

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

**FORM S-1**

REGISTRATION STATEMENT UNDER THE SECURITIES ACT OF 1933

**LIXTE BIOTECHNOLOGY HOLDINGS, INC.**

(Exact name of registrant as specified in its charter)

**Delaware**

(State or other jurisdiction of  
incorporation or organization)

**100**

(Primary standard industrial  
classification code number)

**20-2903526**

(I.R.S. employer  
identification number)

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

(Address, including zip code, and telephone number, including area code, of registrant's principal executive offices)

**Bastiaan van der Baan  
Chief Executive Officer  
680 East Colorado Boulevard, Suite 180  
Pasadena, CA 91101  
(631) 830-7092**

(Name, address, including zip code, and telephone number, including area code, of agent for service)

Copies to:

**David L. Ficksman, Esq.  
TroyGould PC  
1801 Century Park East, 16<sup>th</sup> Floor  
Los Angeles, CA 90067  
Tel: (310) 789-1290**

**Approximate date of commencement of proposed sale to the public:** From time to time after the effective date of this registration statement.

If any of the securities being registered on this Form are to be offered on a delayed or continuous basis pursuant to Rule 415 under the Securities Act of 1933 check the following box. ☒

If this Form is filed to register additional securities for an offering pursuant to Rule 462(b) under the Securities Act, please check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering. ☐

If this Form is a post-effective amendment filed pursuant to Rule 462(c) under the Securities Act, check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering. ☐

If this Form is a post-effective amendment filed pursuant to Rule 462(d) under the Securities Act, check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering. ☐

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer, a smaller reporting company, or an emerging growth company. See the definitions of "large accelerated filer", "accelerated filer", "smaller reporting company", and "emerging growth company" in Rule 12b-2 of the Exchange Act.

Large accelerated filer

☐

Accelerated filer

☐

Non-accelerated filer

☒

Smaller reporting company

☒

Emerging growth company

☐

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 7(a)(2)(B) of the Securities Act. ☐

**The registrant hereby amends this registration statement on such date or dates as may be necessary to delay its effective date until the registrant shall file a further amendment which specifically states that this registration statement shall thereafter become effective in accordance with Section 8(a) of the Securities Act of 1933 or until the registration statement shall become effective on such date as the Securities and Exchange Commission, acting pursuant to said Section 8(a), may determine.**

The information in this prospectus is not complete and may be changed. We may not sell these securities until the registration statement filed with the Securities and Exchange Commission is effective. This prospectus is not an offer to sell these securities and it is not soliciting an offer to buy these securities in any state where the offer or sale is not permitted.

**The information in this prospectus is not complete and may be changed. The securities may not be sold until the registration statement filed with the SEC is declared effective. This prospectus is not an offer to sell these securities and it is not soliciting an offer to buy these securities in any state where the offer or sale is not permitted.**

**Subject to Completion, dated April \_\_, 2025**

## **PRELIMINARY PROSPECTUS**

**467,393 Shares of Common Stock  
434,784 Shares of Common Stock Issuable Upon the Exercise of Outstanding 2025 Warrants  
32,609 Shares of Common Stock Issuable Upon the Exercise of 2025 Placement Agent Warrants**

### **LIXTE BIOTECHNOLOGY HOLDINGS, INC.**

Pursuant to this prospectus, the selling stockholders identified herein are offering on a resale basis 467,393 shares of our common stock, par value \$0.0001 per share, issuable upon exercise of certain common stock warrants (the “2025 Warrants” and the “2025 Placement Agent Warrants”, as defined below). We issued the 2025 Warrants in an exempt private offering (the “Private Placement”) pursuant to a securities purchase agreement, dated February 11, 2025 (the “Purchase Agreement”) with the selling stockholders. We will not receive any of the proceeds from the sale by the selling stockholders of the common stock. However, upon exercise of the 2025 Warrants or the 2025 Placement Agent Warrants by payments of cash, we will receive the respective aggregate exercise prices.

The selling stockholders may sell or otherwise dispose of the common stock covered by this prospectus in a number of different ways and at varying prices. We provide more information about how the selling stockholders may sell or otherwise dispose of the common stock covered by this prospectus in the section entitled “Plan of Distribution”. Discounts, concessions, commissions and similar selling expenses attributable to the sale of common stock covered by this prospectus will be borne by the selling stockholders. We will pay all expenses (other than discounts, concessions, commissions and similar selling expenses) relating to the registration of the common stock with the Securities and Exchange Commission.

You should carefully read this prospectus, together with the documents we incorporate by reference, before you invest in our common stock.

Our common stock is listed on The Nasdaq Capital Market under the symbol “LIXT”. On April 2, 2025, the last reported sale price for our common stock was \$1.22 per share.

**Investing in common stock involves risk. Please read carefully the section entitled “Risk Factors” beginning on page 13 of this prospectus or incorporated by reference.**

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

**The date of this prospectus is April \_\_, 2025.**

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## **ABOUT THIS PROSPECTUS**

You should rely only on the information contained in or incorporated by reference into this prospectus and in any free writing prospectus. We have not and the selling stockholders have not authorized anyone to provide you with information different from that contained in this prospectus. The sale of our securities will only be made in jurisdictions where offers and sales are permitted. The information in this prospectus is accurate only as of the date of this prospectus, and any information we have 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 or any sale of our securities.

Neither we nor the selling stockholders have done anything that would permit this offering or possession or distribution of this prospectus in any jurisdiction where action for that purpose is required, other than in the United States. Persons outside the United States who come into possession of this prospectus must inform themselves about, and observe any restrictions relating to, the offering of our securities and the distribution of this prospectus outside of the United States.

We own or have rights to trademarks or trade names that we use in connection with the operation of our business, including our corporate names, logos and website names. In addition, we own or have the rights to copyrights, trade secrets and other proprietary rights that protect the content of our products. This prospectus may also contain trademarks, service marks and trade names of other companies, which are the property of their respective owners. Our use or display of third parties’ trademarks, service marks, trade names or products in this prospectus is not intended to, and should not be read to, imply a relationship with or endorsement or sponsorship of us. Solely for convenience, some of the copyrights, trade names and trademarks referred to in this prospectus are listed without their ©, ® and ™ symbols, but we will assert, to the fullest extent under applicable law, our rights to our copyrights, trade names and trademarks. All other trademarks are the property of their respective owners.

## PROSPECTUS SUMMARY

The following summary highlights information contained or incorporated by reference elsewhere in this prospectus and does not contain all of the information that you should consider in making your investment decision. Before investing in our common stock, you should carefully read this entire prospectus, including our consolidated financial statements and the related notes and other documents incorporated by reference herein, as well as the information under the caption “Risk Factors” herein and under similar headings in the other documents that are incorporated by reference into this prospectus including documents that are filed after the date hereof. Some of the statements in this prospectus constitute forward-looking statements that involve risks and uncertainties. See “Cautionary Note Regarding Forward-Looking Statements”. Our actual results could differ materially from those anticipated in such forward-looking statements as a result of certain factors, including those discussed in the “Risk Factors” and other sections included in or incorporated by reference herein. In this prospectus, unless otherwise stated or the context otherwise requires, references to “Lixte”, the “Company”, “we”, “us”, “our”, or similar references mean Lixte Biotechnology Holdings, Inc.

### 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, does not have positive cash flows from operations, relies on stock-based compensation for a substantial portion of employee and consultant compensation, and is dependent on periodic access to equity capital to fund its operating requirements.

### Description of Business

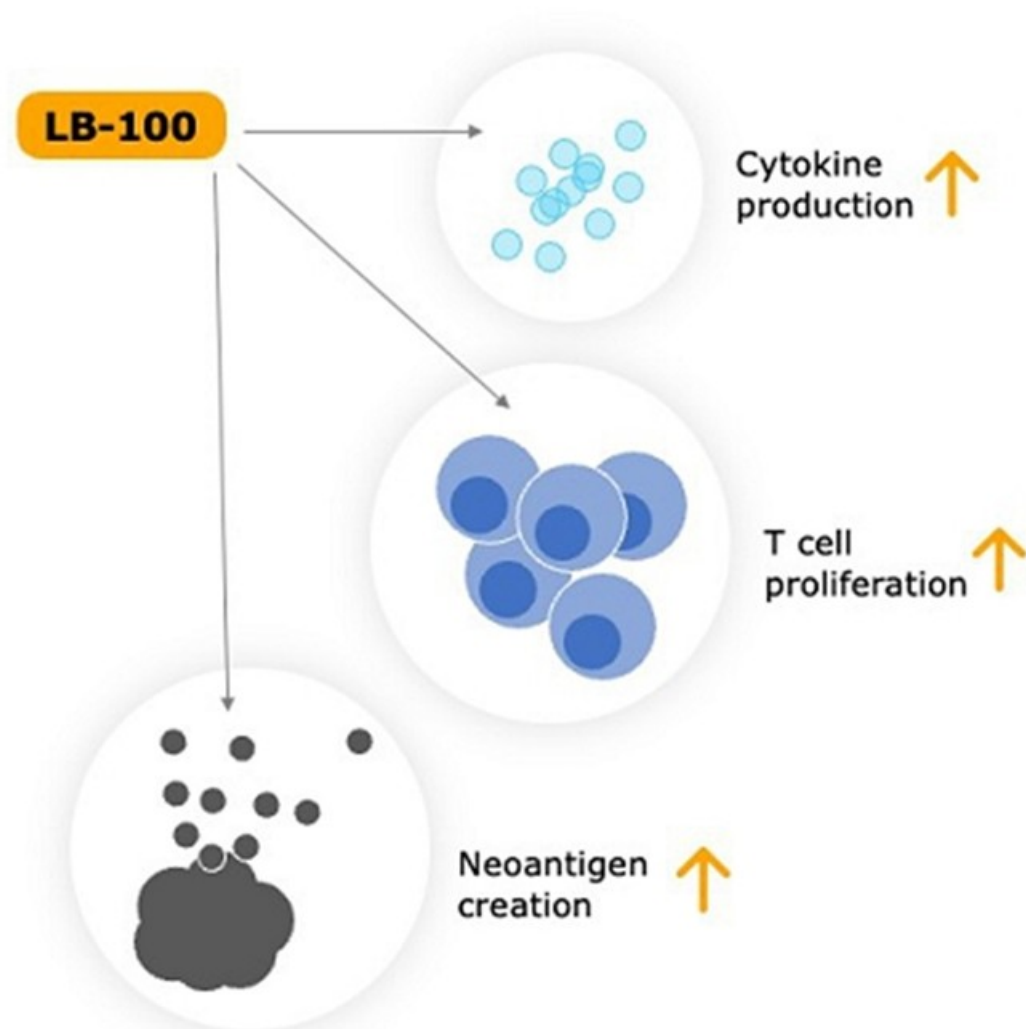
Most cancer patients are treated with either chemotherapy or immunotherapy or both. These therapies often have limited benefit and there is a high unmet medical need to enhance their effects. In many preclinical models we have shown that LB-100 enhances the effect of both chemotherapy and Immunotherapy



