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

FORM 10-K

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

For the fiscal year ended December 31, 2021

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

For the transition period from _____ to _____

Commission file number: **000-51476**

LIXTE BIOTECHNOLOGY HOLDINGS, INC.
(Exact name of registrant as specified in its charter)

Delaware	**20-2903526**
(State or other jurisdiction of incorporation or organization)	(I.R.S. Employer Identification Number)
680 East Colorado Boulevard, Suite 180 Pasadena, California	**91101**
(Address of principal executive offices)	(Zip Code)

Registrant's telephone number: **(631) 830-7092**

Securities registered pursuant to Section 12(b) of the Act: Common Stock, $0.0001 par value.

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

Indicate by check mark if the registrant is a well-known seasoned issuer as defined in Rule 405 of the Securities Act. Yes ☐No ☒

Indicate by check mark if the registrant is not required to file reports pursuant to Section 13 or 15(d) of the Exchange Act. Yes ☐No ☒

Indicate by check mark whether the registrant (1) has filed all reports required to be filed by Section 13 or 15(d) of the Securities Exchange Act of 1934 during the preceding 12 months (or for such shorter period that the registrant was required to file such reports), and (2) has been subject to such filing requirements for the past 90 days. Yes ☒ No ☐

Indicate by check mark whether the registrant has submitted electronically every Interactive Data File required to be submitted pursuant to Rule 405 of Regulation S-T (§ 232.405 of this chapter) during the preceding 12 months (or for such shorter period that the registrant was required to submit such files). Yes ☒ No ☐

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

Large accelerated filer	☐	Accelerated filer	☐
Non-accelerated filer	☒	Smaller reporting company	☒
		Emerging growth company	☐

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised accounting standards provided pursuant to Section 13(a) of the Exchange Act. ☐

Indicate by check mark whether the registrant has filed a report on and attestation to its management's assessment of the effectiveness of its internal control over financial reporting under Section 404(b) of the Sarbanes-Oxley Act (15 U.S.C. 7262(b)) by the registered public accounting firm that prepared or issued its audit report. ☐

Indicate by check mark whether registrant is a shell company (as defined in Rule 12b-2 of the Exchange Act):
Yes ☐ No ☒

The aggregate market value of the common stock held by non-affiliates of the registrant as of June 30, 2021 was approximately **$**0,550,000.

The Company had 13,746,593 shares of common stock, $0.0001 par value, issued and outstanding as of March 11, 2022.

Documents incorporated by reference: None.

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Introductory Comment

Throughout this Annual Report on Form 10-K, the terms "we," "us," "our," "our company," "Lixte," the "Company" and the "Registrant" refer to Lixte Biotechnology Holdings, Inc., a Delaware corporation, and Lixte Biotechnology, Inc., a Delaware corporation, our wholly-owned subsidiary.

FORWARD-LOOKING STATEMENTS

This Annual Report on Form 10-K (the "Report") contains certain forward-looking statements. For example, statements regarding our financial position, business strategy and other plans and objectives for future operations, and assumptions and predictions about future product demand, supply, manufacturing, costs, marketing and pricing factors are all forward-looking statements. These statements are generally accompanied by words such as "intend," "anticipate," "believe," "estimate," "potential(ly)," "continue," "forecast," "predict," "plan," "may," "will," "could," "would," "should," "expect" or the negative of such terms or other comparable terminology. We believe that the assumptions and expectations reflected in such forward-looking statements are reasonable, based on information available to us on the date hereof, but we cannot assure you that these assumptions and expectations will prove to have been correct or that we will take any action that we may presently be planning. However, these forward-looking statements are inherently subject to known and unknown risks and uncertainties. Actual results or experience may differ materially from those expected or anticipated in the forward-looking statements. Factors that could cause or contribute to such differences include, but are not limited to, regulatory policies, competition from other similar businesses, and market and general policies, competition from other similar businesses, and market and general economic factors. This discussion should be read in conjunction with the consolidated financial statements and notes thereto included in this Report.

If one or more of these or other risks or uncertainties materialize, or if our underlying assumptions prove to be incorrect, actual results may vary materially from what we project. Any forward-looking statement you read in this Report reflects our current views with respect to future events and is subject to these and other risks, uncertainties and assumptions relating to our operations, results of operations, growth strategy, and liquidity. All subsequent forward-looking statements attributable to us or individuals acting on our behalf are expressly qualified in their entirety by this paragraph. You should specifically consider the factors identified in this Report, which would cause actual results to differ before making an investment decision. We are under no duty to update any of these forward-looking statements after the date of this Report or to conform these statements to actual results.

PART I

ITEM 1. BUSINESS

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 animal models. 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.

Description of Business; Research; Clinical Trial Activities

Our primary focus is developing new treatments for human cancers for which better therapies are urgently needed.

