

PROSPECTUS SUPPLEMENT  
(To Prospectus Dated February 5, 2021)



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LIXTE BIOTECHNOLOGY HOLDINGS, INC.  
180,000 Shares of Common Stock  
Pre-Funded Warrants to Purchase up to 403,334 Shares of Common Stock  
Up to 403,334 Shares of Common Stock underlying such Pre-Funded Warrants

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We are offering (i) 180,000 shares of our common stock, par value \$0.001 per share (“Common Stock”), at a price of \$6.00 per share and (ii) pre-funded warrants (the “Pre-Funded Warrants”) to purchase up to 403,334 shares of our Common Stock at a price of \$5.9999 per Pre-Funded Warrant, each pursuant to this prospectus supplement, the accompanying prospectus, and a securities purchase agreement entered into on July 18, 2023 (the “Purchase Agreement”), between the Company and an institutional investor thereto (the “Purchaser”). Each Pre-Funded Warrant will have an exercise price of \$0.0001, will be immediately exercisable, and is valid and exercisable until all Pre-Funded Warrants are exercised in full. This prospectus supplement also relates to the offering of the shares of Common Stock issuable upon exercise of such Pre-Funded Warrants.

In a concurrent private placement (the “Concurrent Private Placement”), we are also selling to the Purchaser of our shares of Common Stock and Pre-Funded Warrants in this offering, warrants (the “Common Warrants” and, collectively with the Pre-Funded Warrants, the “Warrants”) to purchase up to 583,334 shares of our Common Stock. Each Common Warrant will have an initial exercise price of \$6.00 per share and will be immediately exercisable for a term of five years from issuance. The Common Warrants and the shares of Common Stock issuable upon exercise of the Common Warrants are not being registered under the Securities Act of 1933, as amended (the “Securities Act”), and are not being offered pursuant to this prospectus supplement and the accompanying prospectus and are being offered pursuant to the exemption provided in Section 4(a)(2) under the Securities Act and Rule 506(b) promulgated thereunder.

Our Common Stock is listed on The Nasdaq Capital Market under the symbol “LIXT”. The last sale price of our Common Stock on July 17, 2023, as reported by The Nasdaq Capital Market, was \$7.53 per share. There is no established public trading market for the Pre-Funded Warrants or Common Warrants and we do not expect a market to develop. Without an active trading market, the liquidity of the Pre-Funded Warrants and Common Warrants will be limited. In addition, we do not intend to have the Pre-Funded Warrants or Common Warrants admitted to trading on The Nasdaq Capital Market or listed on any other national securities exchange or any other trading system.

The aggregate market value of our outstanding Common Stock held by non-affiliates was \$11,103,685 based on 1,665,956 shares of outstanding Common Stock, of which 1,474,593 shares were held by non-affiliates, and a per share price of \$7.53 based on the closing sale price of our Common Stock on July 17, 2023.

Pursuant to General Instruction I.B.6 of Form S-3, in no event will we sell our securities in a public primary offering with a value exceeding more than one-third of our public float in any 12-month period so long as our public float remains below \$75,000,000. We have not sold any securities pursuant to General Instruction I.B.6. of Form S-3 during the prior 12 calendar month period that ends on and includes the date of this prospectus (excluding this offering).

All share and per share amounts presented herein have been retroactively adjusted to reflect the 1-for-10 reverse split of the Company’s common stock effective June 2, 2023.

**Investing in any of our securities involves a high degree of risk. See “Risk Factors” beginning on page S-6 of this prospectus supplement and page 5 of the accompanying prospectus.**

We have retained A.G.P./Alliance Global Partners (“A.G.P.” or the “Placement Agent”) to act as our exclusive placement agent in connection with the securities offered by this prospectus supplement. A.G.P. is not purchasing or selling any of these securities nor is it required to sell any specific number or dollar amount of securities, but has agreed to use its reasonable best efforts to sell the securities offered by this prospectus supplement. We have agreed to pay A.G.P. a cash fee equal to 6.0% of the aggregate gross proceeds raised in this offering as set forth in the table below.

	Per Share	Per Pre-Funded Warrant	Total <sup>(1)</sup>
Public offering price	\$ 6.00	\$ 5.9999	\$ 3,500,004
Placement agent fees <sup>(2)</sup>	\$ 0.36	\$ 0.359994	\$ 210,000
Proceeds, before expenses, to us	\$ 5.64	\$ 5.6399	\$ 3,290,003

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

(2)We have also agreed to issue the Placement Agent or its respective designees warrants (the “placement agent warrants”) to purchase 35,000 shares of Common Stock, and to reimburse certain expenses of the Placement Agent in connection with this offering. The placement agent warrants or the shares underlying the placement agent warrants are not being registered hereby.

Delivery of the securities offered pursuant to this prospectus supplement and the accompanying prospectus is expected to be made on or about July 20, 2023, subject to the satisfaction of certain closing conditions.

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

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Sole Placement Agent

**A.G.P.**

The date of this prospectus supplement is July 18, 2023.

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

### ABOUT THIS PROSPECTUS SUPPLEMENT

This prospectus supplement and the accompanying prospectus relate to the sale of our securities registered for sale under our Registration Statement on Form S-3 (File No. 333-252430) (the “Registration Statement”), which the Securities and Exchange Commission (the “Commission” or the “SEC”) declared effective on February 5, 2021.

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

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

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

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

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## CAUTIONARY NOTE REGARDING FORWARD-LOOKING STATEMENTS

This prospectus supplement, the accompanying prospectus and the documents incorporated by reference herein and therein may contain forward looking statements that involve risks and uncertainties. All statements other than statements of historical fact contained in this prospectus supplement, the accompanying prospectus and the documents incorporated by reference herein and therein, including statements regarding future events, our future financial performance, business strategy, and plans and objectives of management for future operations, are forward-looking statements. We have attempted to identify forward-looking statements by terminology including “anticipates,” “believes,” “can,” “continue,” “could,” “estimates,” “expects,” “intends,” “may,” “plans,” “potential,” “predicts,” “should,” or “will” or the negative of these terms or other comparable terminology. Although we do not make forward looking statements unless we believe we have a reasonable basis for doing so, we cannot guarantee their accuracy. These statements are only predictions and involve known and unknown risks, uncertainties and other factors, including the risks outlined under “Risk Factors” or elsewhere in this prospectus supplement, the accompanying prospectus and the documents incorporated by reference herein and therein, which may cause our or our industry’s actual results, levels of activity, performance or achievements expressed or implied by these forward-looking statements. Moreover, we operate in a highly regulated, very competitive, and rapidly changing environment. New risks emerge from time to time and it is not possible for us to predict all risk factors, nor can we address the impact of all factors on our business or the extent to which any factor, or combination of factors, may cause our actual results to differ materially from those contained in any forward-looking statements.

We have based these forward-looking statements largely on our current expectations and projections 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 financial needs. These forward-looking statements are subject to certain risks and uncertainties that could cause our actual results to differ materially from those reflected in the forward-looking statements. Factors that could cause or contribute to such differences include, but are not limited to, those discussed (i) in our Annual Report on Form 10-K for the fiscal year ended December 31, 2022, (ii) in this prospectus supplement and the accompanying prospectus, and in particular, the risks discussed below and under the heading “Risk Factors” and (iii) those discussed in other documents we file with the SEC. The following discussion should be read in conjunction with the consolidated financial statements for the fiscal years ended December 31, 2022 and 2021 and the notes incorporated by reference herein. We undertake no obligation to revise or publicly release the results of any revision to these forward-looking statements, except as required by law. 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 statement.

You should not place undue reliance on any forward-looking statement, each of which applies only as of the date of this prospectus supplement. You are advised to consult any further disclosures we make on related subjects in our reports on Forms 10-Q, 8-K and 10-K filed with the SEC.

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## PROSPECTUS SUPPLEMENT SUMMARY

*This summary highlights certain information about us, this offering and selected information contained elsewhere in this prospectus supplement and in the documents incorporated by reference. This summary is not complete and does not contain all of the information that you should consider before deciding whether to invest in our shares of common stock. For a more complete understanding of our company and this offering, we encourage you to read and consider carefully the more detailed information contained in or incorporated by reference in this prospectus supplement, including the information contained under the heading “Risk Factors” beginning on page S-6 of this prospectus supplement, and the information included in any free writing prospectus that we have authorized for use in connection with this offering.*

*Throughout this prospectus supplement, the terms “we,” “us,” “our,” and “our company” refer to Lixte Biotechnology Holdings, Inc., a Delaware corporation, and its consolidated subsidiaries unless the context requires otherwise.*

### Company Overview

The Company is a drug discovery company that uses biomarker technology to identify enzyme targets associated with serious common diseases and then designs novel compounds to attack those targets. The Company’s corporate office is located in Pasadena, California.

The Company’s product pipeline is primarily focused on inhibitors of protein phosphatases, used alone and in combination with cytotoxic agents and/or x-ray and immune checkpoint blockers. The Company believes that inhibitors of protein phosphatases have broad therapeutic potential not only for cancer but also for other debilitating and life-threatening diseases. The Company is directing its efforts on clinical development of a specific protein phosphatase inhibitor, referred to as LB-100, which has been shown to have clinical anti-cancer activity at doses that produce little or no toxicity.

The Company’s activities are subject to significant risks and uncertainties, including the need for additional capital. The Company has 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 infusions of equity capital to fund its operating requirements.

