding arising out of or based upon the indenture or the transactions contemplated thereby may be instituted in the federal courts of the United States of America located in the City of New York or the courts of the State of New York in each case located in the City of New York, and we, the trustee and the holder of the debt securities (by their acceptance of the debt securities) irrevocably submit to the non-exclusive jurisdiction of such courts in any such suit, action or proceeding. The indenture further provides that service of any process, summons, notice or document by mail (to the extent allowed under any applicable statute or rule of court) to such party's address set forth in the indenture will be effective service of process for any suit, action or other proceeding brought in any such court. The indenture further provides that we, the trustee and the holders of the debt securities (by their acceptance of the debt securities) irrevocably and unconditionally waive any objection to the laying of venue of any suit, action or other proceeding in the courts specified above and irrevocably and unconditionally waive and agree not to plead or claim any such suit, action or other proceeding has been brought in an inconvenient forum.

DESCRIPTION OF WARRANTS

We may issue warrants for the purchase of shares of Common Stock or Preferred Stock or for the purchase of debt securities. We may issue warrants independently or together with other securities, and the warrants may be attached to or separate from any offered securities. If a series of warrants will be issued under a separate warrant agreement to be entered into between us and the investors or a warrant agent, we will so specify in the applicable prospectus supplement.

The following summary of the material terms of the warrants and warrant agreements is subject to, and qualified in its entirety by reference to, all of the provisions of the warrants and any warrant agreement applicable to a particular series of warrants. The terms of any warrants offered under a prospectus supplement may differ from the terms described below. We urge you to read the applicable prospectus supplement and any related free writing prospectus, as well as the complete warrants and any warrant agreements that contain the terms of the warrants.

The material terms of any issue of warrants will be described in the prospectus supplement relating to the issue. Those terms may include:

- the number of shares of Common Stock or Preferred Stock purchasable upon the exercise of warrants to purchase such shares and the price at which such number of shares may be purchased upon exercise;

- a summary of the terms (including, without limitation, liquidation, dividend, conversion and voting rights) of the series of Preferred Stock purchasable upon exercise of warrants to purchase Preferred Stock as set forth in the certificate of designations for such series of Preferred Stock;

- the principal amount of debt securities that may be purchased upon exercise of a debt warrant and the exercise price for the warrants;
- the date, if any, on and after which the warrants and the related debt securities, Preferred Stock or Common Stock will be separately transferable;
- the terms of any rights to redeem or call the warrants;
- the date on which the right to exercise the warrants will commence and the date on which the right will expire;
- the material U.S. federal income tax consequences applicable to the warrants; and
- any additional material terms of the warrants, including terms, procedures, and limitations relating to the exchange, exercise and settlement of the warrants.

Holders of equity warrants will not be entitled:

- to vote, consent or received dividends;
- receive notice as stockholders with respect to any meeting of stockholders for the election of our directors or any other matter; or
- exercise any rights as stockholders of Lixte Biotechnology Holdings, Inc.

Each warrant will entitle its holder to purchase the principal amount of debt securities or the number of shares of Preferred Stock or Common Stock at the exercise price set forth in, or calculable as set forth in, the applicable prospectus supplement. Unless we otherwise specify in the applicable prospectus supplement, holders of the warrants may exercise the warrants at any time up to the specified time on the expiration date that we set forth in the applicable prospectus supplement. After the close of business on the expiration date, unexercised warrants will become void. A holder of warrant certificates may exchange them for new warrant certificates of different denominations, present them for registration of transfer and exercise them at the corporate trust office of the warrant agent or any other office indicated in the applicable prospectus supplement. Until any warrants to purchase debt securities are exercised, the holder of the warrants will not have any rights of holders of the debt securities that can be purchased upon exercise, including any rights to receive payments of principal, premium or interest on the underlying debt securities or to enforce covenants in the applicable indenture. Until any warrants to purchase Common Stock or Preferred Stock are exercised, the holders of the warrants will not have any rights of holders of the underlying Common Stock or Preferred Stock, including any rights to receive dividends or payments upon any liquidation, dissolution or winding up on the Common Stock or Preferred Stock, if any.