Our drug discovery process is based on discerning clues to potential new targets for disease treatments reported in the increasingly large body of literature identifying the molecular variants which characterize human cancers and other non-cancer disorders. We design drugs for which there are existing data suggesting that they may affect the altered pathways of the cancer cell and may be given safely to humans. We seek to rapidly arrive at patentable structures through analysis of the literature rather than screening of thousands of structures for activity against a particular biochemical pathway.

This approach has led to the development of two classes of drugs for the treatment of cancer, consisting of protein phosphatase inhibitors (PTase-i), designated by us as the LB-100 series of compounds, and histone deacetylase inhibitors (HDACi), designated by us as the LB-200 series of compounds.

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.

Effective treatment of brain tumors depends upon the ability of compounds to penetrate a physiological barrier known as the "blood-brain barrier" which protects the brain from exposure to potentially toxic substances in the blood. Because there is no certainty that our compounds will be active against tumors confined to the brain, the LB-100 compounds have been studied against a variety of common and rare cancer types and have been shown to potentiate the activity of standard anti-cancer drugs in animal models of breast and pancreatic cancer, melanoma, pheochromocytomas and sarcomas. Because the LB-100 compounds appear to exert their ability to improve the effectiveness of different forms of chemotherapy and radiation therapy by inhibiting a process upon which most, if not all, cancer cell types depend on to survive treatment, we believe the LB-100 series of compounds may be useful against most, if not all, cancer types.

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 our 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.

Clinical Trial Agreements

Moffitt Cancer Center Clinical Trial Research Agreement

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, the Company received approval from the U.S. Food and Drug Administration for its Investigational New Drug Application ("IND") 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. An interim analysis will be done after the first 21 patients are entered. If there are 3 or more responders but fewer than 7, an additional 20 patients will be entered. If at any point there are 7 or more responders, this will be sufficient evidence to support continued development of LB-100 for the treatment of low and intermediate-1 risk MDS. Recruitment has been slow and the Covid-19 pandemic has further reduced recruitment of patients into the protocol. At the current rate of accrual, the clinical trial is expected to be completed by June 30, 2025. However, with additional funds, the Company would consider adding two additional MDS centers to the Phase 2 portion of the study to accelerate patient accrual.

Spanish Sarcoma Group Collaboration Agreement

Effective July 31, 2019, the Company entered into a Collaboration Agreement for an Investigator-Initiated Clinical Trial with the Spanish Sarcoma Group (Grupo Español de Investigación en Sarcomas or "GEIS"), Madrid, Spain, to carry out a study entitled "Randomized phase I/II trial of LB-100 plus doxorubicin vs. doxorubicin alone in first line of advanced soft tissue sarcoma". The purpose of this clinical trial is to obtain information with respect to the efficacy and safety of LB-100 combined with doxorubicin in soft tissue sarcomas. Doxorubicin is the global standard for initial treatment of advanced soft tissue sarcomas ("ASTS"). Doxorubicin alone has been the mainstay of first line treatment of ASTS for over 40 years, with little 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.

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

The Company had previously expected that this clinical trial would commence during the quarter ended June 30, 2020. However, during July 2020, the Spanish regulatory authority advised the Company that although it had approved the scientific and ethical basis of the protocol, it required that the Company manufacture new inventory of LB-100 under current Spanish pharmaceutical manufacturing standards. These regulations were adopted subsequent to the production of the Company's existing LB-100 inventory.

A new batch of LB 100 has been prepared and is now undergoing the multitude of analytical studies of the formulated product necessary to gain approval for use in the European Union. Regulatory reviews by the European Union have been delayed, as a result of which the final review of the clinical product by Spanish regulatory authorities will also be delayed. Accordingly, the clinical trial is now estimated to begin during the quarter ending June 30, 2022 and be completed by June 30, 2025.

The interim analysis of this clinical trial could indicate either inferiority or superiority of LB-100 plus doxorubicin as compared to doxorubicin alone. A positive study would have the potential to change the standard therapy for this disease after four decades of failure to improve the marginal benefit of doxorubicin alone.

In order to manufacture a new inventory supply of LB-100 for the GEIS clinical trial, the Company has engaged a number of vendors to carry out the multiple tasks needed to make and gain approval of a new clinical product for investigational study in Spain. These tasks include the synthesis under good manufacturing practices (GMP) of the active pharmacologic ingredient (API), with documentation of each of the steps involved by an independent auditor. The API is then transferred to a vendor that prepares the clinical drug product, also under GMP conditions documented by an independent auditor. The clinical drug product is then sent to a vendor to test for purity and sterility, provide appropriate labels, store the drug, and distribute the drug to the clinical centers for use in the clinical trials. A formal application documenting all steps taken to prepare the clinical drug product for clinical use must be submitted to the appropriate regulatory authorities for review and approval before being used in a clinical trial.