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### Recent Developments

*News Release:* On July 17, 2023, the Company issued a news release announcing that a recently posted article in BioRxiv based on the results of a collaboration between the Company and the Netherlands Cancer Institute, shows that inhibition of PP2A in colon cancer cells, using LIXTE’s lead clinical compound LB-100, leads to major changes in the way cancer cells process their mRNAs.

Based on this finding, the Company indicated that cancer cells are predicted to produce a significant number of aberrant proteins that can be recognized by the immune system. This newly discovered mechanism, by which LB-100 turns immunologically “cold” tumors “hot,” adds to several additional mechanisms that have recently been described through which LB-100 sensitizes cancer cells to immune checkpoint blockade.

The Company said the new research also shows that disruption of proper mRNA maturation induced by LB-100 leads to a reduced ability of the cancer cells to deal with DNA damage. This finding concurs with multiple pre-clinical studies demonstrating synergy between LB-100 and radiotherapy or different chemotherapies in various cancer models.

The July 13, 2023 *BioRxiv* article, titled “PP2A Inhibition Instructs Spliceosome Phosphorylation to Create Splicing Vulnerability in Colon Adenocarcinoma,” was authored by Dias et. al. from the Netherlands Cancer Institute, in a collaboration that the Company initiated in 2021 with a team of scientists headed by René Bernards, a Professor of Molecular Carcinogenesis at the Netherlands Cancer Institute and a member of the Company’s Board of Directors.

*Moffitt Clinical Trial:* Effective August 20, 2018, the Company entered into a five-year Clinical Trial Research Agreement with the Moffitt Cancer Center and Research Institute Hospital Inc., Tampa, Florida. Pursuant to the Clinical Trial Research Agreement, Moffitt agreed to conduct and manage a Phase 1b/2 clinical trial to evaluate the therapeutic benefit of the Company’s lead anti-cancer clinical compound LB-100 to be administered intravenously in patients with low or intermediate-1 risk myelodysplastic syndrome (MDS).

In November 2018, the Company received approval from the U.S. Food and Drug Administration for its Investigational New Drug Application to conduct a Phase 1b/2 clinical trial to evaluate the therapeutic benefit of LB-100 in patients with low and intermediate-1 risk MDS who have failed or are intolerant of standard treatment. Patients with MDS, although usually older, are generally well except for severe anemia requiring frequent blood transfusions. This Phase 1b/2 clinical trial utilized LB-100 as a single agent in the treatment of patients with low and intermediate-1 risk MDS, including patients with del(5q) myelodysplastic syndrome (del5qMDS) failing first line therapy.

During the three months ended June 30, 2023, the Phase 1b/2 clinical trial at the Moffitt Cancer Center evaluating LB-100 in patients with MDS was closed by the principal investigator because of low accrual to the study. In this clinical trial, single agent LB-100 was used on a new schedule of days 1, 3, and 5 every 3 weeks. It was determined that patients found it too challenging to go for an infusion given on this schedule. The Company is not employing this schedule in its other clinical trials. Although the Maximally Tolerated Dose (MTD) was not achieved, there was no dose-limiting toxicity on this schedule at doses that were even greater than those which were above the MTD in the Phase 1 clinical trial of LB-100 on the Monday, Tuesday, Wednesday schedule.

The Company has decided not to pursue further studies in MDS, as other opportunities in much more common diseases have become available. For example, the Company is now focusing on documenting clear-cut potentiation of cytotoxic treatment as in the ongoing study of advanced soft tissue sarcoma and small cell lung cancer. In addition, new data has directed the Company's resources to demonstrate that the striking potentiation of immunotherapy in diverse common cancers also occurs in the clinic. The Company will maintain its patent positions in MDS in the possibility that other cancer centers would be interested in partnering with the Company.

*City of Hope Clinical Trial:* In July 2023, the Company was notified that one of three centers accruing patients to its Phase 1b trial in small cell lung cancer has a shortage of carboplatin and will be placed on a temporary enrollment hold as a result.

## Corporate Information

We are incorporated in Delaware, and our principal place of business is located at 680 East Colorado Boulevard, Suite 180, Pasadena, California 91101. Our telephone number is (631) 830-7092. Our corporate website address is [www.lixte.com](http://www.lixte.com). Information contained on or accessible through our website is not a part of this prospectus, and the inclusion of our website address in this prospectus is an inactive textual reference only.

Our common stock and warrants trade on The Nasdaq Capital Market under the symbols "LIXT" and "LIXTW", respectively.

Our principal Internet address is [www.lixte.com](http://www.lixte.com). Information contained on, or that can be accessed through, our website, is not, and shall not be deemed to be, incorporated in this prospectus supplement or considered a part thereof. We make available free of charge on [www.lixte.com](http://www.lixte.com) our annual, quarterly and current reports, and amendments to those reports, as soon as reasonably practicable after we electronically file such material with, or furnish it to, the SEC. The SEC maintains an Internet site that contains reports, proxy and information statements, and other information regarding issuers that file electronically with the SEC at <http://www.sec.gov>.

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## THE OFFERING

Issuer	Lixte Biotechnology Holdings, Inc.
Common Stock offered by us	180,000 shares of Common Stock at a price of \$6.00 per share.
Pre-Funded Warrants offered	We are also offering Pre-Funded Warrants to purchase up to 403,334 shares of Common Stock in lieu of shares of Common Stock to the Purchaser whose purchase of shares of Common Stock in this offering would otherwise result in the Purchaser, together with its affiliates and certain related parties, beneficially owning more than 9.99% of our outstanding Common Stock immediately following the consummation of this offering. Each Pre-Funded Warrant is exercisable for one share of our Common Stock. The purchase price of each Pre-Funded Warrant is equal to the price at which the share of Common Stock is being sold to the public, minus \$0.0001 per share. The Pre-Funded Warrants are exercisable immediately, at an exercise price of \$0.0001 per share, and may be exercised at any time until all of the Pre-Funded Warrants are exercised in full. This offering also relates to the shares of Common Stock issuable upon exercise of the Pre-Funded Warrants sold in this offering.
Concurrent Private Placement of Common Warrants offered	<p>In the Concurrent Private Placement and pursuant to the Purchase Agreement, we are also selling to the Purchaser, for no additional consideration, Common Warrants to purchase up to 583,334 shares of our Common Stock. The Common Warrants have an exercise price of \$6.00 per share.</p> <p>The Common Warrants will be immediately exercisable for a term of five years from issuance. The Common Warrants and the shares issuable upon exercise thereof are not being registered under the Securities Act of 1933, as amended (the "Securities Act") and are not offered pursuant to this prospectus supplement and the accompanying prospectus. The Common Warrants are being offered pursuant to an exemption from the registration requirements of the Securities Act provided in Section 4(a)(2) of the Securities Act and 506(b) promulgated thereunder. See "Private Placement Transaction."</p> <p>Under the Purchase Agreement, the Company has agreed to file a registration statement with the SEC covering the resale of the shares underlying the Common Warrants issued in the Concurrent Private Placement.</p>
Common Stock to be outstanding after the offering	2,249,290 shares (as of July 18, 2023), assuming the issuance of 403,334 shares of Common Stock upon the exercise of the Pre-Funded Warrants.
Use of proceeds	We estimate the net proceeds to us from this offering will be approximately \$3,290,003, after deducting the placement agent fee and estimated offering expenses payable by us, and excluding the proceeds, if any, from the exercise of the Pre-Funded Warrants offered hereby. We intend to use the net proceeds from this offering for working capital and general corporate purposes including for further clinical development of our lead compound LB-100. See "Use of Proceeds."
Risk factors	An investment in our securities involves a high degree of risk. See "Risk Factors" beginning on page S-6 for a discussion of certain factors that you should consider when evaluating an investment in our securities.
NASDAQ symbols	Our Common Stock and Warrants are listed on The Nasdaq Capital Market under the symbol "LIXT" and "LIXTW", respectively.

The number of shares of our common stock to be outstanding after this offering as shown above is based on 1,665,956 shares outstanding as of March 31, 2023, as adjusted for the 1-for-10 reverse stock split of June 2, 2023, and excludes as of that date:

- 72,917 shares of common stock issuable upon conversion of 350,000 shares of Series A Preferred Stock outstanding at a conversion rate of 0.2083 common shares per preferred share, reflecting an effective conversion price of \$48.00 per common share.
- 388,229 shares of common stock issuable upon exercise of outstanding common stock options issued to members of management, consultants, and directors at a weighted average exercise price of \$29.26 per common share.
- 190,031 shares of common stock issuable upon exercise of outstanding common stock warrants at an average exercise price of \$50.16 per common share.
- 153,021 shares of common stock reserved for future grants pursuant to the 2020 Stock Incentive Plan.
- 35,000 shares of common stock issuable upon exercise of warrants issued to the placement agent as part of the offering on July 18, 2023 at an exercise price of \$6.60 per common share (110% of the offering price of \$6.00 per share).
- 583,334 shares of Common Stock issuable upon exercise of the Common Warrants to be issued to the Purchasers in the Concurrent Private Placement.