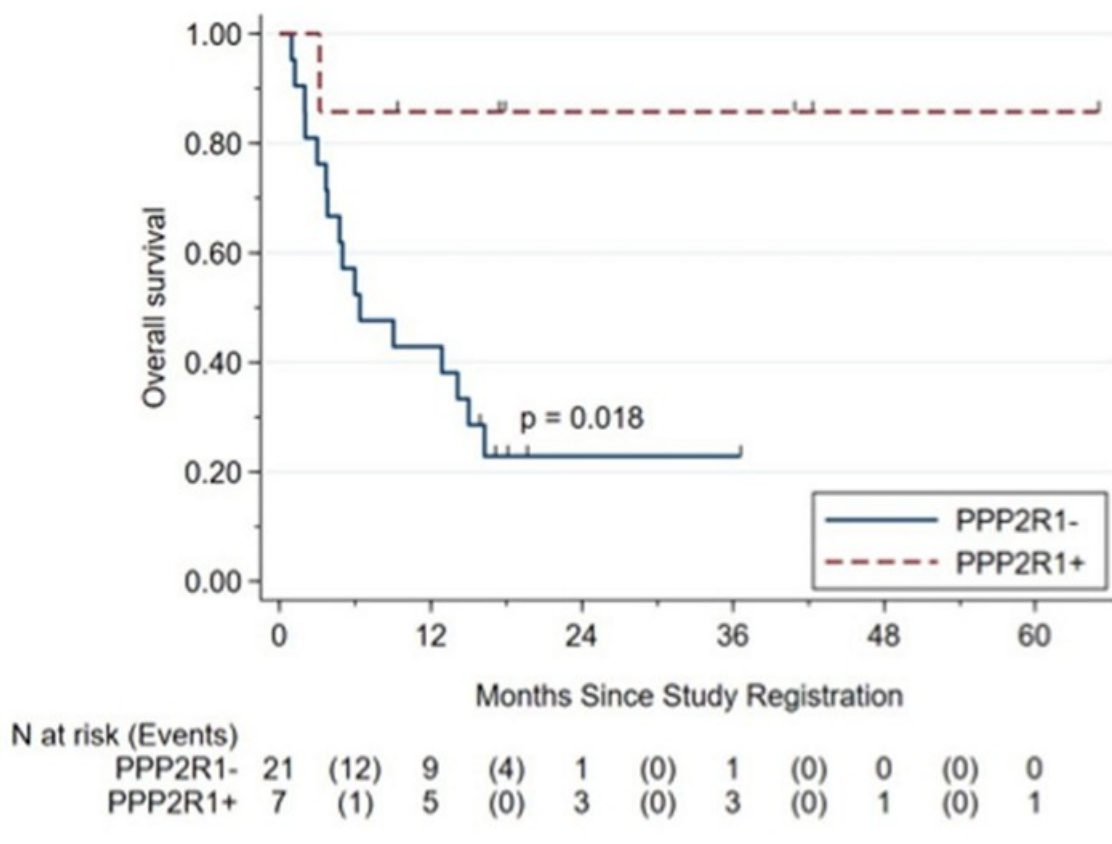
LB-100, a small molecule potent inhibitor of PP2A, was designed and developed by us. Numerous preclinical studies have documented that LB-100 potentiates most if not all anti-cancer drugs that damage DNA. LB-100 is not associated with any increase in cytotoxicity when given with cytotoxic drugs. This 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/m<sup>2</sup> 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
<b>LB-100 + Immunotherapy</b>	Ovarian Clear Cell Cancer	NCT06065462				Actively Recruiting at MD Anderson And Northwestern. GSK sponsored
<b>LB-100 + Immunotherapy</b>	Metastatic MSI Low Colon Cancer	NCT06012734				Open at Netherlands Cancer Institute Roche sponsored.
<b>LB-100 + Chemotherapy</b>	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 patients 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 regimen 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

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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 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 at “Item 7. Management’s Discussion and Analysis of Financial Condition and Results of Operations – Specific Risks Associated with the Company’s Business Activities – Serious Adverse Events”.

#### 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.

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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.

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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.

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## **Nasdaq Compliance**

On August 23, 2024, we announced via Current Report on Form 8-K that we received a letter from the Listing Qualifications Department (the “Staff”) of the Nasdaq

Stock Market LLC (“Nasdaq”) on August 19, 2024 indicating that we were not in compliance with the minimum stockholders’ equity requirement of \$2,500,000 for continued listing on the Nasdaq Capital Market under Listing Rule 5550(b) (the “Stockholders’ Equity Requirement”).

On October 3, 2024, we submitted a plan to the Staff to regain compliance with the Stockholders’ Equity Requirement, which outlined our proposed initiatives to regain compliance by raising equity capital through various registered equity offerings.

On October 21, 2024, the Staff provided notice (the “Notice”) to us that it had granted an extension through February 18, 2025 to regain compliance with the Stockholders’ Equity Requirement, which required that we complete our capital raising initiatives and evidence compliance with the Stockholders’ Equity Requirement through filing a Current Report on Form 8-K with the Securities and Exchange Commission providing certain required information.

As of February 18, 2025, we had not regained compliance with the Stockholders’ Equity Requirement. Accordingly, on February 19, 2025, we received a Staff determination letter from the Staff stating that we did not meet the terms of the extension because we did not complete our proposed financing initiatives to regain compliance.

We timely requested a Hearing before a Nasdaq Hearings Panel (the “Panel”), which automatically stayed Nasdaq’s suspension or delisting of our common shares and warrants pending the Panel’s decision. Pursuant to the Nasdaq Listing Rules, the Panel has the discretion to grant us an additional extension through no later than August 18, 2025. However, there can be no assurances that the Hearings Panel will grant us an extension of time to regain compliance, or that we will be able to regain compliance during an extension period. During the hearings process our common shares and warrants will continue to trade on The Nasdaq Capital Market.

We intend to take reasonable measures available to regain compliance under Nasdaq’s listing rules and to remain listed on Nasdaq. However, there can be no assurances that we will ultimately regain compliance with the Stockholders’ Equity Rule, or be able to maintain compliance with all other applicable requirements for continued listing on Nasdaq. Our failure to meet these requirements may result in our securities being delisted from Nasdaq.

## **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 our Board of Directors. Our common stock and Common Warrants are traded on Nasdaq under the symbols “LIXT” and “LIXTW”, respectively. 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 Nasdaq.

Our principal address is 680 East Colorado Boulevard, Suite 180, Pasadena, CA 91101. 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.

## **July 2023 Financing**

On July 20, 2023, we sold 583,334 shares of common stock at a price of \$6.00 per share to an institutional investor and raised gross proceeds of approximately \$3,500,000. As part of this financing, we sold warrants to the institutional investor to purchase 583,334 shares of common stock (the “2023 Warrants”). The 2023 Warrants had an initial exercise price of \$6.00 per share, were immediately exercisable upon issuance, and expire five years thereafter on July 20, 2028. We also issued warrants to the placement agent to purchase 35,000 shares of common stock at an exercise price of \$6.60 per share and expiring on July 20, 2028 (the “2023 Placement Agent Warrants”).

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The exercise prices of the warrants issued to the institutional investor and to the placement agent are subject to customary adjustments for stock splits, stock dividends, stock combinations, reclassifications, reorganizations, or similar events affecting our common stock. In addition, the warrants issued to the institutional investor contain a “fundamental transaction” provision whereby in the event of a fundamental transaction (including a sale or transfer of assets or ownership of the Company as defined in the warrant agreement) within our control, the holder of the unexercised common stock warrants would be entitled to receive, in exchange for extinguishment of the warrants, cash consideration equal to a Black-Scholes valuation, as defined in the warrant agreement. If such fundamental transaction is not within our control, the warrant holder would only be entitled to receive the same form of consideration (and in the same proportion) as the holders of our common stock.

Accordingly, in the event of a change in control of the Company or a sale or transfer of all or substantially all of our assets, as defined in the 2023 Warrants, to the extent that the warrants issued to the institutional investor are outstanding at the effective date that such a transaction is closed, this “fundamental transaction” provision would entitle the holder to substantial cash consideration, thus reducing the amounts to be retained by us or potentially distributable to our stockholders.

## **February 2025 Financing**

On February 11, 2025, we entered into a Securities Purchase Agreement (the “Purchase Agreement”) with two institutional investors (the “Selling Stockholders”). Pursuant to the Purchase Agreement, on February 13, 2025, we sold 434,784 shares of common stock at a price of \$2.415 per share and raised gross proceeds of approximately \$1,050,000. As part of this financing, we sold warrants to the institutional investors to purchase 434,784 shares of common stock (the “2025 Warrants”). Such Warrants had an initial exercise price of \$2.29 per share, were immediately exercisable upon issuance, and expire five years thereafter on February 13, 2030. We also issued warrants to the placement agent to purchase 32,609 shares of common stock at an exercise price of \$3.0188 per share and expiring on February 13, 2030 (the “2025 Placement Agent Warrants”).

The exercise prices of the warrants issued to the institutional investors and to the placement agent are subject to customary adjustments for stock splits, stock dividends, stock combinations, reclassifications, reorganizations, or similar events affecting our common stock. In addition, the warrants issued to the institutional investors contain a “fundamental transaction” provision whereby in the event of a fundamental transaction (including a sale or transfer of assets or ownership of the Company as defined in the warrant agreement) within our control, the holders of the unexercised common stock warrants would be entitled to receive, in exchange for extinguishment of the warrants, cash consideration equal to a Black-Scholes valuation, as defined in the warrant agreement. If such fundamental transaction is not within our control, the warrant holders would only be entitled to receive the same form of consideration (and in the same proportion) as the holders of our common stock.

Accordingly, in the event of a change in control of the Company or a sale or transfer of all or substantially all of our assets, as defined in the 2025 Warrants, to the extent that the warrants issued to the institutional investors are outstanding at the effective date that such a transaction is closed, this “fundamental transaction” provision would entitle the holders to substantial cash consideration, thus reducing the amounts to be retained by us or potentially distributable to our stockholders.

Pursuant to the Purchase Agreement, we agreed to file a registration statement on Form S-1 for the resale by the selling stockholders of the shares of common stock issuable upon exercise of the 2025 Warrants and the 2025 Placement Agent Warrants.

We are filing the registration statement of which this prospectus forms a part to satisfy our obligations under the Purchase Agreement.

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## THE OFFERING

<i>Issuer:</i>	Lixte Biotechnology Holdings, Inc.
<i>Number of shares of common stock being offered by Selling Stockholders:</i>	Up to 467,393 shares of common stock.
<i>Number of shares of common stock outstanding immediately prior to this offering:</i>	2,684,074 shares of common stock.
<i>Number of shares of common stock to be outstanding immediately after this offering:</i>	Up to 3,151,467 shares <sup>(1)</sup>
<i>Use of proceeds:</i>	We will not receive any of the proceeds from the sale of shares of our common stock being offered for sale by the Selling Stockholders. However, upon any cash exercise of the 2025 Warrants and the 2025 Placement Agent Warrants, we will receive gross proceeds of up to \$1,094,095.
<i>Nasdaq trading symbol:</i>	Our common stock currently trades on Nasdaq under the symbol “LIXT”.
<i>Transfer agent and registrar:</i>	The transfer agent and registrar for our common stock is Computershare Trust Company, N.A.
<i>Risk factors:</i>	The securities offered by this prospectus are speculative and involve a high degree of risk. Investors purchasing securities should not purchase the securities unless they can afford the loss of their entire investment. See “Risk Factors” beginning on page 13.

(1) Immediately after this offering, the Company will have 3,151,467 shares of common stock outstanding assuming exercise of the 2025 Warrants and the 2025 Placement Agent Warrants as set forth above and will exclude:

- 72,917 shares of our common stock issuable upon the conversion of 350,000 shares of Series A Convertible Preferred Stock outstanding at a conversion rate of 0.2083 common shares per preferred share, reflecting a conversion price of \$48.00 per common share;
- 662,078 shares of common stock issuable upon the exercise of common stock options issued to members of management, consultants, and directors at a weighted average exercise price of \$11.526 per share;
- 808,365 shares of common stock issuable upon exercise of outstanding common stock warrants at an average exercise price of \$16.4074 per common share, including 137,700 shares of common stock issuable upon exercise of 137,700 publicly traded warrants at \$57.00 per common share through November 30, 2025; and
- 133,339 shares of common stock reserved for future grants pursuant to our 2020 Stock Incentive Plan, as amended (the “2020 Plan”).