DESCRIPTION OF RIGHTS

General

We may issue rights to our stockholders to purchase shares of our common stock, preferred stock or the other securities described in this prospectus. We may offer rights separately or together with one or more additional rights, debt securities, preferred stock, common stock or warrants, or any combination of those securities in the form of units, as described in the applicable prospectus supplement. Each series of rights will be issued under a separate rights agreement to be entered into between us and a bank or trust company, as rights agent. The rights agent will act solely as our agent in connection with the certificates relating to the rights of the series of certificates and will not assume any obligation or relationship of agency or trust for or with any holders of rights certificates or beneficial owners of rights. The following description sets forth certain general terms and provisions of the rights to which any prospectus supplement may relate. The particular terms of the rights to which any prospectus supplement may relate and the extent, if any, to which the general provisions may apply to the rights so offered will be described in the applicable prospectus supplement. To the extent that any particular terms of the rights, rights agreement or rights certificates described in a prospectus supplement differ from any of the terms described below, then the terms described below will be deemed to have been superseded by that prospectus supplement. We encourage you to read the applicable rights agreement and rights certificate for additional information before you decide whether to purchase any of our rights. We will provide in a prospectus supplement the following terms of the rights being issued:

- the date of determining the stockholders entitled to the rights distribution;
- the aggregate number of shares of common stock, preferred stock or other securities purchasable upon exercise of the rights;
- the exercise price;
- the aggregate number of rights issued;
- whether the rights are transferrable and the date, if any, on and after which the rights may be separately transferred;
- the date on which the right to exercise the rights will commence, and the date on which the right to exercise the rights will expire;
- the method by which holders of rights will be entitled to exercise;
- the conditions to the completion of the offering, if any;
- the withdrawal, termination and cancellation rights, if any;
- whether there are any backstop or standby purchaser or purchasers and the terms of their commitment, if any;
- whether stockholders are entitled to oversubscription rights, if any;
- any applicable material U.S. federal income tax considerations; and
- any other terms of the rights, including terms, procedures and limitations relating to the distribution, exchange and exercise of the rights, as applicable.

Each right will entitle the holder of rights to purchase for cash the principal amount of shares of common stock, preferred stock or other securities at the exercise price provided in the applicable prospectus supplement. Rights may be exercised at any time up to the close of business on the expiration date for the rights provided in the applicable prospectus supplement.

Holders may exercise rights as described in the applicable prospectus supplement. Upon receipt of payment and the rights certificate properly completed and duly executed at the corporate trust office of the rights agent or any other office indicated in the prospectus supplement, we will, as soon as practicable, forward the shares of common stock, preferred stock or other securities, as applicable, purchasable upon exercise of the rights. If less than all of the rights issued in any rights offering are exercised, we may offer any unsubscribed securities directly to persons other than stockholders, to or through agents, underwriters or dealers or through a combination of such methods, including pursuant to standby arrangements, as described in the applicable prospectus supplement.

Rights Agent

The rights agent for any rights we offer will be set forth in the applicable prospectus supplement.

DESCRIPTION OF UNITS

We may issue units consisting of any combination of the other types of securities offered under this prospectus in one or more series. We may evidence each series of units by unit certificates that we will issue under a separate unit agreement. We may enter into unit agreements with a unit agent. Each unit agent will be a bank or trust company that we select. We will indicate the name and address of the unit agent in the applicable prospectus supplement relating to a particular series of units.

The following description, together with the additional information included in any applicable prospectus supplement, summarizes the general features of the units that we may offer under this prospectus. You should read any prospectus supplement and any free writing prospectus that we may authorize to be provided to you related to the series of units being offered, as well as the complete unit agreements that contain the terms of the units. Specific unit agreements will contain additional important terms and provisions and we will file each unit agreement as an exhibit to the registration statement of which this prospectus is a part, or will incorporate by reference from another report that we file with the SEC, the form of each unit agreement relating to units offered under this prospectus.

If we offer any units, certain terms of that series of units will be described in the applicable prospectus supplement, including, without limitation, the following, as applicable:

- the title of the series of units;
- identification and description of the separate constituent securities comprising the units;
- the price or prices at which the units will be issued;
- the date, if any, on and after which the constituent securities comprising the units will be separately transferable;
- the material U.S. federal income tax considerations applicable to the units; and
- any other material terms of the units and their constituent securities.