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

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## RISK FACTORS

*Investing in our shares of common stock involves a high degree of risk and uncertainty. You should carefully consider these risk factors, together with all of the other information included or incorporated by reference in this prospectus supplement and the accompanying prospectus, as modified and superseded, before you decide to invest in our securities, including without limitation the risk factors listed under Part I, Item 1A. Risk Factors of our most recent Annual Report on Form 10-K and in our most recent Quarterly Report on Form 10-Q filed with the SEC. The occurrence of any of the following risks could harm our business. In that case, the trading price of our common stock could decline, and you may lose all or part of your investment. Additional risks and uncertainties not presently known to us or that we currently deem immaterial may also impair our operations. You should also refer to the other information contained in this prospectus supplement, the accompanying prospectus and the documents incorporated by reference into this prospectus supplement and the accompanying prospectus, including our financial statements and the notes to those statements and the information set forth in the section entitled "Cautionary Note Regarding Forward-Looking Statements."*

### Risks Related to our Business

***Our independent registered public accounting firm has expressed substantial doubt about our ability to continue as a going concern.***

The Company's consolidated financial statements have been presented on the basis that it will continue as a going concern, which contemplates the realization of assets and satisfaction of liabilities in the normal course of business. The Company has no recurring source of revenue and has experienced negative operating cash flows since inception, and management has stated that substantial doubt exists about the Company's ability to continue as a going concern. As a result, our independent registered public accounting firm has included an explanatory paragraph in their report that accompanies our audited consolidated financial statements as of and for the year ended December 31, 2022, with respect to this uncertainty. This going concern opinion could materially limit our ability to raise additional funds through the sale of equity securities in the future, and subsequent reports by our independent registered public accounting firm on our consolidated financial statements may also include an explanatory paragraph with respect to our ability to continue as a going concern.

***We need significant additional financing to fund our operations and complete the development 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.***

We expect that our existing cash resources as of December 31, 2022, in addition to the expected proceeds of this offering, will provide sufficient working capital resources to fund our operations, including our clinical trial programs with respect to the development of our lead anti-cancer clinical compound LB-100, through approximately the second quarter of 2024. Our existing cash resources will not be sufficient to complete development of and obtain regulatory approval for our lead product candidate, and we will need to raise significant additional capital to help us do so. The Company estimates that it will need to raise additional capital to fund its operations, including its various clinical trial commitments, during the latter part of the fiscal year ending December 31, 2023. In addition, our operating plan might change as a result of many factors currently unknown to us, including possible additional clinical trials, and we might need additional funds sooner than planned.

We expect to expend substantial resources for the foreseeable future to continue the clinical development of our lead product candidate and the advancement and expansion of our preclinical research pipeline. These expenditures will include costs associated with research and development, conducting preclinical studies and clinical trials and potentially obtaining regulatory approvals.

Budgets and future capital requirements depend on many factors, including:

- the scope, progress, results and costs of our ongoing and planned development programs for our lead product candidate, as well as any additional clinical trials we undertake;
- the timing of, and the costs involved in, obtaining regulatory approvals for our lead drug candidate if our clinical trials are successful;
- our ability to establish and maintain strategic licensing or other arrangements and the financial terms of such agreements;
- the costs to in-license future product candidates or technologies;
- the costs involved in preparing, filing, prosecuting, maintaining, expanding, defending and enforcing patent claims, including litigation costs and the outcome of such litigation;
- the costs in defending and resolving future derivative and securities class action litigation;
- our operating expenses; and
- the emergence of competing technologies or other adverse market developments.

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Additional funds might not be available when we need them on terms that are acceptable to us, or at all. We have no committed source of additional capital. If adequate funds are not available to us on a timely basis, we might not be able to continue as a going concern or we might be required to delay, limit, reduce or terminate preclinical studies,

clinical trials or other development activities for our product candidates or target indications.

## **Risks Related to Owning our Securities**

***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.***

We are a “smaller reporting company,” as defined in the Regulation S-K of the Securities Act of 1933, as amended (the “Securities Act”), which allows us to take advantage of certain exemptions from various reporting requirements that are applicable to other public companies that are not smaller reporting companies, including (1) not being required to comply with the auditor attestation requirements of Section 404 of the Sarbanes-Oxley Act of 2002, and (2) reduced disclosure obligations regarding executive compensation in our periodic reports and proxy statements. In addition, as an emerging growth company, we are only required to provide two years of audited financial statements in this document. As a result of these reduced reporting and disclosure requirements our financial statements might not be comparable to SEC registrants not classified as emerging growth companies.

We cannot predict if investors will find our common stock less attractive because we might rely on these exemptions. If some investors find our common stock less attractive as a result, there might be a less active trading market for our common stock and our stock price might be more volatile.

Our independent registered public accounting firm is not be required to formally attest to the effectiveness of our internal control over financial reporting until we are no longer a “smaller reporting company”. We cannot assure you that there will not be material weaknesses or significant deficiencies in our internal controls in the future.

Investors might find our common stock less attractive as a result of our election to utilize these exemptions, which could result in a less active trading market for our common stock and/or the market price of our common stock might be more volatile.

***The Warrants are speculative in nature.***

The Warrants offered in this Offering do not confer any rights of common stock ownership on their holders, such as voting rights or the right to receive dividends, but rather merely represent the right to acquire shares of common stock at a fixed price. Specifically, holders of the Warrants may exercise their right to acquire the common stock and pay an exercise price of \$6.00 per share. Furthermore, each Warrant will expire five (5) years from the original issuance date. In the event our common stock price does not exceed the exercise price of the Warrants during the period when the Warrants are exercisable, the Warrants might not have any value.

***Holders of the Warrants will have no rights as a common stockholder until they acquire our common stock.***

Until the acquisition of shares of our common stock upon exercise of the Warrants, a holder will have no rights with respect to shares of our common stock issuable upon exercise of the Warrant. Upon exercise of a Warrant, a holder will be entitled to exercise the rights of a common stockholder as to the security exercised only as to matters for which the record date occurs after the exercise.

***Provisions of the Warrants could discourage an acquisition of us by a third party.***

Certain provisions of the Warrants could make it more difficult or expensive for a third party to acquire us. The Warrants prohibit us from engaging in certain transactions constituting “fundamental transactions” unless, among other things, the surviving entity assumes our obligations under the Warrants. These and other provisions of the Warrants could prevent or deter a third party from acquiring us even where the acquisition could be beneficial to you.

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

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

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

- reputational issues;
- competition from existing technologies and products or new technologies and products that might emerge;
- announcements of acquisitions, partnerships, collaborations, joint ventures, new products, capital commitments, or other events by us or our competitors;
- changes in general economic, political and market conditions in or any of the regions in which we conduct our business;

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- changes in industry conditions or perceptions;
- changes in valuations of similar companies or groups of companies;
- analyst research reports, recommendation and changes in recommendations, price targets, and withdrawals of coverage;
- departures and additions of key personnel;
- disputes and litigations related to intellectual properties, proprietary rights, and contractual obligations;
- changes in applicable laws, rules, regulations, or accounting practices and other dynamics; and
- other events or factors, many of which might be out of our control.

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

#### **Risks Related to the Company's Common Stock**

*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.*

If our stockholders sell substantial amounts of our common stock in the public market, the market price of our common stock could fall. Moreover, the perceived risk of this potential dilution could cause stockholders to attempt to sell their shares and investors to short our common stock. These sales also might make it more difficult for us to sell equity or equity-related securities in the future at a time and price that we deem reasonable or appropriate.

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*Market and economic conditions might negatively impact our business, financial condition and share price.*

Concerns over medical epidemics, energy costs, geopolitical issues, the U.S. mortgage market and a deteriorating real estate market, unstable global credit markets and financial conditions, and volatile oil prices have led to periods of significant economic instability, diminished liquidity and credit availability, declines in consumer confidence and discretionary spending, diminished expectations for the global economy and expectations of slower global economic growth, increased unemployment rates, and increased credit defaults in recent years. Our general business strategy might be adversely affected by any such economic downturns (including the impact related to the recent COVID-19 pandemic), volatile business environments and continued unstable or unpredictable economic and market conditions. If these conditions continue to deteriorate or do not improve, it might make any necessary debt or equity financing more difficult to complete, more costly, and more dilutive. Failure to secure any necessary financing in a timely manner and on favorable terms could have a material adverse effect on our growth strategy, financial performance, and share price and could require us to delay or abandon development or commercialization plans.

*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.*

The trading market for our common stock will rely in part on the research and reports that industry or financial analysts publish about us, our business, our markets and our competitors. We do not control these analysts. If securities analysts do not cover our common stock, the lack of research coverage might adversely affect the market price of our common stock. Furthermore, if one or more of the analysts who do cover us downgrade our stock or if those analysts issue other unfavorable commentary about us or our business, our stock price would likely decline. If one or more of these analysts cease coverage of us or fails to regularly publish reports on us, we could lose visibility in the market and interest in our stock could decrease, which in turn could cause our stock price or trading volume to decline and might also impair our ability to expand our business with existing customers and attract new customers.

*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 expect that significant additional capital will be needed in the future to continue our planned operations, including increased marketing, hiring new personnel, commercializing our intended product, and continuing activities as an operating public company. To the extent we raise additional capital by issuing equity securities, our stockholders might experience substantial dilution. We might sell common stock, convertible securities or other equity securities in one or more transactions at prices and in a manner we determine from time to time. If we sell common stock, convertible securities or other equity securities in more than one transaction, investors might be materially diluted by subsequent sales. Such sales might also result in material dilution to our existing stockholders, and new investors could gain rights superior to our existing stockholders.

*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 currently anticipate that we will retain future earnings for the development, operation and expansion of our business and do not anticipate declaring or paying any cash dividends for the foreseeable future. Any return to stockholders will therefore be limited to the increase, if any, of our share price.