## RISK FACTORS

*Investing in our common stock is highly speculative and involves a significant degree of risk. You should carefully consider the following risks and uncertainties as well as the risks and uncertainties described in the section entitled “Risk Factors” contained in our Annual Report on Form 10-K for the fiscal year ended December 31, 2024, filed with the Securities and Exchange Commission, which filings are incorporated in this prospectus by reference in their entirety, as well as in any prospectus supplement hereto. These risk factors could materially and adversely affect our business, results of operations or financial condition. Our business faces significant risks and the risks described below or incorporated by reference herein may not be the only risks we face. Additional risks not presently known to us or that we currently believe are immaterial may materially affect our business, results of operations, or financial condition. If any of these risks occur, the trading price of our common stock could decline and you may lose all or part of your investment.*

### 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 assurance 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 is preparing 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 February 2025, a total of 78 patient have received or are receiving experimental treatment with LB-100. It is expected that it will take at least two months to prepare a detailed response to the IRB, during which time the Company intends to update the safety overview of LB-100.

### **Risks Related to this Offering and Ownership of our Securities**

***We have a history of losses, expect to continue to incur losses in the near term and may not achieve or sustain profitability in the future, and as a result, our management has identified, and our auditors agreed that there is a substantial doubt about our ability to continue as a going concern.***

We have incurred significant losses since our inception. We experienced net losses of \$3,585,965 and \$5,087,029 for the years ended December 31, 2024 and 2023, respectively. We expect our operating losses will continue, or even increase, at least through the near term. You should not rely upon our past results as indicative of future performance. We will not reach profitability in the near future or at any specific time in the future.

The report of our independent registered public accounting firm that accompanies our audited consolidated financial statements in our Annual Report on Form 10-K for the fiscal year ended December 31, 2024 contains an explanatory paragraph regarding substantial doubt about our ability to continue as a going concern. Our consolidated financial statements do not include any adjustments that might result if we are unable to continue as a going concern. If we are unable to continue as a going concern, holders of our securities might lose their entire investment.

***We are currently not in compliance with the Nasdaq continued listing requirements. If we are unable to regain compliance with Nasdaq's listing requirements, our securities could be delisted, which could affect our common stock's market price and liquidity and reduce our ability to raise capital.***

On August 23, 2024, we announced via Current Report on Form 8-K that we received a letter from the Listing Qualifications Department (the "Staff") of the Nasdaq Stock Market LLC ("Nasdaq") on August 19, 2024 indicating that we were not in compliance with the minimum stockholders' equity requirement of \$2,500,000 for continued listing on the Nasdaq Capital Market under Listing Rule 5550(b) (the "Stockholders' Equity Requirement").

On October 3, 2024, we submitted a plan to the Staff to regain compliance with the Stockholders' Equity Requirement, which outlined our proposed initiatives to regain compliance by raising equity capital through various registered equity offerings.

On October 21, 2024, the Staff provided notice (the "Notice") to us that it had granted an extension through February 18, 2025 to regain compliance with the Stockholders' Equity Requirement, which required that we complete our capital raising initiatives and evidence compliance with the Stockholders' Equity Requirement through filing a Current Report on Form 8-K with the Securities and Exchange Commission providing certain required information.

As of February 18, 2025, we had not regained compliance with the Stockholders' Equity Requirement. Accordingly, on February 19, 2025, we received a Staff determination letter from the Staff stating that we did not meet the terms of the extension because we did not complete our proposed financing initiatives to regain compliance.

We timely requested a Hearing before a Nasdaq Hearings Panel (the "Panel"), which automatically stayed Nasdaq's suspension or delisting of our common shares and warrants pending the Panel's decision. Pursuant to the Nasdaq Listing Rules, the Panel has the discretion to grant us an additional extension through no later than August 18, 2025. However, there can be no assurances that the Hearings Panel will grant us an extension of time to regain compliance, or that we will be able to regain compliance during an extension period. During the hearings process our common shares and warrants will continue to trade on The Nasdaq Capital Market.

We intend to take reasonable measures available to regain compliance under Nasdaq's listing rules and to remain listed on Nasdaq. However, there can be no assurances that we will ultimately regain compliance with the Stockholders' Equity Rule, or be able to maintain compliance with all other applicable requirements for continued listing on Nasdaq. Our failure to meet these requirements may result in our securities being delisted from Nasdaq.

We cannot assure you that we will be able to regain compliance with Nasdaq listing standards. Our failure to continue to meet these requirements would result in our common stock being delisted from Nasdaq, and if our common stock is delisted, the warrants issued in our public offering would also be delisted. We and holders of our securities could be materially adversely impacted if our securities are delisted from Nasdaq. In particular:

- we may be unable to raise equity capital on acceptable terms or at all;
- we may lose the confidence of our clinical partners, which would jeopardize our ability to continue our clinical trials as currently conducted;
- the price of our common stock will likely decrease as a result of the loss of market efficiencies associated with Nasdaq and the loss of federal pre-emption of state securities laws;
- holders may be unable to sell or purchase our securities when they wish to do so;
- we may become subject to stockholder litigation;
- we may be unable to attract, or we may lose the interest of, institutional investors in our common stock;
- we may lose media and analyst coverage;
- our common stock could be considered a "penny stock", which would likely limit the level of trading activity in the secondary market for our common stock; and
- we would likely lose any active trading market for our common stock, as it may only be traded on one of the over-the-counter markets, if at all.

***We will have to seek to raise additional funds to fund our operations, including the various clinical trials being currently conducted or will be conducted in the future. Depending on the terms available to us, if these fund raising activities result in significant dilution, they may negatively impact the trading price of our common stock.***

Any additional financing that we secure may require the granting of rights, preferences or privileges senior to, *opari passu* with, those of our common stock. Any issuances by us of equity securities may be at or below the prevailing market price of our common stock and in any event may have a dilutive impact on your ownership interest, which could cause the market price of our common stock to decline. We may also raise additional funds through the incurrence of debt or the issuance or sale of other securities or instruments senior to our shares of common stock, which may be highly dilutive. The holders of any securities or instruments we may issue may have rights superior to the rights of our common stockholders. If we experience dilution from the issuance of additional securities and we grant superior rights to new securities over holders of our common stock, it may negatively impact the trading price of our common stock and you may lose all or part of your investment.

***As part of the Company's ongoing process of evaluating various alternatives to obtain the capital required to fund its operations and maintain its listing on Nasdaq, management may decide to consider a wide variety of strategic alternatives, and there can be no assurances that any such transaction, if implemented, would enhance stockholder value, and could be highly dilutive to existing stockholders.***

The Company is evaluating various alternatives to obtain the capital required to fund its operations and maintain its listing on Nasdaq, including merger or acquisition opportunities (including reverse mergers) and funding transactions involving a change in control. There can be no assurances that the evaluation process will result in the

identification of an appropriate transaction, the negotiation and execution of a definitive agreement to effect such a transaction, or that any such transaction will ultimately be approved by the Company's stockholders and then be consummated. Depending on various factors, many of which are outside the control of the Company, our failure to enter into and consummate a strategic transaction could have a material adverse effect on our ability to continue to operate and finance our business, and on the market price of our common stock. Even if such a strategic transaction is consummated, there can be no assurances that it will enhance stockholder value, and it may result in substantial dilution to existing stockholders. Any potential transaction would be dependent on a number of factors that may be outside of our control, including, among other things, market conditions, industry trends, the interest of third parties in a potential transaction with the Company, and the availability of appropriate financing for such a transaction. If we are unable to raise the required capital to fund our operations, or to enter into a strategic transaction in the near future, we may not be able to maintain our listing on Nasdaq, and we may need to curtail or cease operations, which could result in a total loss of stockholders' investment.

***The price of our common stock or warrants might fluctuate substantially.***

You should consider an investment in our common stock and warrants to be risky. Some factors that might cause the market price of our common stock or warrants 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.

***Provisions of the Warrants issued in the 2023 Financing and 2025 Financing could discourage an acquisition of us by a third party.***

Certain provisions of the 2023 Warrants and 2025 Warrants could make it more difficult or expensive for a third party to acquire us. Such Warrants prohibit us from

engaging in certain transactions constituting “fundamental transactions” unless, among other things, the surviving entity assumes our obligations under such Warrants. These and other provisions of the Common Warrants offered by this prospectus could prevent or deter a third party from acquiring us even where the acquisition could be beneficial to you. Also, we may be required to redeem these Warrants for a cash payment calculated pursuant to the Black-Scholes option-pricing model.

***An active, liquid and orderly trading market for our common stock may not develop, the price of our stock may be volatile, and you could lose all or part of your investment.***

Even though our common stock is currently listed on Nasdaq, we cannot predict the extent to which investor interest in our Company will lead to the development of an active trading market in our securities or how liquid that market might become. If such a market does not develop or is not sustained, it may be difficult for you to sell your shares of common stock at the time you wish to sell them, at a price that is attractive to you, or at all. There could be extreme fluctuations in the price of our common stock if there are a limited number of shares in our public float.

The trading price of our common stock may be highly volatile and could be subject to wide fluctuations in response to various factors, some of which are beyond our control. Our stock price could be subject to wide fluctuations in response to a variety of factors, which include:

- whether we achieve our anticipated corporate objectives;
- actual or anticipated fluctuations in our quarterly or annual operating results;
- changes in our financial or operational estimates;
- our ability to implement our operational plans;
- changes in the economic performance or market valuations of companies similar to ours; and
- general economic or political conditions in the United States or elsewhere.

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In addition, broad market and industry factors may seriously affect the market price of companies’ stock, including ours, regardless of actual operating performance. In the past, following periods of volatility in the overall market and the market price of a particular company’s securities, securities class action litigation has often been instituted against these companies. This litigation, if instituted against us, could result in substantial costs and a diversion of our management’s attention and resources.

***Our outstanding Warrants may cause the trading price of our common stock to decrease.***

Depending on the price of our common stock, the number of shares of common stock issuable pursuant to the exercise of the Warrants issued in the 2023 Financing and 2025 Financing, could result in an immediate decrease in the trading price of our common stock. If the bid price of our common stock falls below \$1.00 per share for 30 consecutive business days, we would no longer meet Nasdaq’s minimum bid price requirement and our common stock would be subject to delisting. We cannot predict the effect, if any, that the availability of shares for future sale represented by such Warrants will have on the trading price of our common stock from time to time.

***If our shares of common stock become subject to the penny stock rules, it would become more difficult to trade our shares.***

The Securities and Exchange Commission has adopted rules that regulate broker-dealer practices in connection with transactions in penny stocks. Penny stocks are generally equity securities with a price of less than \$5.00, other than securities registered on certain national securities exchanges or authorized for quotation on certain automated quotation systems, provided that current price and volume information with respect to transactions in such securities is provided by the exchange or system. If we do not retain a listing on Nasdaq and if the price of our common stock is less than \$5.00, our common stock will be deemed a penny stock. The penny stock rules require a broker-dealer, before a transaction in a penny stock not otherwise exempt from those rules, to deliver a standardized risk disclosure document containing specified information. In addition, the penny stock rules require that before effecting any transaction in a penny stock not otherwise exempt from those rules, a broker-dealer must make a special written determination that the penny stock is a suitable investment for the purchaser and receive (i) the purchaser’s written acknowledgment of the receipt of a risk disclosure statement; (ii) a written agreement to transactions involving penny stocks; and (iii) a signed and dated copy of a written suitability statement. These disclosure requirements may have the effect of reducing the trading activity in the secondary market for our common stock, and therefore stockholders may have difficulty selling their shares.