LEGAL OWNERSHIP OF SECURITIES

We may issue securities in registered form or in the form of one or more global securities. We describe global securities in greater detail below. We refer to those persons who have securities registered in their own names on the books that we or any applicable trustee, depositary or warrant agent maintain for this purpose as the “holders” of those securities. These persons are the legal holders of the securities. We refer to those persons who, indirectly through others, own beneficial interests in securities that are not registered in their own names, as “indirect holders” of those securities. As discussed below, indirect holders are not legal holders, and investors in securities issued in book-entry form or in street name will be indirect holders.

Book-Entry Holders

We may issue securities in book-entry form only, as we will specify in the applicable prospectus supplement. This means securities may be represented by one or more global securities registered in the name of a financial institution that holds them as depositary on behalf of other financial institutions that participate in the depositary’s book-entry system. These participating institutions, which are referred to as participants, in turn, hold beneficial interests in the securities on behalf of themselves or their customers.

Only the person in whose name a security is registered is recognized as the holder of that security. Securities issued in global form will be registered in the name of the depositary or its participants. Consequently, for securities issued in global form, we will recognize only the depositary as the holder of the securities, and we will make all payments on the securities to the depositary. The depositary passes along the payments it receives to its participants, which in turn pass the payments along to their customers who are the beneficial owners. The depositary and its participants do so under agreements they have made with one another or with their customers; they are not obligated to do so under the terms of the securities.

As a result, investors in book-entry securities will not own securities directly. Instead, they will own beneficial interests in a global security, through a bank, broker or other financial institution that participates in the depositary's book-entry system or holds an interest through a participant. As long as the securities are issued in global form, investors will be indirect holders, and not holders, of the securities.

Street Name Holders

We may terminate a global security or issue securities in non-global form. In these cases, investors may choose to hold their securities in their own names or in "street name". Securities held by an investor in street name would be registered in the name of a bank, broker or other financial institution that the investor chooses, and the investor would hold only a beneficial interest in those securities through an account he or she maintains at that institution.

For securities held in street name, we will recognize only the intermediary banks, brokers and other financial institutions in whose names the securities are registered as the holders of those securities, and we will make all payments on those securities to them. These institutions pass along the payments they receive to their customers who are the beneficial owners, but only because they agree to do so in their customer agreements or because they are legally required to do so. Investors who hold securities in street name will be indirect holders, not holders, of those securities.

Legal Holders

Our obligations, as well as the obligations of any applicable trustee and of any third parties employed by us or a trustee, run only to the legal holders of the securities. We do not have obligations to investors who hold beneficial interests in global securities, in street name or by any other indirect means. This will be the case whether an investor chooses to be an indirect holder of a security or has no choice because we are issuing the securities only in global form.

For example, once we make a payment or give a notice to the holder, we have no further responsibility for the payment or notice even if that holder is required, under agreements with depositary participants or customers or by law, to pass it along to the indirect holders but does not do so. Similarly, we may want to obtain the approval of the holders to amend an indenture, to relieve us of the consequences of a default or of our obligation to comply with a particular provision of the indenture or for other purposes. In such an event, we would seek approval only from the holders, and not the indirect holders, of the securities. Whether or how the holders contact the indirect holders is the responsibility of the holders.

Special Considerations for Indirect Holders

If you hold securities through a bank, broker or other financial institution, either in book-entry form or in street name, you should check with your own institution to find out:

- the performance of third-party service providers;
- how it handles securities payments and notices;
- whether it imposes fees or charges;
- how it would handle a request for the holders' consent, if ever required;
- whether and how you can instruct it to send you securities registered in your own name so you can be a holder, if that is permitted in the future;

- how it would exercise rights under the securities if there were a default or other event triggering the need for holders to act to protect their interests; and
- if the securities are in book-entry form, how the depositary's rules and procedures will affect these matters.

Global Securities

A global security is a security that represents one or any other number of individual securities held by a depositary. Generally, all securities represented by the same global securities will have the same terms.

Each security issued in book-entry form will be represented by a global security that we deposit with and register in the name of a financial institution or its nominee that we select. The financial institution that we select for this purpose is called the depositary. Unless we specify otherwise in the applicable prospectus supplement, DTC will be the depositary for all securities issued in book-entry form.