*We might be at risk of securities class action litigation.*

We might be at risk of securities class action litigation. In the past, biotechnology and pharmaceutical companies have experienced significant stock price volatility, particularly when associated with binary events such as clinical trials and product approvals. If we face such litigation, it could result in substantial costs and a diversion of management's attention and resources, which could harm our business and results in a decline in the market price of our common stock.

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***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.***

Our Certificate of Incorporation and our Amended and Restated Bylaws, and Delaware law could make it more difficult for a third party to acquire us, even if closing such a transaction would be beneficial to our stockholders. We are authorized to issue up to 10,000,000 shares of preferred stock. This preferred stock might be issued in one or more series, the terms of which might be determined at the time of issuance by our Board of Directors without further action by stockholders. The terms of any series of preferred stock might include voting rights (including the right to vote as a series on particular matters), preferences as to dividend, liquidation, conversion and redemption rights and sinking fund provisions. We have designated 350,000 shares of preferred stock as Series A Convertible Preferred Stock, all of which are issued and outstanding. The issuance of any preferred stock could materially adversely affect the rights of the holders of our common stock, and therefore, reduce the value of our common stock. In particular, specific rights granted to future holders of preferred stock could be used to restrict our ability to merge with, or sell our assets to, a third party and thereby preserve control by the present management.

Provisions of our Certificate of Incorporation and our Amended and Restated Bylaws and Delaware law also could have the effect of discouraging potential acquisition proposals or making a tender offer or delaying or preventing a change in control, including changes a stockholder might consider favorable. Such provisions might also prevent or frustrate attempts by our stockholders to replace or remove our management. In particular, the certificate of incorporation and bylaws and Delaware law, as applicable, among other things:

- provide the Board of Directors with the ability to alter the bylaws without stockholder approval;
- place limitations on the removal of directors;
- establishing advance notice requirements for nominations for election to the Board of Directors or for proposing matters that can be acted upon at stockholder meetings; and
- provide that vacancies on the Board of Directors might be filled by a majority of directors in office, although less than a quorum.

***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.***

As a publicly traded company we incur significant additional legal, accounting and other expenses. The obligations of being a public company in the United States require significant expenditures and will place significant demands on our management and other personnel, including costs resulting from public company reporting obligations under the Exchange Act and the rules and regulations regarding corporate governance practices, including those under the Sarbanes-Oxley Act, the Dodd-Frank Wall Street Reform and Consumer Protection Act, and the listing requirements of the stock exchange on which our securities are listed. These rules require the establishment and maintenance of effective disclosure and financial controls and procedures, internal control over financial reporting and changes in corporate governance practices, among many other complex rules that are often difficult to implement, monitor and maintain compliance with. Moreover, despite recent reforms made possible by the JOBS Act, the reporting requirements, rules, and regulations will make some activities more time-consuming and costly, particularly after we are no longer an “emerging growth company”. In addition, we expect these rules and regulations to make it more difficult and more expensive for us to obtain director and officer liability insurance. Our management and other personnel will need to devote a substantial amount of time to ensure that we comply with all of these requirements and to keep pace with new regulations, otherwise we might fall out of compliance and risk becoming subject to litigation or being delisted, among other potential problems.

***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.***

Section 404 of Sarbanes-Oxley requires annual management assessments of the effectiveness of our internal control over financial reporting. If we fail to comply with the rules under Sarbanes-Oxley related to disclosure 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. If material weaknesses or significant deficiencies are discovered or if we otherwise fail to achieve and maintain the adequacy of our internal control, we might not be able to ensure that we can conclude on an ongoing basis that we have effective internal controls over financial reporting in accordance with Section 404 of Sarbanes-Oxley. Moreover, effective internal controls are necessary for us to produce reliable financial reports and are important to helping prevent financial fraud. If we cannot provide reliable financial reports or prevent fraud, our business and operating results could be harmed, investors could lose confidence in our reported financial information, and the trading price of our common stock could drop significantly.

## **Risks Related to this Offering**

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

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

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

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

***There is no public market for the Warrants to purchase Common Stock being offered in this offering and the Concurrent Private Placement.***

There is no established public trading market for the Warrants being offered in this offering and the Concurrent Private Placement, and we do not expect a market to develop. In addition, we do not intend to apply for listing the Warrants on The Nasdaq Capital Market, or any other national securities exchange or any other trading system. Without an active market, the liquidity of the Warrants will be limited.



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

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## DILUTION

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

After giving effect to the issuance and sale of 180,000 shares of Common Stock at an offering price of \$6.00 per share and 403,334 Pre-Funded Warrants at an offering price of \$5.9999 per Pre-Funded Warrant and the exercise of all of the Pre-Funded Warrants at an exercise price of \$0.0001 per share, and after deducting estimated offering expenses payable by us in this offering, our pro forma net tangible book value as of March 31, 2023 would have been \$7,205,833, or \$3.20 per share of Common Stock. This represents an immediate increase in pro forma net tangible book value of \$0.75 per share to our existing stockholders and an immediate dilution in pro forma net tangible book value of \$2.80 per share to investors participating in this offering.

The following table illustrates this dilution on a per share basis:

Offering price per share		\$	6.00
Historical net tangible book value per share as of March 31, 2023	\$	2.45	
Increase in net tangible book value pro share attributable to this offering	\$	0.75	
Pro forma net tangible book value per share after this offering		\$	3.20
Dilution per share to new investors participating in this offering		\$	2.80

The table and calculations set forth above are based on the number of shares of Common Stock outstanding as of April 18, 2023 and assumes no exercise of any outstanding options or warrants. To the extent that outstanding options or warrants are exercised, new options or other equity grants are issued under or outside of our equity incentive plans or we otherwise issue additional shares of Common Stock in the future, there will be further dilution to new investors participating in this offering.

The number of shares of our common stock to be outstanding after this offering as shown above is based on 1,665,956 shares outstanding as of March 31, 2023, as adjusted for the 1-for-10 reverse stock split of June 2, 2023, and excludes as of that date:

- 72,917 shares of common stock issuable upon conversion of 350,000 shares of Series A Preferred Stock outstanding at a conversion rate of 0.2083 common shares per preferred share, reflecting an effective conversion price of \$48.00 per common share.
- 388,229 shares of common stock issuable upon exercise of outstanding common stock options issued to members of management, consultants, and directors at a weighted average exercise price of \$29.26 per common share.
- 190,031 shares of common stock issuable upon exercise of outstanding common stock warrants at an average exercise price of \$50.16 per common share.
- 153,021 shares of common stock reserved for future grants pursuant to the 2020 Stock Incentive Plan.
- 35,000 shares of common stock issuable upon exercise of warrants issued to the placement agent as part of the offering on July 18, 2023 at an exercise price of \$6.60 per common share (110% of the offering price of \$6.00 per share).
- 583,334 shares of Common Stock issuable upon exercise of the Common Warrants to be issued to the Purchasers in the Concurrent Private Placement.

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## USE OF PROCEEDS

Assuming all of the shares offered in this offering are sold, we estimate that our net proceeds from this offering will be approximately \$3,290,003.

We intend to use the net proceeds of this offering for continuing operating expenses and working capital.

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

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## DESCRIPTION OF SECURITIES

*The shares of Common Stock and Warrants and the shares of Common Stock issuable upon exercise of the Warrants offered in this offering will be issued pursuant to a securities purchase agreement, or Purchase Agreement, between each of the investors and us. We urge you to review the Purchase Agreement, the form of Pre-Funded Warrant and the form of Common Warrant, which will be filed as exhibits to a Current Report on Form 8-K.*

*The following brief summary of the material terms and provisions of the Warrants is subject to, and qualified in its entirety by, the form of Pre-Funded Warrant and the form of Common Warrant. This prospectus supplement also relates to the offering of the shares of our Common Stock issuable upon exercise, if any, of the Warrants issued to the investors in this offering.*

### Common Stock

We are authorized to issue 100,000,000 shares of Common Stock, par value \$0.0001 per share, and 10,000,000 shares of preferred stock, par value \$0.0001 per share.

On June 2, 2023, the Company effected a 1-for-10 reverse split of its issued and outstanding shares of Common Stock. While the Certificate of Amendment reduced the number

of outstanding shares of Common Stock, it did not reduce the number of authorized shares of Common Stock or preferred stock.

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

A description of the general terms and provisions of our Common Stock and each other class of our securities that qualifies or limits our Common Stock is set forth under the caption "Description of Capital Stock" on page 7 of the accompanying prospectus.

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### **Pre-Funded Warrants**

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

*Exercisability.* The holder may exercise the Pre-Funded Warrants immediately and at any time until the Pre-Funded Warrants are exercised in full. The Pre-Funded Warrants are exercisable, at the option of the holder, in whole or in part, by delivering to us a written exercise notice accompanied, within one trading day, by payment in full for the number of shares of our Common Stock purchased upon such exercise. The holder of Pre-Funded Warrants does not have the right to exercise any portion of the Pre-Funded Warrant if the holder would have beneficially owned in excess of 9.99% of the shares of our Common Stock outstanding immediately after giving effect to such purchase. This percentage may, however, be raised or lowered to an amount not to exceed 4.99% at the option of the holder upon at least 61 days' prior notice from the holder to us.

*Cashless Exercise.* At any time when a registration statement covering the issuance or resale of the shares of Common Stock issuable upon exercise of the Pre-Funded Warrants is not effective, the holder may exercise its Pre-Funded Warrants on a cashless basis. When exercised on a cashless basis, a portion of the Pre-Funded Warrants are cancelled in payment of the purchase price payable in respect of the number of shares of our Common Stock purchasable upon such exercise.