***If we were to dissolve, the holders of our securities may lose all or substantial amounts of their investments.***

If we were to dissolve as a corporation, as part of ceasing to do business or otherwise, we will be required to pay all amounts owed to any creditors before distributing any assets to holders of our capital stock. There is a risk that in the event of such a dissolution, there will be insufficient funds to repay amounts owed to holders of any of our indebtedness and insufficient assets to distribute to our capital stockholders, in which case investors could lose their entire investment.

***If securities or industry analysts do not publish or cease publishing research or reports about us, our business or our market, or if they change their recommendations regarding our securities adversely, our stock price and trading volume could decline.***

The trading market for our common stock is influenced by the research and reports that industry or securities analysts may publish about us, our business, our market or our competitors. If any of the analysts who may cover us change their recommendation regarding our common stock adversely, or provide more favorable relative recommendations about our competitors, our stock price would likely decline. If any of the analysts who may cover us were to cease coverage of our Company or fail to regularly publish reports on us, we could lose visibility in the financial markets, which in turn could cause our stock price or trading volume to decline.

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***In making your investment decision, you should understand that neither we nor the Selling Stockholders have authorized any other party to provide you with information concerning us or this offering.***

You should carefully evaluate all of the information in this prospectus before investing in our company. We may receive media coverage regarding our company, including coverage that is not directly attributable to statements made by our officers, that incorrectly reports on statements made by our officers or employees, or that is misleading as a result of omitting information provided by us, our officers or employees. We and the placement agent have not authorized any other party to provide you with information concerning us or this offering, and you should not rely on unauthorized information in making an investment decision.

#### **CAUTIONARY NOTE REGARDING FORWARD-LOOKING STATEMENTS**

This prospectus, and the documents incorporated by reference herein may 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 facts contained in this prospectus, including statements regarding our future results of operations and financial position, business strategy and plans and our objectives for future operations, are forward-looking statements. The words “anticipate”, “believe”, “could”, “estimate”, “expect”, “forecast”, “intend”, “may”, “plan”, “potential”, “should”, “will”, “would”, “might”, and similar expressions are intended to identify forward-looking statements. These forward-looking statements are subject to certain risks and uncertainties that could cause actual results to differ materially from historical results or anticipated results, including:

- 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 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;
- 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; and
- 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 caution you that the foregoing list may not contain all of the forward-looking statements made in this prospectus. We have based these forward-looking statements largely on our current expectations about future events and financial trends that we believe may affect our financial condition, results of operations, business strategy, short term and long-term business operations and objectives, and financial needs. These forward-looking statements are subject to a number of risks, uncertainties and assumptions, including those described in “Risk Factors”. Moreover, we operate in a very competitive and rapidly changing environment. New risks emerge from time to time. It is not possible for our management to predict all risks, nor can we assess the impact of all factors on our business or the extent to which any factor, or combination of factors, may cause actual results to differ materially from those contained in any forward-looking statements we may make. In light of these risks, uncertainties and assumptions, the forward-looking events and circumstances discussed in this prospectus may not occur and actual results could differ materially and adversely from those anticipated or implied in the forward-looking statements.

You should not rely upon forward-looking statements as predictions of future events. Although we believe that the expectations reflected in the forward-looking statements are reasonable, we cannot guarantee that the future results, levels of activity, performance or events and circumstances reflected in the forward-looking statements will be achieved or occur. We undertake no obligation to update publicly any forward-looking statements for any reason after the date of this prospectus to conform these statements to actual results or to changes in our expectations.

You should read this prospectus and the documents that we reference in this prospectus and have filed with the Securities and Exchange Commission as exhibits to the registration statement of which this prospectus is a part with the understanding that our actual future results, levels of activity, performance and events and circumstances may be materially different from what we expect.

## USE OF PROCEEDS

We will not receive any of the proceeds from any sale or other disposition of the common stock covered by this prospectus. All proceeds from the sale of the common stock will be paid directly to the selling stockholders. However, we will receive proceeds upon the cash exercise of the 2025 Warrants and the 2025 Placement Agent Warrants. Assuming full cash exercise of the 2025 Warrants and the 2025 Placement Agent Warrants, we would receive approximately \$1,094,095. We currently intend to use any cash proceeds from a Warrant exercise for working capital and continuing operating expenses, including, without limitation, for further clinical development of our lead compound LB-100.

## CAPITALIZATION

The following table sets forth our capitalization as of December 31, 2024 as follows:

- on an actual basis; and
- on an as adjusted basis, to reflect (i) the issuance of 434,784 common shares included in the sale of 434,784 units on February 11, 2025, (ii) the issuance of 434,784 common shares issuable upon exercise of the warrants included in the sale of 434,784 units on February 11, 2025, at an exercise price of \$2.29 per share; and (iii) the issuance of 32,609 common shares issuable upon exercise of the warrants issued to the placement agent in the sale of 434,784 units on February 11, 2025.

	As of December 31, 2024	
	Actual	As Adjusted
Cash	\$ 1,038,952	\$ 2,928,800
Stockholders' equity:		
Preferred stock, \$0.0001 par value per share, 10,000,000 shares authorized, issued and outstanding 350,000 shares	\$ 3,500,000	\$ 3,500,000
Common stock, \$0.0001 par value per share; 100,000,000 shares authorized, 2,249,290 issued and outstanding		
shares actual, and 3,151,467 shares, on an as adjusted basis	225	315
Additional paid-in capital	49,394,687	51,284,445
Accumulated deficit	(52,067,693)	(52,068,693)
Total stockholders' equity	827,219	2,717,067
Total capitalization	\$ 827,219	\$ 2,717,067

As of March 31, 2025, the Company will have 3,151,467 shares of common stock outstanding assuming exercise of the 434,784 warrants and the 32,609 warrants as set forth in the table above and will exclude:

- 72,917 shares of our common stock issuable upon the conversion of 350,000 shares of Series A Convertible Preferred Stock outstanding at a conversion rate of 0.2083 common shares per preferred share, reflecting a conversion price of \$48.00 per common share;
- 662,078 shares of common stock issuable upon the exercise of common stock options issued to members of management, consultants, and directors at a weighted average exercise price of \$11.526 per share;
- 808,365 shares of common stock issuable upon exercise of outstanding common stock warrants at an average exercise price of \$16.4074 per common share, including 137,700 shares of common stock issuable upon exercise of 137,700 publicly traded warrants at \$57.00 per common share through November 30, 2025; and
- 133,339 shares of common stock reserved for future grants pursuant to our 2020 Stock Incentive Plan, as amended (the “2020 Plan”).

### SELECTED HISTORICAL FINANCIAL DATA

#### Consolidated Statements of Operations Data

	Years Ended December 31,	
	2024	2023
Revenues	\$ —	\$ —
Costs and expenses:		
Research and development costs	726,232	898,100
General and administrative costs	2,846,557	4,192,136
Total costs and expenses	3,572,789	5,090,236
Loss from operations	(3,572,789)	(5,090,236)
Interest income	7,048	17,486
Interest expense	(16,821)	(16,233)
Foreign currency gain (loss)	(3,403)	1,954
Net loss	\$ (3,585,965)	\$ (5,087,029)
Net loss per common share – basic and diluted	\$ (1.59)	\$ (2.66)
Weighted average common shares outstanding – basic and diluted	2,249,290	1,915,838

#### Consolidated Balance Sheet Data

	December 31,	
	2024	2023
Total current assets	\$ 1,145,503	\$ 4,308,620
Total assets	\$ 1,145,503	\$ 4,308,620
Total current liabilities	\$ 318,824	\$ 313,858
Total liabilities	\$ 318,824	\$ 313,858
Stockholders' equity:		
Preferred Stock, \$0.0001 par value; authorized – 10,000,000 shares; issued and outstanding – 350,000 shares of Series A Convertible Preferred Stock, \$10.00 per share stated value, liquidation preference based on assumed conversion into common shares – 72,917 shares	\$ 3,500,000	\$ 3,500,000
Common stock, \$0.0001 par value; authorized – 100,000,000 shares; issued and outstanding – 2,249,290 shares at December 31, 2024 and 2023, respectively	225	225
Additional paid-in capital	49,394,687	48,976,265
Accumulated deficit	(52,067,693)	(48,481,728)
Total stockholders' equity	\$ 827,219	\$ 3,994,762

### DESCRIPTION OF SECURITIES

#### General

Our certificate of incorporation, as amended, authorizes the issuance of up to 100,000,000 shares of common stock, par value \$0.0001 per share, and up to 10,000,000 shares of preferred stock, par value \$0.0001 per share. As of March 31, 2025, there were 2,684,074 shares of common stock outstanding, which were held by 46 stockholders of record, and 350,000 shares of Series A Convertible Preferred Stock outstanding convertible into 72,917 shares of common stock.

On June 2, 2023, we effected a reverse stock split of our common stock at a ratio of 1-for-10. All share and per share information presented in this prospectus reflects the effect of the reverse stock split.

#### Common Stock

Each holder of common stock is entitled to one vote for each share of common stock held on all matters submitted to a vote of the stockholders, including the election of directors. Our certificate of incorporation, as amended and bylaws do not provide for cumulative voting rights.

Subject to preferences that may be applicable to any then outstanding preferred stock, the holders of our outstanding shares of common stock are entitled to receive

dividends, if any, as may be declared from time to time by our Board of Directors out of legally available funds. In the event of our liquidation, dissolution or winding up, holders of common stock will be entitled to share ratably in the net assets legally available for distribution to stockholders after the payment of all of our debts and other liabilities, subject to the satisfaction of any liquidation preference granted to the holders of any outstanding shares of preferred stock.

Holders of our common stock have no pre-emptive, conversion or subscription rights, and there are no redemption or sinking fund provisions applicable to the common stock. The rights, preferences and privileges of the holders of common stock are subject to, and may be adversely affected by, the rights of the holders of shares of any series of our preferred stock that are outstanding or that we may designate and issue in the future.

## **Preferred Stock**

Our Board of Directors is authorized, without vote or action by our stockholders, to issue from time to time up to an aggregate of 10,000,000 shares of preferred stock in one or more series and to fix or alter the designations, preferences, rights and any qualifications, limitations or restrictions of the shares of each of these series, including, if applicable, the dividend rights and preferences, conversion rights, voting rights, terms and rights of redemption, including without limitation sinking fund provisions, redemption price or prices, liquidation rights and preferences, and the number of shares constituting any series. The issuance of preferred stock may have the effect of delaying, deferring or preventing a change in control of us without further action by our stockholders and may adversely affect the dividend, liquidation and voting and other rights of the holders of common stock. The issuance of preferred stock with voting and conversion rights may adversely affect the voting power of the holders of common stock, including the loss of voting control to others. We currently have no plans to issue any additional shares of preferred stock.

We believe that the ability to issue preferred stock without the expense and delay of a special stockholders' meeting provides us with increased flexibility in structuring possible future financings and acquisitions, and in meeting other corporate needs that might arise. This also permits the Board of Directors of the Company to issue preferred stock containing terms which could impede the completion of a takeover attempt. This could discourage an acquisition attempt or other transaction which stockholders might believe to be in their best interests or in which they might receive a premium for their stock over the then market price of the stock.

## **Warrants**

In connection with the 2023 Financing and 2025 Financing, we issued warrants to purchase a total of 1,085,727 shares to the investors and placement agents, including Warrants to purchase 583,334 shares of common stock exercisable at \$6.00 per share to the investor in the 2023 Financing and Warrants to purchase 434,784 shares of common stock exercisable at \$2.29 per share to the investors in the 2025 Financing.