A global security may not be transferred to or registered in the name of anyone other than the depositary, its nominee or a successor depositary, unless special termination situations arise. We describe those situations below under the section entitled "Special Situations When a Global Security Will Be Terminated" in this prospectus. As a result of these arrangements, the depositary, or its nominee, will be the sole registered owner and holder of all securities represented by a global security, and investors will be permitted to own only beneficial interests in a global security. Beneficial interests must be held by means of an account with a broker, bank or other financial institution that in turn has an account with the depositary or with another institution that does. Thus, an investor whose security is represented by a global security will not be a holder of the security, but only an indirect holder of a beneficial interest in the global security.

If the prospectus supplement for a particular security indicates that the security will be issued in global form only, then the security will be represented by a global security at all times unless and until the global security is terminated. If termination occurs, we may issue the securities through another book-entry clearing system or decide that the securities may no longer be held through any book-entry clearing system.

Special Considerations for Global Securities

The rights of an indirect holder relating to a global security will be governed by the account rules of the investor's financial institution and of the depositary, as well as general laws relating to securities transfers. We do not recognize an indirect holder as a holder of securities and instead deal only with the depositary that holds the global security.

If securities are issued only in the form of a global security, an investor should be aware of the following:

- an investor cannot cause the securities to be registered in his or her name, and cannot obtain non-global certificates for his or her interest in the securities, except in the special situations described below;
- an investor will be an indirect holder and must look to his or her own bank or broker for payments on the securities and protection of his or her legal rights relating to the securities, as described above;
- an investor may not be able to sell interests in the securities to some insurance companies and to other institutions that are required by law to own their securities in non-book-entry form;
- an investor may not be able to pledge his or her interest in a global security in circumstances where certificates representing the securities must be delivered to the lender or other beneficiary of the pledge in order for the pledge to be effective;
- the depositary's policies, which may change from time to time, will govern payments, transfers, exchanges and other matters relating to an investor's interest in a global security;

- we and any applicable trustee have no responsibility for any aspect of the depositary's actions or for its records of ownership interests in a global security, nor do we or any applicable trustee supervise the depositary in any way;

- the depositary may, and we understand that DTC will, require that those who purchase and sell interests in a global security within its book-entry system use immediately available funds, and your broker or bank may require you to do so as well; and

- financial institutions that participate in the depositary's book-entry system, and through which an investor holds its interest in a global security, may also have their own policies affecting payments, notices and other matters relating to the securities.

There may be more than one financial intermediary in the chain of ownership for an investor. We do not monitor and are not responsible for the actions of any intermediary.

Special Situations When a Global Security Will Be Terminated

In a few special situations described below, the global security will terminate and interests in it will be exchanged for physical certificates representing those interests. After that exchange, the choice of whether to hold securities directly or in street name will be the responsibility of the investor. Investors must consult their own banks or brokers to learn how to have their interests in securities transferred to their own names so that they will be direct holders. We have described the rights of holders and street name investors above.

Unless we provide otherwise in the applicable prospectus supplement, the global security will terminate when the following special situations occur:

- if the depositary notifies us that it is unwilling, unable or no longer qualified to continue as depositary for that global security and we do not appoint another institution to act as depositary within 90 days;

- if we notify any applicable trustee that we wish to terminate that global security; or

- if an event of default has occurred with regard to securities represented by that global security and has not been cured or waived.

The applicable prospectus supplement may also list additional situations for terminating a global security that would apply only to the particular series of securities covered by the applicable prospectus supplement. When a global security terminates, the depositary, and not we or any applicable trustee, is responsible for deciding the names of the institutions that will be the initial direct holders.

PLAN OF DISTRIBUTION

We may sell the securities offered by this prospectus from time to time pursuant to underwritten public offerings, negotiated transactions, block trades or a combination of these methods or through underwriters or dealers, through agents and/or directly to one or more purchasers. The securities may be distributed from time to time in one or more transactions:

- at a fixed price or prices, which may be changed;

- at market prices prevailing at the time of sale;

- at prices related to such prevailing market prices; or

- at negotiated prices.

Each time that we sell securities offered by this prospectus, we will provide a prospectus supplement or supplements that will describe the method of distribution and set forth the terms and conditions of the offering of such securities, including the offering price of the securities and the proceeds to us.

Offers to purchase the securities being offered by this prospectus may be solicited directly. Agents may also be designated to solicit offers to purchase the securities from time to time. Any agent involved in the offer or sale of our securities will be identified in a prospectus supplement.