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

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

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

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

### **PRIVATE PLACEMENT TRANSACTION**

#### **Common Warrants**

*Unregistered.* In the Concurrent Private Placement, we are offering Common Warrants to purchase up to 583,334 shares of our Common Stock at an exercise price of \$6.00 per share. The exercise price and number of shares of Common Stock issuable upon the exercise of the Common Warrants will be subject to adjustment in the event of any stock dividend and split, reverse stock split, recapitalization, reorganization or similar transaction, as described in the Common Warrants.

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*Exercisability.* Each Common Warrant will be immediately exercisable for a term of five years from issuance. The Common Warrants are exercisable, at the option of the holder, in whole or in part, by delivering to us a written exercise notice accompanied, within one trading day, by payment in full for the number of shares of our Common Stock purchased upon such exercise (except in the case of a cashless exercise discussed below). The holder of Common Warrants does not have the right to exercise any portion of the Common Warrant if the holder would beneficially own in excess of 4.99% or 9.99%, as applicable, of the shares of our Common Stock outstanding immediately after giving effect to such purchase. This percentage may, however, be raised or lowered to an amount not to exceed 9.99% at the option of the holder upon at least 61 days' prior notice from the holder to us.

*Cashless Exercise.* The Common Warrants and the shares issuable upon exercise thereof are not being registered under the Securities Act and are not offered pursuant to this prospectus supplement and the accompanying prospectus. The Common Warrants are being offered pursuant to an exemption from the registration requirements of the Securities Act provided in Section 4(a)(2) of the Securities Act. Accordingly, the investor may only sell Common Stock issued upon exercise of the Common Warrants pursuant to an effective registration statement under the Securities Act covering the resale of those shares, an exemption under Rule 144 under the Securities Act or another applicable exemption under the Securities Act. At any time when a registration statement covering the issuance or resale of the shares of Common Stock issuable upon exercise of the Common Warrants is not effective, the holder may exercise its Common Warrants on a cashless basis. When exercised on a cashless basis, a portion of the Common Warrant is cancelled in payment of the purchase price payable in respect of the number of shares of our Common Stock purchasable upon such exercise.

*Exercise Price.* The exercise price of Common Stock purchasable upon exercise of the Common Warrants is \$6.00 per share. The exercise price and the number of shares issuable upon exercise of the Common Warrants is subject to appropriate adjustment in the event of recapitalization events, stock dividends, stock splits, stock combinations or similar events affecting our Common Stock.

*Transferability.* The Common Warrants may be transferred at the option of the holder without obtaining our consent.

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

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

**Registration Rights.** We have agreed to file a registration statement covering the resale of the shares of Common Stock underlying the Common Warrants within 30 days of the date of the Purchase Agreement. We must use commercially reasonable efforts to cause such registration statement to become effective within 60 days (90 days in the event the SEC elects to review such registration statement) following the filing of such registration statement and to keep such registration statement effective at all times until the Purchaser no longer owns any Common Warrants or shares of Common Stock underlying such Common Warrants.

## PLAN OF DISTRIBUTION

A.G.P./Alliance Global Partners has agreed to act as our exclusive placement agent in connection with this offering subject to the terms and conditions of the placement agency agreement dated July 18, 2023 (the “Placement Agency Agreement”). The Placement Agent is not purchasing or selling any of the securities offered by this prospectus supplement, nor is it required to arrange the purchase or sale of any specific number or dollar amount of securities, but has agreed to use its reasonable best efforts to arrange for the sale of all of the securities offered hereby. We have entered into the Purchase Agreement directly with the Purchaser in connection with this offering. The Purchase Agreement contains customary representations, warranties and covenants.

We will deliver the securities being issued to the Purchaser upon receipt of funds for the purchase of the securities offered pursuant to this prospectus supplement. We expect to deliver the shares of Common Stock and Pre-Funded Warrants being offered hereby on or about July 20, 2023.

We have agreed to indemnify the Placement Agent and specified other persons against specified liabilities, including liabilities under the Securities Act, and to contribute to payments the Placement Agent may be required to make in respect thereof.

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## Fees and Expenses

We have engaged A.G.P. as our exclusive placement agent in connection with this offering. This offering is being conducted on a reasonable “best efforts” basis and the Placement Agent has no obligation to buy any of the securities from us or to arrange for the purchase or sale of any specific number or dollar amount of securities. We have agreed to pay the Placement Agent a fee based on the aggregate proceeds as set forth in the table below:

	Per Share	Per Pre-Funded Warrant	Total <sup>(1)</sup>
Public offering price	\$ 6.00	\$ 5.9999	\$ 3,500,004
Placement agent fees <sup>(2)</sup>	\$ 0.36	\$ 0.3599	\$ 210,000
Proceeds, before expenses, to us	\$ 5.64	\$ 5.6399	\$ 3,290,003

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

(2) We have agreed to pay the Placement Agent a placement agent’s fee equal to 6.0% of the aggregate purchase price of the securities sold in this offering.

We estimate the total expenses payable by us for this offering (excluding the placement agent fee) will be approximately \$165,000, which amount includes: (i) a non-accountable expense allowance payable to the placement agent of \$15,000; (ii) reimbursement of the accountable expenses of the placement agent of \$75,000 related to the legal fees of the placement agent being paid by us (none of which has been paid in advance); and (iii) other estimated expenses of approximately \$75,000 which include our legal, accounting, and printing costs and various fees associated with the registration and listing of our securities.

## Placement Agent Warrants

We have agreed to issue warrants to the Placement Agent (the “Placement Agent Warrants”) to purchase up to 35,000 shares of our Common Stock, which represent 6.0% of the number of securities being sold in this offering. The Placement Agent Warrants will have substantially the same terms as the Common Warrants sold in the Concurrent Private Placement and have the same registration rights provided to the Purchaser under the Purchase Agreement.

## Regulation M

The Placement Agent may be deemed to be an underwriter within the meaning of Section 2(a)(11) of the Securities Act, and any commissions received by it and any profit realized on the resale of the securities sold by it while acting as principal might be deemed to be underwriting discounts or commissions under the Securities Act. As an underwriter, the Placement Agent would be required to comply with the requirements of the Securities Act and the Securities Exchange Act of 1934, as amended (the “Exchange Act”), including, without limitation, Rule 415(a)(4) under the Securities Act and Rule 10b-5 and Regulation M under the Exchange Act. These rules and regulations may limit the timing of purchases and sales of our securities by the Placement Agent acting as principal. Under these rules and regulations, the Placement Agent:

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

## Lock-Up Agreements

Our directors and officers have entered into lock-up agreements. Under these agreements, these individuals agreed, subject to specified exceptions, not to sell or transfer any shares of Common Stock or securities convertible into, or exchangeable or exercisable for, Common Stock during a period ending 90 days after the completion of this offering, without first obtaining the written consent of the Placement Agent. Specifically, these individuals agreed, in part, subject to certain exceptions, not to:

- offer for sale, sell, pledge, or otherwise transfer or dispose of (or enter into any transaction or device that is designed to, or could be expected to, result in the transfer or disposition by any person at any time in the future of) any shares of Common Stock or securities convertible into or exercisable or exchangeable for Common Stock;

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- enter into any swap or other derivatives transaction that transfers to another, in whole or in part, any of the economic benefits or risks of ownership of shares of Common Stock; or
- make any demand for or exercise any right or cause to be filed a registration statement, including any amendments thereto, with respect to the registration of any of our securities.

## No Sales of Similar Securities

We have agreed, subject to certain exceptions, not to issue, enter into any agreement to issue or announce the issuance or proposed issuance of, any shares of Common Stock (or securities convertible into or exercisable for Common Stock) or, subject to certain exceptions, file any registration statement, including any amendments or supplements thereto

(other than the prospectus supplement, registration statement or amendment to the registration statement relating to the securities offered hereunder and a registration statement on Form S-8), until 90 days after the completion of this offering. We have also agreed not to enter into a variable rate transaction (as defined in the securities purchase agreement) for 180 days after the completion of this offering.

#### Listing

Our common stock and warrants are listed on The Nasdaq Capital Market under the symbols “LIXT” and “LIXTW”, respectively.

#### Transfer Agent and Registrar

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

#### Other Activities and Relationships

The Placement Agent and certain of its affiliates are full service financial institutions engaged in various activities, which may include securities trading, commercial and investment banking, financial advisory, investment management, investment research, principal investment, hedging, financing and brokerage activities. The Placement Agent and certain of its affiliates may in the future perform various commercial and investment banking and financial advisory services for us, for which they will receive customary fees and expenses. However, except as disclosed in this prospectus supplement, we have no present arrangements with the Placement Agents for any services.

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### LEGAL MATTERS

The validity of the shares of common stock offered hereby will be passed upon for us by TroyGould PC, Los Angeles, California. Thompson Hine LLP, New York, New York, will advise on certain legal matters in connection with the offering on behalf of the Placement Agent.

#### EXPERTS

Weinberg & Company, P.A., an independent registered public accounting firm, audited our consolidated financial statements included in our Annual Report on Form 10-K for the fiscal year ended December 31, 2022, as set forth in their report, which includes an explanatory paragraph as to the Company’s ability to continue as a going concern, dated March 29, 2023, which is incorporated by reference in this prospectus supplement and elsewhere in the registration statement. Our consolidated financial statements are incorporated by reference in reliance on Weinberg & Company, P.A.’s report, given on the authority of such firm as experts in accounting and auditing.