The exercise prices of the Warrants are subject to customary adjustments for stock splits, stock dividends, stock combinations, reclassifications, reorganizations, or similar events affecting our common stock. In addition, the Warrants contain a "fundamental transaction" provision which provides that if any defined fundamental transactions are within our control and are consummated, the holder of the unexercised common stock Warrants would be entitled to receive, at its option, in exchange for extinguishment of such Warrants, cash consideration equal to a Black-Scholes valuation amount, as defined in the Warrant agreement. The fundamental transaction provision includes (i) a sale, lease, assignment, transfer, conveyance or other disposition of all or substantially all of assets in one or a series of related transactions, or (ii) a change in control of the Company by which it, directly or indirectly, in one or more related transactions, consummates a stock or share purchase agreement or other business combination with another person or group, whereby such other person or group acquires more than 50% of the voting power of our common equity.

If such fundamental transaction is not within our control, including not being approved by our Board of Directors, the Warrant holder would only be entitled to receive the same type or form of consideration (and in the same proportion) equal to the Black-Scholes valuation amount of the remaining unexercised portion of the Warrant on the date of consummation of such fundamental transaction as the holders of our common stock receive. Accordingly, these Warrants are classified as a component of permanent stockholders' equity. We will account for any cash payment for a Warrant redemption as a distribution from stockholders' equity, as and when a fundamental transaction is consummated and such cash payment is required to be made.

## **Anti-Takeover Effects of Certain Provisions in our Certificate and Bylaws**

### ***Exclusive Forum***

The certificate of incorporation provides that, unless we consent to the selection of an alternative forum, the Court of Chancery of the State of Delaware shall be the sole and exclusive forum for (i) any derivative action or proceeding brought on our behalf, (ii) any action asserting a claim of breach of fiduciary duty owed by any of our directors, officers, or other employee to us or to our stockholders, (iii) any action asserting a claim against us arising pursuant to any provision of the Delaware General Corporation Law, the certificate of incorporation or the bylaws or (iv) any action asserting a claim governed by the internal affairs doctrine. However, this provision does not apply to suits brought to enforce a duty or liability created by the Exchange Act. In addition, the Court of Chancery of the State of Delaware and the federal district courts will have concurrent jurisdiction for the resolution of any suit brought to enforce any duty or liability created by the Securities Act. Notwithstanding the foregoing, the inclusion of such provisions in the certificate of incorporation will not be deemed to be a waiver by us or our stockholders of the obligation to comply with federal securities laws, rules and regulations.

Although we believe these provisions benefit the Company by providing increased consistency in the application of Delaware law in the types of lawsuits to which it applies, these provisions may have the effect of discouraging lawsuits against the Company's directors and officers. Furthermore, the enforceability of choice of forum provisions in other companies' certificates of incorporation has been challenged in legal proceedings, and it is possible that a court could find these types of provisions to be inapplicable or unenforceable.

### ***Advance Notice of Stockholder Proposals and Nominations***

Our bylaws include an advance notice procedure for stockholders to nominate candidates for election as directors or to bring other business before any meeting of our stockholders. The stockholder notice procedure provides that only persons who are nominated by, or at the direction of, the Board of Directors, or by a stockholder who has given timely written notice prior to the meeting at which directors are to be elected, will be eligible for election as directors and that, at a stockholders' meeting, only such business may be conducted as has been brought before the meeting by, or at the direction of, the Board of Directors or by a stockholder who has given timely written notice of such stockholder's intention to bring such business before such meeting.

Under the stockholder notice procedure, for notice of stockholder nominations or other business to be made at a stockholders' meeting to be timely, such notice must be received by us not earlier than the close of business on the 120th calendar day and not later than the close of business on the 90th calendar day prior to the one-year anniversary of the immediately preceding year's annual meeting or as otherwise provided in the bylaws.

A stockholder's notice to us proposing to nominate a person for election as a director or proposing other business must contain certain information specified in the bylaws, including the identity and address of the nominating stockholder, a representation that the stockholder is a record holder of our stock entitled to vote at the meeting and information regarding each proposed nominee or each proposed matter of business that would be required under the federal securities laws to be included in a proxy statement soliciting proxies for the proposed nominee or the proposed matter of business.



The stockholder notice procedure may have the effect of precluding a contest for the election of directors or the consideration of stockholder proposals if the proper procedures are not followed, and of discouraging or deterring a third party from conducting a solicitation of proxies to elect its own slate of directors or to approve its own proposal, without regard to whether consideration of such nominees or proposals might be harmful or beneficial to us and our stockholder.

#### ***Restrictions on Call of Special Meetings***

Our bylaws provide that special meetings of stockholders can only be called by the Board of Directors, Chief Executive Officer or President (in the absence of a Chief Executive Officer), but not by our stockholders or any other person or persons.

#### ***No Cumulative Voting***

The certificate of incorporation does not authorize cumulative voting for the election of directors.

#### ***Preferred Stock Authorization***

Our Board of Directors, without stockholder approval, has the authority under our certificate of incorporation to issue preferred stock with rights superior to the rights of the holders of common stock. As a result, preferred stock, while not intended as a defensive measure against takeovers, could be issued quickly and easily, could adversely affect the rights of holders of common stock and could be issued with terms calculated to delay or prevent a change of control of the Company or make removal of management more difficult.

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#### **Selling Stockholders**

The common stock being offered by the selling stockholders are those issuable to the selling stockholder upon exercise of the 2025 Warrants and the 2025 Placement Agent Warrants. For additional information regarding the issuance of the 2025 Warrants and the 2025 Placement Agent Warrants, see “2025 Financing” above. We are registering the shares of common stock in order to permit the selling stockholders to offer the shares for resale from time to time. Except for the beneficial ownership of securities of the Company, including the 2025 Warrants and the 2025 Placement Agent Warrants, neither the selling stockholders nor any persons who have control over the selling stockholders has had any material relationship with us within the past three years.

The table below lists the selling stockholders and other information regarding the beneficial ownership (as determined under Section 13(d) of the Exchange Act) of the shares of Common Stock by the selling stockholders. The second column lists the number of shares of Common Stock beneficially owned by the selling stockholders, based on their ownership of the shares of Common Stock, options to purchase Common Stock, and warrants to purchase Common Stock, as of March 31, 2025, assuming exercise in full of the 2025 Warrants and the 2025 Placement Agent Warrants held by the selling stockholders on that date, without regard to any limitations on exercises. The third column lists the maximum number of shares of Common Stock that may be sold or otherwise disposed of by the selling stockholders pursuant to the registration statement of which this prospectus forms a part. The selling stockholders may sell or otherwise dispose of some, all or none of its shares. The fourth column assumes the sale of all of the shares of Common Stock offered by the selling stockholders pursuant to this prospectus, without regard to any limitations on exercises.

Under the terms of the 2025 Warrants, the selling stockholders may not exercise the Warrants to the extent such exercise would cause the selling stockholders, together with their affiliates and attribution parties, to beneficially own a number of shares of common stock which would exceed 4.99% or 9.99%, as applicable, of our then outstanding common stock following such exercise, excluding for purposes of such determination the shares of common stock issuable upon exercise of the Warrants which have not been exercised. The number of shares of common stock owned prior to the offering in the second column and the number of shares of common stock owned after the offering in the fourth column do not reflect this limitation. The selling stockholders may sell all, some or none of their shares in this offering. See “Plan of Distribution”.

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Name of Selling Stockholder	Number of Shares of Common Stock Owned Prior to this Offering	Maximum Number of Shares of Common Stock to be Sold Pursuant to this Prospectus	Shares Owned Immediately After Sale of Maximum Number of Shares in this Offering	
			Number	Percentage of Outstanding Shares of Common Stock <sup>(3)</sup>
Intracoastal Capital LLC <sup>(1)</sup>	219,495	217,392	2,103	**%
Gundyco ITF Orca Capital <sup>(2)</sup>	217,392	217,392	0	0%
Michael Vasinkevich <sup>(4)</sup>	20,910	20,910	0	0%
Noam Rubinstein <sup>(4)</sup>	10,272	10,272	0	0%
Craig Schwabe <sup>(4)</sup>	1,101	1,101	0	0%
Charles Worthman <sup>(4)</sup>	326	326	0	0%
<b>Total</b>	<b>469,496</b>	<b>467,393</b>	<b>2,103</b>	<b>**%</b>

\*Less than 1.0%

- (1) Represents (i) 2,103 shares of common stock issuable upon exercise of our public warrants and (ii) 217,392 shares of common stock issuable upon exercise of Warrants. The securities are held by Intracoastal Capital LLC., a Delaware limited liability company (“Intracoastal”). The Warrants are subject to a beneficial ownership limitation of 4.99%, which such limitation restricts the selling stockholder from exercising that portion of the Warrants that would result in the Selling Stockholder and its affiliates owning, after exercise, a number of shares of common stock in excess of the beneficial ownership limitation. The address of Intracoastal is 245 Palm Trail, Delray Beach, Florida 33483.

- (2) Represents 217,392 shares of common stock issuable upon exercise of Warrants. The securities are held by Orca Capital AG, a German corporation. The Warrants are subject to a beneficial ownership limitation of 4.99%, which such limitation restricts the selling stockholder from exercising that portion of the Warrants that would result in the Selling Stockholder and its affiliates owning, after exercise, a number of shares of common stock in excess of the beneficial ownership limitation. The address of Orca Capital AG is Sperling 2 85276, Hettenshausen, Germany.
- (3) Percentages are based on 3,151,467 shares of common stock assumed to be outstanding immediately after this offering.
- (4) Represents shares of common stock issuable upon exercise of the 2025 Placement Agent Warrants issued as compensation to H.C. Wainwright & Co., LLC, as our exclusive placement agent, in conjunction with the February 2025 Financing. Each of the selling stockholders is affiliated with H.C. Wainwright & Co., LLC, a registered broker dealer with a registered address of H.C. Wainwright & Co., LLC, 430 Park Ave, 3rd Floor, New York, NY 10022, and has sole voting and dispositive power over the securities held. The selling stockholder acquired the 2025 Placement Agent Warrants in the ordinary course of business and, at the time the 2025 Placement Agent Warrants were acquired, the selling stockholder had no agreement or understanding, directly or indirectly, with any person to distribute such securities.

### **Plan of Distribution**

The selling stockholders and any of their pledges, assignees and successors-in-interest may from time to time, sell any or all of their shares of common stock covered hereby on The Nasdaq Capital Market or any other stock exchange, market or trading facility on which the common stock is traded or in private transactions. These sales may be at fixed or negotiated prices. The selling stockholders may use any one or more of the following methods when selling shares of common stock:

- ordinary brokerage transactions and transactions in which the broker-dealer solicits purchasers;
- block trades in which the broker-dealer will attempt to sell the shares as agent but may position and resell a portion of the block as principal to facilitate the transaction;
- purchases by a broker-dealer as principal and resale by the broker-dealer for its account;
- an exchange distribution in accordance with the rules of the applicable exchange;
- privately negotiated transactions;
- settlement of short sales;
- in transactions through broker-dealers that agree with the selling stockholder to sell a specified number of shares of common stock at a stipulated price per share;
- through the written settlement of options or other hedging transactions, whether through an options exchange or otherwise;
- a combination of any such methods of sale; or
- any other method permitted pursuant to applicable law.

The selling stockholders may also sell shares of common stock under Rule 144 or any other exemption from registration under the Securities Act, if available, rather than under this prospectus.