If a dealer is utilized in the sale of the securities being offered by this prospectus, the securities will be sold to the dealer, as principal. The dealer may then resell the securities to the public at varying prices to be determined by the dealer at the time of resale.

If an underwriter is utilized in the sale of the securities being offered by this prospectus, an underwriting agreement will be executed with the underwriter at the time of sale and the name of any underwriter will be provided in the prospectus supplement that the underwriter will use to make resales of the securities to the public. In connection with the sale of the securities, we, or the purchasers of securities for whom the underwriter may act as agent, may compensate the underwriter in the form of underwriting discounts or commissions. The underwriter may sell the securities to or through dealers, and those dealers may receive compensation in the form of discounts, concessions or commissions from the underwriters and/or commissions from the purchasers for which they may act as agent. Unless otherwise indicated in a prospectus supplement, an agent will be acting on a best efforts basis and a dealer will purchase securities as a principal, and may then resell the securities at varying prices to be determined by the dealer.

Any compensation paid to underwriters, dealers or agents in connection with the offering of the securities, and any discounts, concessions or commissions allowed by underwriters to participating dealers will be provided in the applicable prospectus supplement. Underwriters, dealers and agents participating in the distribution of the securities may be deemed to be underwriters within the meaning of the Securities Act, and any discounts and commissions received by them and any profit realized by them on resale of the securities may be deemed to be underwriting discounts and commissions. We may enter into agreements to indemnify underwriters, dealers and agents against civil liabilities, including liabilities under the Securities Act, or to contribute to payments they may be required to make in respect thereof and to reimburse those persons for certain expenses.

Any Common Stock issued by us under this prospectus will be listed on The Nasdaq Capital Market, but any other securities may or may not be listed on a national securities exchange. To facilitate the offering of securities, certain persons participating in the offering may engage in transactions that stabilize, maintain or otherwise affect the price of the securities. This may include over-allotments or short sales of the securities, which involve the sale by persons participating in the offering of more securities than were sold to them. In these circumstances, these persons would cover such over-allotments or short positions by making purchases in the open market or by exercising their over-allotment option, if any. In addition, these persons may stabilize or maintain the price of the securities by bidding for or purchasing securities in the open market or by imposing penalty bids, whereby selling concessions allowed to dealers participating in the offering may be reclaimed if securities sold by them are repurchased in connection with stabilization transactions. The effect of these transactions may be to stabilize or maintain the market price of the securities at a level above that which might otherwise prevail in the open market. These transactions may be discontinued at any time.

If indicated in the applicable prospectus supplement, underwriters or other persons acting as agents may be authorized to solicit offers by institutions or other suitable purchasers to purchase the securities at the public offering price set forth in the prospectus supplement pursuant to delayed delivery contracts providing for payment and delivery on the date or dates stated in the prospectus supplement. These purchasers may include, among others, commercial and savings banks, insurance companies, pension funds, investment companies and educational and charitable institutions.

We may engage in at the market offerings into an existing trading market in accordance with Rule 415(a)(4) under the Securities Act. In addition, we may enter into derivative transactions with third parties, or sell securities not covered by this prospectus to third parties in privately negotiated transactions. If the applicable prospectus supplement so indicates, in connection with those derivatives, the third parties may sell securities covered by this prospectus and the applicable prospectus supplement, including in short sale transactions. If so, the third party may use securities pledged by us or borrowed from us or others to settle those sales or to close out any related open borrowings of stock, and may use securities received from us in settlement of those derivatives to close out any related open borrowings of stock. The third party in such sale transactions will be an underwriter and, if not identified in this prospectus, will be named in the applicable prospectus supplement (or a post-effective amendment). In addition, we may otherwise loan or pledge securities to a financial institution or other third party that in turn may sell the securities short using this prospectus and an applicable prospectus supplement. Such financial institution or other third party may transfer its economic short position to investors in our securities or in connection with a concurrent offering of other securities.

The specific terms of any lock-up provisions in respect of any given offering will be described in the applicable prospectus supplement.

The underwriters, dealers and agents may engage in transactions with us, or perform services for us, in the ordinary course of business for which they receive compensation.