#### WHERE YOU CAN FIND MORE INFORMATION

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

We have filed with the SEC a registration statement on Form S-3 (File No. 333-252430) under the Securities Act with respect to the shares of common stock offered by this prospectus supplement. When used in this prospectus supplement, the term “registration statement” includes amendments to the registration statement as well as the exhibits, schedules, financial statements and notes filed as part of the registration statement or incorporated by reference therein. This prospectus supplement, which constitutes a part of the registration statement, omits some information contained in the registration statement in accordance with SEC rules and regulations. You should review the information and exhibits in the registration statement for further information on us and our consolidated subsidiaries and the common stock we are offering by this prospectus supplement. Statements herein concerning any document we filed as an exhibit to the registration statement or that we otherwise filed with the SEC are not intended to be comprehensive and are qualified by reference to these filings. You should review the complete document to evaluate these statements. You can obtain a copy of the registration statement from the SEC at the address listed above or from the SEC’s website.

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### INCORPORATION OF DOCUMENTS BY REFERENCE

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

- Current Reports on Form 8-K, filed with the SEC on [August 6, 2019](#), [July 17, 2020](#), [August 18, 2020](#), [November 27, 2020](#), [December 2, 2020](#), [January 22, 2021](#), [March 3, 2021](#), [May 14, 2021](#), [June 3, 2021](#), [July 9, 2021](#), [September 20, 2021](#), [October 13, 2021](#), [March 23, 2022](#), [April 15, 2022](#), [May 13, 2022](#), [June 17, 2022](#), [June 23, 2022](#), [June 24, 2022](#), [October 11, 2022](#), [October 18, 2022](#), [November 10, 2022](#), [December 2, 2022](#), [December 6, 2022](#), [December 23, 2022](#), [February 10, 2023](#), [February 15, 2023](#), [April 5, 2023](#), [April 25, 2023](#), [May 10, 2023](#), [May 30, 2023](#), and [June 6, 2023](#);
- Quarterly Reports on Form 10-Q, filed with the SEC on [August 6, 2019](#), [May 11, 2020](#), [August 10, 2020](#), [November 10, 2020](#), [May 12, 2021](#), [August 10, 2021](#), [November 10, 2021](#), [May 10, 2022](#), [August 10, 2022](#), [November 8, 2022](#), and [May 10, 2023](#);
- Annual Reports on Form 10-K, filed with the SEC on [March 25, 2020](#), [March 26, 2021](#), [March 21, 2022](#), and [March 29, 2023](#).

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

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

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

Lixte Biotechnology Holdings, Inc.  
680 East Colorado Boulevard, Suite 180  
Pasadena, California 91101

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

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

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**PROSPECTUS****LIXTE BIOTECHNOLOGY HOLDINGS, INC.****\$20,000,000**

**Common Stock**  
**Preferred Stock**  
**Debt Securities**  
**Warrants**  
**Rights**  
**Units**

From time to time, we may offer and sell up to an aggregate amount of \$20,000,000 of any combination of the securities described in this prospectus in one or more offerings. We may also offer securities as may be issuable upon conversion, redemption, repurchase, exchange or exercise of any securities registered hereunder, including any applicable antidilution provisions. We may sell the securities to or through underwriters and also to other purchasers or through agents. The names of any underwriters or agents, and any fees, discounts or other compensation payable to them will be set forth in the applicable prospectus supplement accompanying this prospectus.

We will provide the specific terms of these offerings in one or more supplements to this prospectus. We may also authorize one or more free writing prospectuses to be provided to you in connection with these offerings. The prospectus supplement and any related free writing prospectus may also update or change information contained in this prospectus. You should carefully read this prospectus, the applicable prospectus supplement and any related free writing prospectus, as well as any documents incorporated by reference, before buying any of the securities being offered. **This prospectus may not be used to consummate a sale of securities unless it is accompanied by the applicable prospectus supplement.**

Our common stock is listed on The Nasdaq Capital Market under the symbol "LIXT." On January 25, 2021, the last reported sale price of our common stock on The Nasdaq Capital Market was \$3.33 per share.

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

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

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

The date of this prospectus is February 5, 2021.

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## ABOUT THIS PROSPECTUS

This prospectus is part of a registration statement that we filed with the Securities and Exchange Commission (the “SEC”) using a “shelf” registration process. Under this shelf registration process, we may, from time to time, offer and sell, either individually or in combination, in one or more offerings, up to a total dollar amount of \$20,000,000 of shares of our common stock (“Common Stock”), preferred stock (“Preferred Stock”), various series of debt securities, rights to purchase shares of our Common Stock or Preferred Stock, and/or warrants to purchase any such securities, either individually or as units comprised of a combination of one or more of the other securities.

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

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

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

Unless the context otherwise indicates, references in this prospectus to “Lixte,” “we,” “us,” “our,” and the “Company” refer, collectively, to Lixte Biotechnology Holdings, Inc., a Delaware corporation. When we refer to “you,” we mean the potential holders of the applicable series of securities.

### NOTE ABOUT FORWARD-LOOKING STATEMENTS

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

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

## PROSPECTUS SUMMARY

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

### *The Company*

#### Company Overview

We are a drug discovery company that uses biomarker technology to identify enzyme targets associated with serious common diseases and then designs novel compounds to attack those targets. Our product pipeline is primarily focused on inhibitors of protein phosphatases, used alone and in combination with cytotoxic agents and/or x-ray and immune checkpoint blockers, and encompasses two major categories of compounds at various stages of pre-clinical and clinical development that we believe have broad therapeutic potential not only for cancer but also for other debilitating and life-threatening diseases.

We have developed two series of pharmacologically active drugs, the LB-100 series and the LB-200 series. We believe that the mechanism by which compounds of the LB-100 series affect cancer cell growth is different from cancer agents currently approved for clinical use. Lead compounds from each series have activity against a broad spectrum of common and rarer human cancers in cell culture systems. In addition, compounds from both series have anti-cancer activity in animal models of glioblastoma multiforme, neuroblastoma, and medulloblastoma, all cancers of neural tissue. Lead compounds of the LB-100 series also have activity against melanoma, breast cancer and sarcoma in animal models and enhance the effectiveness of commonly used anti-cancer drugs in these model systems. 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, our compounds will improve therapeutic benefit without enhancing toxicity in humans.

Our activities are subject to significant risks and uncertainties, including the need for additional capital, as described below. We have not yet commenced any revenue-generating operations, do not have positive cash flows from operations, and are dependent on periodic infusions of equity capital to fund our operating requirements.

## Product Candidates

The LB-100 series consists of novel structures which have the potential to be first in their class and may be useful in the treatment of not only several types of cancer but also vascular and metabolic diseases. The LB-200 series contains compounds which have the potential to be the most effective in its class and may be useful for the treatment of chronic hereditary diseases, such as Gaucher's disease, in addition to cancer and neurodegenerative diseases.

We have demonstrated that lead compounds of both the LB-100 series and the LB-200 are active against a broad spectrum of human cancers in cell culture and against several types of human cancers in animal models. The research on these compounds was initiated in 2006 under a Cooperative Research and Development Agreement, or 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. As discussed below, our primary focus is on the clinical development of LB-100.

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The LB-200 series consists of histone deacetylase inhibitors (HDACi). Many pharmaceutical companies are also developing drugs of this type, and at least two companies have HDACi approved for clinical use, in both cases for the treatment of a type of lymphoma. Despite this significant competition, we have demonstrated that our HDACi have broad activity against many cancer types, have neuroprotective activity, and have anti-fungal activity. In addition, these compounds have low toxicity. LB-200 has not yet 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 pre-clinical development of our LB-200 series of compounds at this time. At this time, we intend to only maintain composition of matter patents for LB-200.

Collaborations with leading academic research centers in the United States, Europe and Asia have established the breadth of activity of LB-100 in pre-clinical models of several major cancers. There is considerable scientific interest in LB-100 because it exerts its activity by a novel mechanism and is the first of its type to be evaluated so broadly in multiple animal models of cancer and now in human beings. LB-100 is one of a series of serine/threonine phosphatase (s/t ptase) inhibitors designed by us. The s/t ptases are ubiquitous enzymes that regulate many cell signaling networks important to cell growth, division and death. The s/t ptases have long been appreciated as potentially important targets for anti-cancer drugs. However, because of the multi-functionality of these enzymes, it had been widely held that pharmacologic inhibitors of s/t ptases would be too toxic to allow their development as anti-cancer treatments, but we have shown that this is not the case. LB-100 was well tolerated at doses associated with objective regression (significant tumor shrinkage) and/or the arresting of tumor progression in patients with progressive cancers.

Pre-clinical studies showed that LB-100 itself inhibits a spectrum of human cancers and that combined with standard cytotoxic drugs and/or radiation, LB-100 potentiates their effectiveness against hematologic and solid tumor cancers without enhancing toxicity. Given at very low doses in animal models of cancer, LB-100 markedly increased the effectiveness of a PD-1 blocker, one of the widely used new immunotherapy drugs. This finding raises the possibility that LB-100 may further expand the value of the expanding field of cancer immunotherapy.

We completed a Phase 1 clinical trial of LB-100 to evaluate its safety that showed it is associated with antitumor activity in humans at doses that are readily tolerable. Responses included objective regression (tumor shrinkage) lasting for 11 months of a pancreatic cancer and cessation of growth (stabilization of disease) for 4 months or more of 9 other progressive solid tumors out of 20 patients who had measurable disease. As Phase 1 clinical trials are fundamentally designed to determine safety of a new compound in humans, we were encouraged by these results. The next step is to demonstrate in Phase 2 clinical trials the efficacy of LB-100 in one or more specific tumor types, against which the compound has well documented activity in pre-clinical models.