Broker-dealers engaged by the selling stockholders may arrange for other brokers-dealers to participate in sales. Broker-dealers may receive commissions or discounts from the selling stockholders (or, if any broker-dealer acts as agent for the purchaser of shares of common stock, from the purchaser) in amounts to be negotiated, but, except as set forth in a supplement to this prospectus, in the case of an agency transaction not in excess of a customary brokerage commission in compliance with Rule 2121 of the Financial Industry Regulatory Authority, or FINRA; and in the case of a principal transaction, a markup or markdown in compliance with FINRA Rule 2121.

In connection with the sale of the shares of common stock covered by this prospectus or interests therein, the selling stockholders may enter into hedging transactions with broker-dealers or other financial institutions, which may in turn engage in short sales of the shares of common stock in the course of hedging the positions they assume. The selling stockholders may also sell shares of common stock short and deliver these shares to close out their short positions, or loan or pledge the shares to broker-dealers that in turn may sell these shares. The selling stockholders may also enter into option or other transactions with broker-dealers or other financial institutions or create one or more derivative securities which require the delivery to such broker-dealer or other financial institution of shares of common stock covered by this prospectus, which shares such broker-dealer or other financial institution may resell pursuant to this prospectus (as supplemented or amended to reflect such transaction).

The selling stockholders and any broker-dealers or agents that are involved in selling the shares of common stock covered hereby may be deemed to be “underwriters” within the meaning of the Securities Act in connection with such sales. In such event, any commissions received by such broker-dealers or agents and any profit on the resale of the shares purchased by them may be deemed to be underwriting commissions or discounts under the Securities Act. Each selling stockholder has informed the Company that it does not have any written or oral agreement or understanding, directly or indirectly, with any person to distribute the shares of common stock.

We are required to pay certain fees and expenses incurred by us incident to the registration of the shares of common stock covered hereby. We have agreed to indemnify the selling stockholders against certain losses, claims, damages and liabilities, including liabilities under the Securities Act.

We agreed to keep the registration statement of which this prospectus forms a part effective until the selling stockholders do not own any 2025 Warrants or common stock issuable upon exercise thereof. The shares of common stock will be sold only through registered or licensed brokers or dealers if required under applicable state securities laws. In addition, in certain states, the shares of common stock covered hereby may not be sold unless they have been registered or qualified for sale in the applicable state or an exemption from the registration or qualification requirement is available and is complied with.

Under applicable rules and regulations under the Securities Exchange Act of 1934, or the Exchange Act, any person engaged in the distribution of the shares of common stock covered hereby may not simultaneously engage in market making activities with respect to the common stock for the applicable restricted period, as defined in Regulation M, prior to the commencement of the distribution. In addition, the selling stockholders will be subject to applicable provisions of the Exchange Act and the rules and regulations thereunder, including Regulation M, which may limit the timing of purchases and sales of the common stock by the selling stockholder or any other person. We will make copies of this prospectus available to the selling stockholders and have informed them of the need to deliver a copy of this prospectus to each purchaser at or prior to the time of the sale (including by compliance with Rule 172 under the Securities Act).

### **Listing**

Our common stock is currently listed on the Nasdaq Capital Market under the symbol “LIXT”. The warrants issued in our November 2020 public offering are currently listed on the Nasdaq Capital Market under the symbol “LIXTW”.

## Transfer Agent and Registrar

The transfer agent and registrar for our common stock and the warrants issued in our November 2020 public offering is Computershare Trust Company, N.A.

## LEGAL MATTERS

The validity of the securities offered by this prospectus will be passed upon by TroyGould PC, Los Angeles, California.

## EXPERTS

Weinberg & Company, P.A., our independent, registered public accounting firm, has audited our consolidated financial statements as of December 31, 2024 and 2023 and for the years then ended included in our Annual Report on Form 10-K for the fiscal year ended December 31, 2024, which is incorporated by reference into this prospectus and elsewhere in the registration statement of which this prospectus is a part. Our 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.

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## INCORPORATION OF CERTAIN INFORMATION BY REFERENCE

The SEC allows us to incorporate by reference into this prospectus certain information we file with it, which means that we can disclose important information by referring you to those documents. The information incorporated by reference is considered to be part of this prospectus. Because we are incorporating by reference future filings with the SEC, this prospectus is continually updated and those future filings may modify or supersede some of the information included or incorporated in this prospectus. We incorporate by reference the documents listed below and all documents subsequently filed with the SEC (excluding any portions of any Form 8-K that are not deemed "filed" pursuant to the General Instructions of Form 8-K) pursuant to Section 13(a), 13(c), 14 or 15(d) of the Exchange Act, after the date of this prospectus and prior to the date this offering is terminated or we issue all of the securities under this prospectus:

- our Annual Report on [Form 10-K](#) for the fiscal year ended December 31, 2024, filed with the SEC on March 24, 2025;
- our Current Reports on Form 8-K filed with the SEC on [January 6, 2025](#), [February 13, 2025](#), [February 21, 2025](#), [February 25, 2025](#), [March 11, 2025](#), [March 11, 2025](#), [March 14, 2025](#), [March 27, 2025](#), and [March 31, 2025](#); and
- the description of our common stock contained in the registration statement on [Form 8-A](#), filed with the SEC on November 17, 2020, and any amendment or report filed for the purpose of updating such description (including [Exhibit 4.1](#) to the Annual Report on Form 10-K for the fiscal year ended December 31, 2023).

To obtain copies of these filings, see "Where You Can Find More Information" in this prospectus. Nothing in this prospectus shall be deemed to incorporate information furnished, but not filed, with the SEC, including pursuant to Item 2.02 or Item 7.01 of Form 8-K and any corresponding information or exhibit furnished under Item 9.01 of Form 8-K.

Information in this prospectus supersedes related information in the documents listed above and information in subsequently filed documents supersedes related information in both this prospectus and the incorporated documents.

## WHERE YOU CAN FIND MORE INFORMATION

We are subject to the periodic reporting requirements of the Exchange Act, and we will file periodic reports, proxy statements and other information with the SEC. These periodic reports, proxy statements and other information are available at [www.sec.gov](http://www.sec.gov). We maintain a website at <https://lixte.com>. We have not incorporated by reference into this prospectus the information contained in, or that can be accessed through, our website, and you should not consider it to be a part of this prospectus. You may access our Annual Reports on Form 10-K, Quarterly Reports on Form 10-Q, Current Reports on Form 8-K and amendments to those reports filed or furnished pursuant to Section 13(a) or 15(d) of the Exchange Act with the SEC free of charge at our website as soon as reasonably practicable after such material is electronically filed with, or furnished to, the SEC. You may also request a copy of these filings (other than exhibits to these documents unless the exhibits are specifically incorporated by reference into these documents or referred to in this prospectus), at no cost, by writing us at 680 East Colorado Boulevard, Suite 180, Pasadena, California 91101 or contacting us at (631) 830-7092.

We have filed with the SEC a registration statement under the Securities Act relating to the offering of these securities. The registration statement, including the attached exhibits, contains additional relevant information about us and the securities. This prospectus does not contain all of the information set forth in the registration statement. You may review a copy of the registration statement and the documents incorporated by reference herein through the SEC's website at [www.sec.gov](http://www.sec.gov).

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## LIXTE BIOTECHNOLOGY HOLDINGS, INC.

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## PROSPECTUS

April \_\_, 2025

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## PART II

## INFORMATION NOT REQUIRED IN PROSPECTUS

### Item 13. Other Expenses of Issuance and Distribution

The following table sets forth the various expenses, all of which will be borne by the registrant, in connection with the sale and distribution of the securities being registered, other than the placement agent fees. All amounts shown are estimates except for the SEC registration fee and the FINRA filing fee.

SEC registration fee		\$	168
Transfer agent and registrar fees			2,000
Accounting fees and expenses			35,000
Legal fees and expenses			50,000
Miscellaneous			2,832
Total		\$	90,000

#### Item 14. Indemnification of Directors and Officers.

Section 102(b)(7) of the Delaware General Corporation Law (“DGCL”) provides that a Delaware corporation, in its certificate of incorporation, may limit the personal liability of a director to the corporation or its stockholders for monetary damages for breach of fiduciary duties as a director, except for liability for any:

- transaction from which the director derived an improper personal benefit;
- act or omission not in good faith or that involved intentional misconduct or a knowing violation of law;
- unlawful payment of dividends or redemption of shares; or
- breach of the director’s duty of loyalty to the corporation or its stockholders.

Under Section 145 of the DGCL, we can indemnify our directors and officers against liabilities they may incur in such capacities, including liabilities under the Securities Act of 1933, as amended (the “Securities Act”). Our certificate of incorporation (Exhibit 3.1 to this registration statement) provides that we must indemnify our directors and officers to the fullest extent permitted by law and requires us to pay expenses incurred in defending or other participating in any proceeding in advance of its final disposition upon our receipt of an undertaking by the director or officer to repay such advances if it is ultimately determined that the director or officer is not entitled to indemnification. Our certificate of incorporation further provides that rights conferred under such certificate of incorporation do not exclude any other right such persons may have or acquire under the certificate of incorporation, the bylaws, any statute, agreement, vote of stockholders or disinterested directors or otherwise.

The certificate of incorporation also provides that, pursuant to Delaware law, our directors shall not be liable for monetary damages for breach of the directors’ fiduciary duty of care to us and our stockholders. This provision in the certificate of incorporation does not eliminate the duty of care, and in appropriate circumstances equitable remedies such as injunctive or other forms of non-monetary relief will remain available under Delaware law. In addition, each director will continue to be subject to liability for breach of the director’s duty of loyalty to us for acts or omissions not in good faith or involving intentional misconduct, or knowing violations of law, for actions leading to improper personal benefit to the director, and for payment of dividends or approval of stock repurchases or redemptions that are unlawful under Delaware law. The provision also does not affect a director’s responsibilities under any other law, such as the federal securities laws or state or federal environmental laws. We also intend to obtain directors’ and officers’ liability insurance pursuant to which our directors and officers are insured against liability for actions taken in their capacities as directors and officers.

In addition, we have entered into agreements to indemnify our directors and certain of our officers in addition to the indemnification provided for in the certificate of incorporation. These agreements, among other things, indemnify our directors and some of our officers for certain expenses (including attorney’s fees), judgments, fines and settlement amounts incurred by such person in any action or proceeding, including any action by or in our right, on account of services by that person as a director or officer of our company or as a director or officer of our subsidiary, or as a director or officer of any other company or enterprise that the person provides services to at our request.

#### Item 15. Recent Sales of Unregistered Securities.

The information below lists all of the securities sold by us during the past three years which were not registered under the Securities Act: None.

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#### Item 16. Exhibits and Financial Statement Schedules.

A list of exhibits to this registration statement is set forth in the Index to Exhibits as presented below.