LEGAL MATTERS

TroyGould PC, Los Angeles, California, has issued an opinion regarding certain legal matters relating to the issuance of the securities offered by this prospectus on behalf of Lixte Biotechnology Holdings, Inc. Additional legal matters may be passed upon for us, or any underwriters, dealers or agents, by counsel that we will name in the applicable prospectus supplement.

EXPERTS

The consolidated financial statements of Lixte Biotechnology Holdings, Inc. appearing in Lixte Biotechnology Holdings, Inc.'s Annual Report on Form 10-K for the fiscal year ended December 31, 2023 have been audited by Weinberg & Company, P.A., an independent registered public accounting firm, as stated in their report thereon, which includes an explanatory paragraph as to the Company's ability to continue as a going concern. Such financial statements have been incorporated herein by reference in reliance on such report given on the authority of such firm as experts in auditing and accounting.

WHERE YOU CAN FIND MORE INFORMATION

We file annual, quarterly and current reports, proxy statements and other information with the SEC. The SEC maintains a website at http://www.sec.gov that contains reports, proxy and information statements and other information regarding us and other issuers that file electronically with the SEC. This prospectus is only part of a registration statement on Form S-3 that we have filed with the SEC under the Securities Act, and therefore omits certain information contained in the registration statement. We have also filed exhibits and schedules with the registration statement that are excluded from this prospectus, and you should refer to the applicable exhibit or schedule for a complete description of any statement referring to any contract or other document. You may access the registration statement of which this prospectus forms a part by visiting http://www.sec.gov.

We also maintain a website at www.lixte.com, through which you can access our SEC filings free of charge. The information set forth on our website is not part of this prospectus. The reference to our website address does not constitute incorporation by reference of the information contained on our website.

INFORMATION INCORPORATED BY REFERENCE

The rules of the SEC allow us to "incorporate by reference" into this prospectus information that we have filed with the SEC under the Commission File No. 001-39717. This means we can disclose important information to you without actually including the specific information in this prospectus by referring you to SEC filings that contain that information. The information incorporated by reference is considered to be a part of this prospectus, provided that it will be automatically updated and superseded by information that we file later with the SEC. This prospectus incorporates by reference the documents listed below:

- Our Annual Report on Form 10-K for the fiscal year ended December 31, 2023, as filed with the SEC on March 19, 2024;
- Our Current Reports on Form 8-K, as filed with the SEC on March 22, 2024 and March 28, 2024;
- the description of the Common Stock incorporated by reference to our Registration Statement on Form 8-A that was filed with the SEC on November 17, 2020, including any amendment or report filed for the purpose of updating such description; and
- all reports and other documents subsequently filed by us pursuant to Sections 13(a), 13(c), 14 and 15(d) of the Exchange Act after the date of this prospectus and prior to the termination or completion of the offering of securities under this prospectus shall be deemed to be incorporated by reference in this prospectus and to be a part hereof from the date of filing such reports and other documents.

Notwithstanding the foregoing, we are not incorporating by reference any documents, portions of documents, exhibits or other information that is deemed to have been furnished to, rather than filed with, the SEC.

Any statement contained in this prospectus or in a document incorporated or deemed to be incorporated by reference into this prospectus shall be deemed to be modified or superseded for purposes of this prospectus to the extent that a statement contained in this prospectus or any other subsequently filed document that is deemed to be incorporated by reference into this prospectus modifies or supersedes the statement. Any statements so modified or superseded shall not be deemed, except as so modified or superseded, to constitute a part of this prospectus.

We will provide without charge to each person, including any beneficial owner, to whom a copy of this prospectus is delivered, upon written or oral request of any such person, a copy of any or all of the documents that has been or may be incorporated by reference into this prospectus (excluding certain exhibits to the documents) at no cost. Any such request to us may be made by writing or telephoning our Investor Relations department at the following address and telephone number:

680 East Colorado Boulevard, Suite 180
Pasadena, California 91101
(631) 830-7092

You may also access these documents on our website, www.lixte.com. The information contained on, or that can be accessed through, our website is not a part of this prospectus. We have included our website address in this prospectus solely as an inactive textual reference.

2,366,503 Shares of Common Stock
Pre-Funded Warrants to Purchase up to 258,859 Shares of Common Stock
Up to 258,859 Shares of Common Stock Underlying the Pre-Funded Warrants

LIXTE BIOTECHNOLOGY HOLDINGS, INC.

The date of this prospectus supplement is June 4, 2026.