## Current Studies

**Moffitt.** Effective August 20, 2018, we entered into a Clinical Trial Research Agreement with the Moffitt Cancer Center and Research Institute Hospital Inc., Tampa, Florida, effective for a term of five years, unless terminated earlier by us pursuant to 30 days written notice. Pursuant to the Clinical Trial Research Agreement, Moffitt agreed to conduct and manage a Phase 1b/2 clinical trial to evaluate the therapeutic benefit of our lead anti-cancer clinical compound LB-100 to be administered intravenously in patients with low or intermediate-1 risk myelodysplastic syndrome (MDS).

In November 2018, we received approval from the U.S. Food and Drug Administration or "FDA" for our Investigational New Drug or "IND" Application to conduct a Phase 1b/2 clinical trial to evaluate the therapeutic benefit of LB-100 in patients with low and intermediate-1 risk MDS who have failed or are intolerant of standard treatment. Patients with MDS, although usually older, are generally well except for severe anemia requiring frequent blood transfusions. This Phase 1b/2 clinical trial utilizes LB-100 as a single agent in the treatment of patients with low and intermediate-1 risk MDS, including patients with del(5q) myelodysplastic syndrome (del5qMDS) failing first line therapy. The bone marrow cells of patients with del5qMDS are deficient in PP2A by virtue of an acquired mutation and are especially vulnerable to further inhibition of PP2A by LB-100. The clinical trial began at a single site in April 2019 and the first patient was entered into the clinical trial in July 2019. A total enrollment of 41 patients is planned.

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**GEIS.** As of 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 clinical trial to obtain information about 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 therapeutic gain 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.

**NCI.** During the fourth quarter of 2019, the National Cancer Institute, or NCI, enrolled the first two patients of a planned eight patient pharmacologic study of the ability of LB-100 to enter the brain and penetrate recurrent brain tumors in patients where surgical removal of the cancers is indicated (clinical trials registry NCT03027388). This study is being conducted and funded by the NCI under a CRADA with us; additional information will be reported by us as it is provided by the NCI.

**City of Hope.** Effective January 18, 2021, we entered into a Clinical Trials Agreement with the City of Hope to carry out a Phase 1b clinical trial of LB-100, combined with a standard regimen for untreated, extensive stage-disease small cell lung cancer (ED-SCLC). LB-100 will be given in combination with carboplatin, etoposide and Atelolizumab, an FDA approved but marginally effective regimen, to previously untreated ED-SCLC patients. The dose of LB-100 will be escalated with fixed doses of the 3-drug regimen to reach a recommended Phase 2 dose (RP2D).

## Risks Associated with Our Business

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

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

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- Our future success is dependent on the regulatory approval of our product candidate.
- Our business may be adversely affected by the ongoing coronavirus pandemic.
- Business interruptions could adversely affect future operations, revenues, and financial conditions, and may increase our cost of expenses.
- Our failure to find third party collaborators to assist or share in the costs of product development could materially harm our business, financial condition, and results of operations.
- If we fail to comply with our obligations under our license agreement with licensors, we could lose rights that are important to our business.
- We may infringe the intellectual property rights of others, which may prevent or delay our product development efforts.
- Our intellectual property may not be sufficient to protect our products from competition.

Our principal place of business is located 248 Route 25A No. 2, East Setauket, NY 11733. (631) 880-2907. Our telephone number is (631) 880-2907. Our corporate website address is [www.lixte.com](http://www.lixte.com). Information contained on or accessible through our website is not a part of this prospectus, and the inclusion of our website address in this prospectus is an inactive textual reference only.

For more information about our company, please refer to other documents that we have filed with the SEC and that are incorporated by reference into this prospectus, as listed under the heading "Incorporation by Reference."

## RISK FACTORS

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

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

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## THE SECURITIES WE MAY OFFER

We may offer shares of Common Stock and Preferred Stock, various series of debt securities, rights to purchase shares of Common Stock and Preferred Stock, and/or warrants to purchase any such securities, either individually or in combination, up to a total dollar amount of \$20,000,000 from time to time under this prospectus, together with any applicable prospectus supplement and any related free writing prospectuses, at prices and on terms to be determined by market conditions at the time of any offering. This prospectus provides you with a general description of the securities we may offer. Each time we offer a type or series of securities under this prospectus, we will provide a prospectus supplement that will describe the specific amounts, prices and other important terms of the securities, including, to the extent applicable:

- designation or classification;
- aggregate principal amount or aggregate offering price;
- maturity;



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

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

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

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

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

**USE OF PROCEEDS**

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

**DESCRIPTION OF CAPITAL STOCK**

*The following is a summary description of the Common Stock, which does not purport to be complete and is summarized from, and is qualified in its entirety by reference to, our Certificate of Incorporation, as amended, and Amended and Restated Bylaws, and Certificate of Designation, to which you should refer and copies of which are incorporated herein by reference as Exhibits 3.1 - 3.4, 3.5 - 3.7, 4.1 and 4.2, respectively, and to the registration statement on Form S-3 of which this prospectus forms a part. The summary below is also qualified by provisions of applicable law, including the Delaware General Corporation Law.*

**Common Stock**

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

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

The holders of a majority of the shares of our capital stock, represented in person or by proxy, are necessary to constitute a quorum for the transaction of business at any meeting. If a quorum is present, an action by stockholders entitled to vote on a matter is approved if the number of votes cast in favor of the action exceeds the number of votes cast in opposition to the action, with the exception of the election of directors, which requires a plurality of the votes cast.

**Preferred Stock**

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

of a majority of the holders of such series. The holders of each tranche of 175,000 shares are entitled to receive a per share dividend equal to 1% of our annual net revenue divided by 175,000, until converted or redeemed. Each share of Series A Convertible Preferred Stock may be converted, at the option of the holder, into 2.083 shares of common stock (subject to customary anti-dilution provisions), and as subject to mandatory conversions at the conversion rate in the event of a merger or sale transaction resulting in gross proceeds to us of at least \$21,875,000. Each share has a liquidation preference based on its assumed conversion into shares of common stock. We have a right to redeem the Series A Convertible Preferred Stock up to the fifth anniversary of their respective closing dates (March 17, 2015 and January 21, 2016) at a price per share equal to \$50.

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

- the title and stated value;
- the number of shares being offered;
- the liquidation preference per share;
- the purchase price per share;
- the dividend rate per share, dividend period and payment dates and method of calculation for dividends;
- whether dividends will be cumulative or non-cumulative and, if cumulative, the date from which dividends will accumulate;
- our right, if any, to defer payment of dividends and the maximum length of any such deferral period;
- the procedures for any auction and remarketing, if any;
- the provisions for a sinking fund, if any;
- the provisions for redemption or repurchase, if applicable, and any restrictions on our ability to exercise those redemption and repurchase rights;
- any listing of the Preferred Stock on any securities exchange or market;
- whether the Preferred Stock will be convertible into Common Stock, and the conversion rate or conversion price, or how they will be calculated, and the exchange period;
- voting rights, if any, of the Preferred Stock;
- preemption rights, if any;

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- restrictions on transfer, sale or other assignment, if any;
- a discussion of any material or special United States federal income tax considerations applicable to the Preferred Stock;
- the relative ranking and preferences of the Preferred Stock as to dividend rights and rights if we liquidate, dissolve or wind up our affairs;
- the limitations on issuances of any class or series of Preferred Stock ranking senior to or on a parity with the series of Preferred Stock being issued as to dividend rights and rights if we liquidate, dissolve or wind up our affairs; and
- any other specific terms, rights, preferences, privileges, qualifications or restrictions of the Preferred Stock.

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

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

##### ***Delaware Law***

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

##### ***Board of Directors Vacancies***

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

##### ***Stockholder Action; Special Meeting of Stockholders***

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

##### ***Advance Notice Requirements for Stockholder Proposals and Director Nominations***

Our Amended and Restated Bylaws provide that stockholders seeking to bring business before our annual meeting of stockholders, or to nominate candidates for election as directors at our annual meeting of stockholders, must provide timely notice of their intent in writing. To be timely, a stockholder's notice must be delivered to the secretary at our principal executive offices not later than the close of business on the 90<sup>th</sup> day nor earlier than the close of business on the 120<sup>th</sup> day prior to the first anniversary

of the preceding year's annual meeting; provided, however, that in the event the date of the annual meeting is more than 30 days before or more than 60 days after such anniversary date, or if no annual meeting was held in the preceding year, notice by the stockholder to be timely must be so delivered not earlier than the close of business on the 120<sup>th</sup> day prior to such annual meeting and not later than the close of business on the later of the 90<sup>th</sup> day prior to such annual meeting or the 10<sup>th</sup> day following the day on which a public announcement of the date of such meeting is first made by us. These provisions may preclude our stockholders from bringing matters before our annual meeting of stockholders or from making nominations for directors at our annual meeting of stockholders.