##### INDEX TO EXHIBITS

Exhibit Number	Description of Document
2.1	<a href="#">Share Exchange Agreement dated as of June 8, 2006 among the Company, John S. Kovach and Lixte Biotechnology, Inc., filed as Exhibit 2.1 to the Company’s Current Report on Form 8-K, as filed with the Securities and Exchange Commission on July 7, 2006 and incorporated herein by reference.</a>
3.1	<a href="#">Certificate of Incorporation, as filed with the Delaware Secretary of State on May 24, 2005, filed as Exhibit 3.1 to the Company’s Registration Statement on Form 10-SB, as filed with the Securities and Exchange Commission on August 3, 2005 and incorporated herein by reference.</a>
3.2	<a href="#">Certificate of Amendment of Certificate of Incorporation, filed as Appendix A to the Company’s Information Statement, as filed with the Securities and Exchange Commission on September 19, 2006 and incorporated herein by reference.</a>
3.3	<a href="#">Certificate of Designations for the Company’s Series A Convertible Preferred Stock, filed as Exhibit 4.01 to the Company’s Current Report on Form 8-K, as filed with the Securities and Exchange Commission on March 18, 2015 and incorporated herein by reference.</a>
3.4	<a href="#">Certificate of Amendment of Certificate of Designations of the Series A Convertible Preferred Stock, filed as Exhibit 3.4 to the Company’s Annual Report on Form 10-K for the fiscal year ended December 31, 2015, as filed with the Securities and Exchange Commission on March 28, 2016 and incorporated herein by reference.</a>
3.5	<a href="#">Amended and Restated Bylaws, filed as Exhibit 3.1 to the Company’s Current Report on Form 8-K, as filed with the Securities and Exchange Commission on November 10, 2022 and incorporated herein by reference.</a>
3.6	<a href="#">Certificate of Amendment of Certificate of Incorporation, filed as Exhibit 3.1 to the Company’s Current Report on Form 8-K, as filed with the Securities and Exchange Commission on November 27, 2020 and incorporated herein by reference.</a>
3.7	<a href="#">Certificate of Amendment to the Certificate of Incorporation of Lixte Biotechnology Holdings, Inc., filed as Exhibit 3.1 to the Company’s Current Report on Form 8-K, as filed with the Securities and Exchange Commission on June 6, 2023 and incorporated herein by reference.</a>
4.1	<a href="#">Description of Registrant’s Securities Registered Pursuant to Section 12 of the Securities Exchange Act of 1934, as amended, filed as Exhibit 4.1 to the Company’s Annual Report on Form 10-K for the fiscal year ended December 31, 2019, as filed with the Securities and Exchange Commission on March 25, 2020 and incorporated herein by reference.</a>

- 4.2 [Form of Public Common Warrant included in Unit, filed as Exhibit 4.2 to the Company's Current Report on Form 8-K, as filed with the Securities and Exchange Commission on November 27, 2020 and incorporated herein by reference.](#)
- 4.3 [Form of Common Stock Purchase Common Warrant, filed as Exhibit 4.1 to the Company's Current Report on Form 8-K, as filed with the Securities and Exchange Commission on July 20, 2023 and incorporated herein by reference.](#)

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- 4.4 [Form of Placement Agent Common Warrant, filed as Exhibit 4.3 to the Company's Current Report on Form 8-K, as filed with the Securities and Exchange Commission on July 20, 2023 and incorporated herein by reference.](#)
- 4.5 [Form of Common Stock Purchase Warrant, filed as Exhibit 4.1 to the Company's Current Report on Form 8-K, as filed with the Securities and Exchange Commission on February 13, 2025 and incorporated herein by reference.](#)
- 4.6 [Form of Placement Agent Warrant, filed as Exhibit 4.2 to the Company's Current Report on Form 8-K, as filed with the Securities and Exchange Commission on February 13, 2025 and incorporated herein by reference.](#)
- 5.1 [Opinion of TroyGould PC\\*](#)
- 10.1 [Master Agreement between Lixte Biotechnology Holdings, Inc. and Theradex Systems, Inc. dated January 12, 2010, filed as Exhibit 10.15 to the Company's Annual Report on Form 10-K for the fiscal year ended December 31, 2012, as filed with the Securities and Exchange Commission on March 15, 2013 and incorporated herein by reference.](#)
- 10.2 [Materials Cooperative Research and Development Agreement between Lixte Biotechnology Holdings, Inc. and the National Institute of Neurological Disorders and Stroke dated October 18, 2013, filed as Exhibit 10.16 to the Company's Annual Report on Form 10-K for the fiscal year ended December 31, 2013, as filed with the Securities and Exchange Commission on March 21, 2014 and incorporated herein by reference.](#)
- 10.3 [Collaboration Agreement between Lixte Biotechnology Holdings, Inc. and BioPharmaWorks LLC effective September 14, 2015, filed as Exhibit 10.01 to the Company's Current Report on Form 8-K, as filed with the Securities and Exchange Commission on September 18, 2015 and incorporated herein by reference.](#)
- 10.4 [Collaboration Agreement for an Investigator-Initiated Clinical Trial between Lixte Biotechnology Holdings, Inc. and the Spanish Sarcoma Group as of July 31, 2019 \(certain portions of this exhibit have been omitted based on a request for confidential treatment filed by the Company with the Securities and Exchange Commission that was granted on September 19, 2019\), filed as Exhibit 10.1 to the Company's Current Report on Form 8-K, as filed with the Securities and Exchange Commission on August 6, 2019 and incorporated herein by reference.](#)
- 10.5 [Employment Agreement Between the Company and Robert N. Weingarten, filed as Exhibit 10.02 to the Company's Current Report on Form 8-K, as filed with the Securities and Exchange Commission on August 18, 2020 and incorporated herein by reference.+](#)
- 10.6 [Employment Agreement Between the Company and Eric Forman, filed as Exhibit 10.02 to the Company's Current Report on Form 8-K, as filed with the Securities and Exchange Commission on July 17, 2020 and incorporated herein by reference.+](#)
- 10.7 [Amendment to Employment Agreement between the Company and Eric Forman, filed as Exhibit 10.21 to the Company's Annual Report on Form 10-K for the fiscal year ended December 31, 2020, as filed with the Securities and Exchange Commission on March 26, 2021.+](#)
- 10.8 [Second Amendment to Employment Agreement between the Company and Eric Forman, filed as Exhibit 10.15 to the Company's Annual Report on Form 10-K for the fiscal year ended December 31, 2022, as filed with the Securities and Exchange Commission on March 29, 2023 and incorporated herein by reference.+](#)

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- 10.9 [Lixte Biotechnology Holdings, Inc. 2020 Stock Incentive Plan, filed as Exhibit 10.1 to the Company Current Report on Form 8-K, as filed with the Securities and Exchange Commission on July 17, 2020 and incorporated herein by reference.+](#)
- 10.10 [Lixte Biotechnology Holdings, Inc. 2020 Stock Incentive Plan \(as amended\), filed as Exhibit 10.1 to the Company's Current Report on Form 8-K, as filed with the Securities and Exchange Commission on November 28, 2023 and incorporated herein by reference.+](#)
- 10.11 [Development Collaboration Agreement by and between Lixte Biotechnology Holdings, Inc. and the Netherlands Cancer Institute, Amsterdam, and Oncode Institute, Utrecht, entered into on October 8, 2021 \(certain portions of this Exhibit have been omitted\), filed as Exhibit 10.1 to the Company's Quarterly Report on Form 10-Q for the quarterly period ended September 30, 2021, as filed with the Securities and Exchange Commission on November 10, 2021 and incorporated herein by reference.](#)
- 10.12 [Insider Trading Policy, filed as Exhibit 10.21 to the Company's Annual Report on Form 10-K for the fiscal year ended December 31, 2022, as filed with the Securities and Exchange Commission on March 29, 2023 and incorporated herein by reference.](#)
- 10.13 [Compensation Clawback Policy, filed as Exhibit 10.16 to the Company's Annual Report on Form 10-K for the fiscal year ended December 31, 2023, as filed with the Securities and Exchange Commission on March 19, 2024 and incorporated herein by reference.+](#)
- 10.14 [Amendment to Contract between Lixte Biotechnology Holdings, Inc. and MRI Global effective April 17, 2022, filed as Exhibit 10.1 to the Company's Quarterly Report on Form 10-Q for the quarterly period ended March 31, 2023, as filed with the Securities and Exchange Commission on May 10, 2023 and incorporated herein by reference.](#)
- 10.15 [Securities Purchase Agreement, filed as Exhibit 10.1 to the Company's Current Report on Form 8-K, as filed with the Securities and Exchange Commission on July 20, 2023 and incorporated herein by reference.](#)
- 10.16 [Employment Agreement between the Company and Bastiaan van der Baan effective September 26, 2023, filed as Exhibit 10.1 to the Company's Current Report on Form 8-K, as filed with the Securities and Exchange Commission on September 27, 2023 and incorporated herein by reference.](#)
- 10.17 [Amendment No. 1 to Development Collaboration Agreement by and between Lixte Biotechnology Holdings, Inc. and the Netherlands Cancer Institute, Amsterdam, and the Oncode Institute, Utrecht, entered into on October 8, 2021, filed as Exhibit 10.3 to the Company's Quarterly Report on Form 10-Q for the quarterly period ended September 30, 2023, as filed with the Securities and Exchange Commission on November 9, 2023 and incorporated herein by reference.](#)

- 10.18 [Amendment No. 2 to Development Collaboration Agreement by and between Lixte Biotechnology Holdings, Inc. and the Netherlands Cancer Institute, Amsterdam, and the Oncode Institute, Utrecht, entered into on October 13, 2023 \(certain portions of this Exhibit have been omitted\), filed as Exhibit 10.1 to the Company's Current Report on Form 8-K, as filed with the Securities and Exchange Commission on October 17, 2023 and incorporated herein by reference.](#)
- 10.19 [Termination letter between H. Lee Moffitt Cancer Center and Research Institute, Inc. and the Company dated October 4, 2023 and effective as of September 30, 2023, filed as Exhibit 10.5 to the Company's Quarterly Report on Form 10-Q for the quarterly period ended September 30, 2023, as filed with the Securities and Exchange Commission on November 9, 2023 and incorporated herein by reference.](#)
- 10.20 [Exclusive Patent License Agreement between Lixte Biotechnology, Inc. and the National Institute of Neurological Disorders and Stroke and the National Cancer Institute, each a component of the National Institute of Health, effective as of February 23, 2024, filed as Exhibit 10.1 to the Company's Current Report on Form 8-K, as filed with the Securities and Exchange Commission on February 26, 2024 and incorporated herein by reference.](#)

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- 10.21 [Consulting Agreement between the Company and Dr. Jan Schellens dated as of May 31, 2024, filed as Exhibit 10.1 to the Company's Current Report on Form 8-K, as filed with the Securities and Exchange Commission on June 5, 2024 and incorporated herein by reference.±](#)
- 10.22 [Clinical Trial Agreement between the Company and the Netherlands Cancer Institute dated as of June 10, 2024, filed as Exhibit 10.1 to the Company's Current Report on Form 8-K, as filed with the Securities and Exchange Commission on June 14, 2024 and incorporated herein by reference.](#)
- 10.23 [Securities Purchase Agreement filed as Exhibit 10.1 to the Company's Current Report on Form 8-K, as filed with the Securities and Exchange Commission on February 13, 2025 and incorporated herein by reference.](#)
- 21.1 [Subsidiaries of the Registrant, filed as Exhibit 21.1 to the Company's Annual Report on Form 10-K for the fiscal year ended December 31, 2022, as filed with the Securities and Exchange Commission on March 29, 2023 and incorporated herein by reference.](#)
- 23.1 [Consent of Weinberg & Company, P.A., Independent Registered Public Accounting Firm\\*](#)
- 23.2 [Consent of TroyGould PC \(included in Exhibit 5.1\)](#)
- 24.1 [Power of Attorney \(included on the signature line\)\\*](#)
- 107 [Filing Fee Table\\*](#)

\* Filed herewith.

+ Indicates a management contract or any compensatory plan, contract or arrangement.

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## Item 17. Undertakings.

The undersigned registrant hereby undertakes:

- (a)(1) To file, during any period in which offers or sales are being made, a post-effective amendment to this registration statement:
- (i) To include any prospectus required by section 10(a)(3) of the Securities Act of 1933;
  - (ii) To reflect in the prospectus any facts or events arising after the effective date of the registration statement (or the most recent post-effective amendment thereof) which, individually or in the aggregate, represent a fundamental change in the information set forth in the registration statement. Notwithstanding the foregoing, any increase or decrease in volume of securities offered (if the total dollar value of securities offered would not exceed that which was registered) and any deviation from the low or high end of the estimated maximum offering range may be reflected in the form of prospectus filed with the SEC pursuant to Rule 424(b) if, in the aggregate, the changes in volume and price represent no more than 20% change in the maximum aggregate offering price set forth in the "Calculation of Registration Fee" table in the effective registration statement; and
  - (iii) To include any material information with respect to the plan of distribution not previously disclosed in the registration statement or any material change to such information in the registration statement;

provided, however, that the undertakings set forth in paragraphs (a)(1)(i), (a)(1)(ii) and (a)(1)(iii) above do not apply if the information required to be included in a post-effective amendment by those paragraphs is contained in reports filed with or furnished to the SEC by the registrant pursuant to section 13 or section 15(d) of the Securities Exchange Act of 1934 that are incorporated by reference in this registration statement or are contained in a form of prospectus filed pursuant to Rule 424(b) that is part of this registration statement.

- (2) That, for the purposes of determining any liability under the Securities Act of 1933, each post-effective amendment that contains a form of prospectus shall be deemed to be a new registration statement relating to the securities offered therein, and the offering of such securities at that time shall be deemed to be the initial bona fide offering thereof.
- (3) To remove from registration by means of a post-effective amendment any of the securities being registered which remain unsold at the termination of the offering.
- (4) That in a primary offering of securities of the undersigned registrant pursuant to this registration statement, regardless of the underwriting method used to sell the securities to the purchaser, if the securities are offered or sold to such purchaser by means of any of the following communications, the undersigned registrant will be a seller to the purchaser and will be considered to offer or sell such securities to such purchaser:
  - (i) Any preliminary prospectus or prospectus of the undersigned registrant relating to the offering required to be filed pursuant to Rule 424;
  - (ii) Any free writing prospectus relating to the offering prepared by or on behalf of the undersigned registrant or used or referred to by the undersigned registrant;

- (iii) The portion of any other free writing prospectus relating to the offering containing material information about the undersigned registrant or its securities provided by or on behalf of the undersigned registrant; and
- (iv) Any other communication that is an offer in the offering made by the undersigned registrant to the purchaser.
- (b) The undersigned registrant hereby undertakes that, for the purposes of determining any liability under the Securities Act of 1933, each filing of the registrant's annual report pursuant to Section 13(a) or 15(d) of the Securities Exchange Act of 1934 (and, where applicable, each filing of an employee benefit plan's annual report pursuant to Section 15(d) of the Securities Exchange Act of 1934) that is incorporated by reference in the registration statement shall be deemed to be a new registration statement relating to the securities offered therein, and the offering of such securities at that time shall be deemed to be the initial bona fide offering thereof.
- (c) Insofar as indemnification for liabilities arising under the Securities Act of 1933 may be permitted to directors, officers and controlling persons of the registrant pursuant to the foregoing provisions, or otherwise, the registrant has been advised that in the opinion of the Securities and Exchange Commission such indemnification is against public policy as expressed in the Act and is, therefore, unenforceable. In the event that a claim for indemnification against such liabilities (other than the payment by the registrant of expenses incurred or paid by a director, officer or controlling person of the registrant in the successful defense of any action, suit or proceeding) is asserted by such director, officer or controlling person in connection with the securities being registered, the registrant will, unless in the opinion of its counsel the matter has been settled by controlling precedent, submit to a court of appropriate jurisdiction the question whether such indemnification by it is against public policy as expressed in the Act and will be governed by the final adjudication of such issue.
- (d) That,
  - (1) For purposes of determining any liability under the Securities Act of 1933, the information omitted from the form of prospectus filed as part of this registration statement in reliance upon Rule 430A and contained in a form of prospectus filed by the registrant pursuant to Rule 424(b)(1) or (4) or 497(h) under the Securities Act of 1933 shall be deemed to be part of this registration statement as of the time it was declared effective.
  - (2) For the purpose of determining any liability under the Securities Act of 1933, each post-effective amendment that contains a form of prospectus shall be deemed to be a new registration statement relating to the securities offered therein, and the offering of such securities at that time shall be deemed to be the initial bona fide offering thereof.

### SIGNATURES

Pursuant to the requirements of the Securities Act of 1933, the registrant has duly caused this registration statement to be signed on its behalf by the undersigned, thereunto duly authorized, in the city of Pasadena, State of California on April 4, 2025.

#### Lixte Biotechnology Holdings, Inc.

By: /s/ Bastiaan van der Baan  
 Name: Bastiaan van der Baan  
 Title: President and Chief Executive Officer  
 (Principal Executive Officer)

### POWER OF ATTORNEY

Each person whose signature appears below appoints Bastiaan van der Baan and Robert Weingarten, and each of them, each of whom may act without the joinder of the other, as their true and lawful attorney-in-fact and agent, with full power of substitution and resubstitution for them and in their name, place and stead, in any and all capacities to sign any and all amendments (including post-effective amendments) to this registration statement (and to any registration statement filed pursuant to Rule 462 under the Securities Act of 1933, as amended), and to file the same, with all exhibits thereto, and other documents in connection therewith, with the Securities and Exchange Commission, granting unto said attorneys-in-fact and agents full power and authority to do and perform each and every act and thing requisite and necessary to be done, as fully to all intents and purposes as they might or would do in person, hereby ratifying and confirming all that said attorneys-in-fact and agents or any of them or their substitute or substitutes, may lawfully do or cause to be done by virtue hereof.

Pursuant to the requirements of the Securities Act of 1933, this registration statement has been signed by the following persons in the capacities and on the dates indicated.

<u>Signature</u>	<u>Title(s)</u>	<u>Date</u>
<u>/s/ Bastiaan van der Baan</u> Bastiaan van der Baan	President and Chief Executive Officer, and Chairman of the Board of Directors (Principal Executive Officer)	April 4, 2025
<u>/s/ Robert Weingarten</u> Robert Weingarten	Vice President and Chief Financial Officer (Principal Financial and Accounting Officer)	April 4, 2025
<u>*</u> Stephen Forman	Director	April 4, 2025
<u>*</u> Yun Yen	Director	April 4, 2025
<u>*</u> Rene Bernards	Director	April 4, 2025
<u>*</u> Regina Brown	Director	April 4, 2025







**TroyGould pc**  
 1801 Century Park East, 16th Floor  
 Los Angeles, California 90067-2367  
**Tel** (310) 553-4441 | **Fax** (310) 201-4746  
[www.troygould.com](http://www.troygould.com)

File No.

April 3, 2025

Lixte Biotechnology Holdings, Inc.  
 680 E. Colorado Blvd., Suite 180  
 Pasadena, CA 91101

Dear Ladies and Gentlemen:

We have acted as counsel to Lixte Biotechnology Holdings, Inc., a Delaware corporation (the “Company”), in connection with the Registration Statement on Form S-1 (the “Registration Statement”), filed by the Company with the Securities and Exchange Commission (the “Commission”) under the Securities Act of 1933, as amended (the “Securities Act”). The Registration Statement relates to the registration for resale by the selling stockholders named in the Registration Statement (the “Selling Stockholders”) of up to 467,393 shares of the Company’s common stock, \$0.0001 par value per share (“Common Stock”) issuable upon the exercise of certain outstanding warrants (the “Warrants”) issued by the Company to the Selling Stockholders or their designees (the “Warrant Shares”).

In connection with our opinion, we have examined the Registration Statement, including the exhibits thereto, the Warrants, and such other documents, corporate records and instruments, and have examined such laws and regulations, as we have deemed necessary for the purposes of this opinion. In making our examination, we have assumed the genuineness of all signatures, the authenticity of all documents submitted to us as originals, the conformity with the originals of all documents submitted to us as copies and the legal capacity of all natural persons. As to matters of fact material to our opinions in this letter, we have relied on certificates and statements from officers and other employees of the Company, public officials and other appropriate persons.

Based on the foregoing and subject to the qualifications set forth below, we are of the opinion that the Warrant Shares initially issuable upon exercise of the Warrants when issued by the Company against payment therefor (not less than par value) in the circumstances contemplated by the Warrants, will have been duly authorized by all necessary corporate action of the Company, and will be validly issued, fully paid and non-assessable.



Lixte Biotechnology Holdings, Inc.  
 April 3, 2025  
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The foregoing opinions are limited to the General Corporation Law of Delaware (which includes those statutory provisions and all applicable provisions of the Delaware Constitution and the reported judicial decisions interpreting such laws), and we express no opinion as to the laws of any other jurisdiction.

The opinions expressed in this opinion letter are as of the date of this opinion letter only and as to laws covered hereby only as they are in effect on that date, and we assume no obligation to update or supplement such opinion to reflect any facts or circumstances that may come to our attention after that date or any changes in law that may occur or become effective after that date. The opinions herein are limited to the matters expressly set forth in this opinion letter, and no opinion or representation is given or may be inferred beyond the opinions expressly set forth in this opinion letter.

We hereby consent to the filing of this opinion with the Commission as an exhibit to the Registration Statement and to the use of this firm’s name under the caption “Legal Matters” in the Registration Statement. In giving this consent, we do not thereby admit that we are within the category of persons whose consent is required under Section 7 of the Securities Act or the rules and regulations of the Commission promulgated thereunder.

Very truly yours,

/s/ TroyGould PC

TroyGould PC

**CONSENT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM**

We consent to the incorporation by reference in this Registration Statement on Form S-1 (File No. 333-\_\_\_\_\_) of our report dated March 24, 2025, relating to the consolidated financial statements of Lixte Biotechnology Holdings, Inc., as of and for the years ended December 31, 2024 and 2023 (which report includes an explanatory paragraph regarding substantial doubt about the Company's ability to continue as a going concern) included in Lixte Biotechnology Holdings, Inc.'s Annual Report on Form 10-K for the fiscal year ended December 31, 2024, filed with the Securities and Exchange Commission. We also consent to the reference to our firm under the caption "Experts" in the Prospectus, which is part of this Registration Statement.

/s/ Weinberg & Company, P.A.  
Los Angeles, California  
April 4, 2025

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## Calculation of Filing Fee Table

**FORM S-1**  
**REGISTRATION STATEMENT UNDER THE SECURITIES ACT OF 1933**  
(Form Type)

**Lixte Biotechnology Holdings, Inc.**  
(Exact Name of Registrant as Specified in its Charter)

Table 1: Newly Registered Securities

Security Type	Security Class Title	Fee Calculation Rule	Amount Registered	Proposed Maximum Offering Price Per Share	Maximum Aggregate Offering Price (1)	Fee Rate	Amount of Registration Fee
<b>Newly Registered Securities</b>							
<b>Fees to Be Paid</b>	Equity	Common Stock underlying the Warrants to purchase Common Stock, par value \$0.0001 per share (2)	457(o)		\$ 1,094,095	0.00015310	\$ 167.51
<b>Fees Previously Paid</b>	-	-	-	-	-	-	-
<b>Total Offering Amounts</b>					\$ 1,094,095		\$ 167.51
<b>Total Fees Previously Paid</b>					\$ -		\$ -
<b>Total Fee Offsets</b>					\$ -		\$ -
<b>Net Fees Due</b>					\$ -		\$ 167.51

- (1) Estimated solely for the purpose of calculating the amount of the registration fee in accordance with Rule 457(o) under the Securities Act of 1933 (the "Securities Act").
- (2) Pursuant to Rule 416 under the Securities Act, the securities registered hereby also include an indeterminate number of additional securities as may from time to time become issuable by reason of stock splits, stock dividends, recapitalizations, or other similar transactions.