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

#### **Transfer Agent and Registrar**

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

#### **NASDAQ Capital Market**

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

#### **DESCRIPTION OF DEBT SECURITIES**

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

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

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

#### **General**

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

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

- the title and ranking of the debt securities (including the terms of any subordination provisions);

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

- the designation of the currency, currencies or currency units in which payment of principal of, and premium and interest on, the debt securities will be made;
- if payments of principal of, or premium or interest on, the debt securities will be made in one or more currencies or currency units other than that or those in which the debt securities are denominated, the manner in which the exchange rate with respect to these payments will be determined;

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

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

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

#### **Transfer and Exchange**

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

#### **Certificated Debt Securities**

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

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

#### **Global Debt Securities and Book-Entry System**

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

#### **Covenants**

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

#### **No Protection in the Event of a Change of Control**

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

#### **Consolidation, Merger and Sale of Assets**

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

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

- certain other conditions are met.

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

#### Events of Default

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

- default in the payment of any interest upon any debt security of that series when it becomes due and payable, and continuance of such default for a period of 30 days (unless the entire amount of the payment is deposited by us with the trustee or with a paying agent prior to the expiration of the 30-day period);

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

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

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

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

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

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

- that holder has previously given to the trustee written notice of a continuing event of default with respect to debt securities of that series; and

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

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

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

#### Modification and Waiver

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

- to cure any ambiguity, defect or inconsistency;
- to comply with covenants in the indenture described above under the heading “Consolidation, Merger and Sale of Assets”;
- to provide for uncertificated securities in addition to or in place of certificated securities;
- to add guarantees with respect to debt securities of any series or secure debt securities of any series;

- to surrender any of our rights or powers under the indenture;
- to add covenants or events of default for the benefit of the holders of debt securities of any series;
- to comply with the applicable procedures of the Depositary;
- to make any change that does not adversely affect the rights of any holder of debt securities;
- to provide for the issuance of and establish the form and terms and conditions of debt securities of any series as permitted by the indenture;
- to effect the appointment of a successor trustee with respect to the debt securities of any series and to add to or change any of the provisions of the indenture to provide for or facilitate administration by more than one trustee; or
- to comply with requirements of the SEC in order to effect or maintain the qualification of the indenture under the Trust Indenture Act of 1939.

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

- reduce the amount of debt securities whose holders must consent to an amendment, supplement or waiver;
- reduce the rate of or extend the time for payment of interest (including default interest) on any debt security;
- reduce the principal of or premium on or change the fixed maturity of any debt security or reduce the amount of, or postpone the date fixed for, the payment of any sinking fund or analogous obligation with respect to any series of debt securities;
- reduce the principal amount of discount securities payable upon acceleration of maturity;
- waive a default or event of default in the payment of the principal of, or premium or interest on, any debt security (except a rescission of acceleration of the debt securities of any series by the holders of at least a majority in aggregate principal amount of the outstanding debt securities of that series and a waiver of the payment default that resulted from such acceleration);
- make the principal of, or premium or interest on, any debt security payable in a currency other than that stated in the debt security;
- make any change to certain provisions of the indenture relating to, among other things, the right of the holders of debt securities to receive payment of the principal of, and premium and interest on, those debt securities and to institute suit for the enforcement of any such payment and to waivers or amendments; or
- waive a redemption payment with respect to any debt security.

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

#### **Defeasance of the Debt Securities and Certain Covenants in Certain Circumstances**

##### **Legal Defeasance**

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

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

##### **Defeasance of Certain Covenants**

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

- we may omit to comply with the covenant described under the heading “Consolidation, Merger and Sale of Assets” and certain other covenants set forth in the indenture, as well as any additional covenants that may be set forth in the applicable prospectus supplement; and
- any omission to comply with those covenants will not constitute a default or an event of default with respect to the debt securities of that series (a “covenant defeasance”).

The conditions include:

- depositing with the trustee cash and/or U.S. government obligations or, in the case of debt securities denominated in a single currency other than U.S. dollars, cash and/or government obligations of the government that issued or caused to be issued such currency, that, through the payment of interest and principal in accordance with their terms, will provide cash in an amount sufficient in the opinion of a nationally recognized firm of independent public accountants or investment bank to pay and discharge each installment of principal of, premium and interest on, and any mandatory sinking fund payments in respect of, the debt securities of that series on the stated maturity of those payments in accordance with the terms of the indenture and those debt securities; and
- delivering to the trustee an opinion of counsel to the effect that we have received from, or there has been published by, the U.S. Internal Revenue Service a ruling or, since the date of execution of the indenture, there has been a change in the applicable U.S. federal income tax law, in either case to the effect that, and based thereon such opinion shall confirm that, the holders of the debt securities of that series will not recognize income, gain or loss for U.S. federal income tax purposes as a result of the deposit and related covenant defeasance and will be subject to U.S. federal income tax on the same amounts and in the same manner and at the same times as would have been the case if the deposit and related covenant defeasance had not occurred.

#### **No Personal Liability of Directors, Officers, Employees or Stockholders**

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

#### **Governing Law**

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

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

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

#### **DESCRIPTION OF WARRANTS**

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

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

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

- the number of shares of Common Stock or Preferred Stock purchasable upon the exercise of warrants to purchase such shares and the price at which such number of shares may be purchased upon exercise;
- a summary of the terms (including, without limitation, liquidation, dividend, conversion and voting rights) of the series of Preferred Stock purchasable upon exercise of warrants to purchase Preferred Stock as set forth in the certificate of designations for such series of Preferred Stock;

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

Holders of equity warrants will not be entitled:

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

Each warrant will entitle its holder to purchase the principal amount of debt securities or the number of shares of Preferred Stock or Common Stock at the exercise

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

## DESCRIPTION OF RIGHTS

### *General*

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

- the date of determining the stockholders entitled to the rights distribution;

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

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

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

### *Rights Agent*

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

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## DESCRIPTION OF UNITS

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

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



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

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

#### LEGAL OWNERSHIP OF SECURITIES

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

#### Book-Entry Holders

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

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

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

#### Street Name Holders

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

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

#### Legal Holders

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

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

#### Special Considerations for Indirect Holders

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

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

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

### **Global Securities**

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

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

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

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

### **Special Considerations for Global Securities**

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

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

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

- the depositary's policies, which may change from time to time, will govern payments, transfers, exchanges and other matters relating to an investor's interest in a global security;
- we and any applicable trustee have no responsibility for any aspect of the depositary's actions or for its records of ownership interests in a global security, nor do we or any applicable trustee supervise the depositary in any way;
- the depositary may, and we understand that DTC will, require that those who purchase and sell interests in a global security within its book-entry system use immediately available funds, and your broker or bank may require you to do so as well; and
- financial institutions that participate in the depositary's book-entry system, and through which an investor holds its interest in a global security, may also have their own policies affecting payments, notices and other matters relating to the securities.

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

### **Special Situations When a Global Security Will Be Terminated**

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

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

- if the depositary notifies us that it is unwilling, unable or no longer qualified to continue as depositary for that global security and we do not appoint another institution to act as depositary within 90 days;
- if we notify any applicable trustee that we wish to terminate that global security; or
- if an event of default has occurred with regard to securities represented by that global security and has not been cured or waived.

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

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

- at a fixed price or prices, which may be changed;
- at market prices prevailing at the time of sale;
- at prices related to such prevailing market prices; or
- at negotiated prices.

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

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

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

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

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

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

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

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

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

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

#### LEGAL MATTERS

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

#### EXPERTS

The financial statements of Lixte Biotechnology Holdings, Inc. as of December 31, 2019, and 2018 and for the years then ended, incorporated by reference in this prospectus have been so incorporated in reliance on the report of Weinberg & Co., P.A., an independent registered public accounting firm, given on the authority of said firm as experts in auditing and accounting.

## WHERE YOU CAN FIND MORE INFORMATION

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

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

## INFORMATION INCORPORATED BY REFERENCE

The rules of the SEC allow us to “incorporate by reference” into this prospectus information that we have filed with the SEC under the Commission File No. 000-51436. This means we can disclose important information to you without actually including the specific information in this prospectus by referring you to SEC filings that contain that information. The information incorporated by reference is considered to be a part of this prospectus, provided that it will be automatically updated and superseded by information that we file later with the SEC. This prospectus incorporates by reference the documents listed below:

- Our Annual Report on Form 10-K for the year ended [December 31, 2019](#) filed with the SEC on March 25, 2020; and

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- Our Quarterly Report on Form 10-Q for the quarters ended [March 31, 2020](#), [June 30, 2020](#) and [September 30, 2020](#) filed with the SEC on May 11, 2020, August 10, 2020 and November 11, 2020, respectively;
- Our Current Reports on Form 8-K filed with the SEC on July 17, 2020, [August 18, 2020](#), [November 27, 2020](#), [December 2, 2020](#) and [January 22, 2021](#);
- the description of the Common Stock incorporated by reference to our Registration Statement on [Form 8-A](#) that was filed with the SEC on November 17, 2020, including any amendment or report filed for the purpose of updating such description; and
- all reports and other documents subsequently filed by us pursuant to Sections 13(a), 13(c), 14 and 15(d) of the Exchange Act after the date of this prospectus and prior to the termination or completion of the offering of securities under this prospectus shall be deemed to be incorporated by reference in this prospectus and to be a part hereof from the date of filing such reports and other documents.

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

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

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

248 Route 25A No. 2  
East Setauket, NY 11733  
Attention: Vice President Business Administration  
Telephone: (631) 880-2907

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

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**LIXTE BIOTECHNOLOGY HOLDINGS, INC.**

**180,000 Shares of Common Stock  
Pre-Funded Warrants to Purchase up to 403,334 Shares of Common Stock  
Up to 403,334 Shares of Common Stock underlying such Pre-Funded Warrants**

**Sole Placement Agent**

# **A.G.P.**

**The date of this prospectus supplement is July 18, 2023.**

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