On November 2, 2021, the Company entered into a Development Agreement with Famar Health Care Services Madrid SA to prepare a new batch of clinical LB-100 for use in clinical trials to be conducted in the European Union.

NCI Pharmacologic Study

In May 2019, the National Cancer Institute (NCI) initiated a glioblastoma (GBM) pharmacologic clinical trial. During the fourth quarter of 2019, the 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 Cooperative Research and Development Agreement, with the Company being required to provide the LB-100 clinical compound.

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

The NCI study is designed to determine the extent to which LB-100 enters recurrent malignant gliomas. Patients having surgery to remove one or more tumors will receive one dose of LB-100 prior to surgery and have blood and tumor tissue analyzed to determine the amount of LB-100 present and to determine whether the cells in the tumors show the biochemical changes expected to be present if LB-100 reaches its molecular target. The goal is to obtain data in up to eight patients. As a result of the innovative design of the NCI study, data from so few patients should be sufficient to provide a sound rationale for conducting a larger clinical trial to determine the effectiveness of adding LB-100 to the standard treatment regimen for GBMs.

The neurosurgical unit at the NCI, which had been closed due to the Covid-19 epidemic, has reopened, and patient accrual has resumed. Patient entry remains at two, with the goal to enter eight patients before analyzing results. There is an urgent need to improve therapy for this type of aggressive brain tumor. If the NCI study shows that LB-100 does penetrate the brain, a clinical study of LB-100 in combination with standard therapy for GBM, the drug temozolomide and radiation, both of which have been well documented in pre-clinical studies to be significantly enhanced by LB-100, would be of significant interest to neuro-oncologists frustrated by decades of limited advances in therapy for this common brain tumor in adults.

Clinical Research Support Agreement with City of Hope National Medical Center

Effective January 18, 2021, the Company executed a Clinical Research Support Agreement with the City of Hope National Medical Center, an NCI-designated

comprehensive cancer center, and City of Hope Medical Foundation (collectively, "City of Hope"), to carry out a Phase 1b clinical trial of LB-100, the Company's first-in-class protein phosphatase inhibitor, combined with a standard regimen for treatment of untreated extensive- stage disease small cell lung cancer (ED-SCLC). LB-100 will be given in combination with carboplatin, etoposide and atezolizumab, an FDA-approved but marginally effective regimen, to previously untreated ED-SCLC patients. The dose of LB-100 will be escalated with the standard fixed doses of the 3-drug regimen to reach a recommended Phase 2 dose (RP2D). Patient entry will be expanded so that a total of 12 patients will be evaluable at the RP2D to confirm the safety of the LB-100 combination and to look for potential therapeutic activity as assessed by objective response rate, duration of overall response, progression-free-survival and overall survival.

The clinical trial was initiated on March 9, 2021, with patient accrual expected to take approximately two years to complete. If LB-100 does potentiate the benefit of the standard regimen, some evidence could be noted at 12 months into the clinical trial, but an assessment of potential increased activity is likely to require at least 24 months. The Company is currently seeking to add two additional centers to increase the rate of accrual. The Company expects this clinical trial to be completed by June 30, 2024.

This clinical trial is based upon a target of 42 enrollees. If a significant number of patients fail during the dose-escalation process, an increase of up to 12 patients would likely be necessary. The Company currently expects that enrollment in this clinical trial will range from approximately 18 to 30 enrollees, with 24 enrollees as the most likely number. Should fewer than 42 enrollees be required, the Company has agreed to compensate City of Hope on a per enrollee basis

Clinical Trial Monitoring Agreements

Moffitt. On September 12, 2018, the Company finalized a work order agreement with Theradex Systems, Inc. ("Theradex"), an international contract research organization ("CRO"), to monitor the Phase 1b/2 clinical trial being managed and conducted by Moffitt. The clinical trial began in April 2019 and the first patient was entered into the clinical trial in July 2019. At the current rate of accrual, the clinical trial is expected to be completed by June 30, 2025.

City of Hope. On February 5, 2021, the Company signed a new work order agreement with Theradex to monitor the City of Hope investigator-initiated clinical trial in small cell lung cancer in accordance with FDA requirements for oversight by the sponsoring party.

Patent and License Agreements

On March 22, 2018, the Company entered into a Patent Assignment and Exploitation Agreement with INSERM TRANSFERT SA, acting as delegatee of the French National Institute of Health and Medical Research, for the assignment to the Company of INSERM'S interest in United States Patent No. 9,833,450 entitled "Oxabicyloheptanes and Oxabicycloheptenes for the Treatment of Depressive and Stress Disorders", which was filed with the United States Patent and Trademark Office in the name of INSERM and the Company as co-owners on February 19, 2015 and granted on May 12, 2017, and related patent applications and filings. INSERM is a French public institution dedicated to research in the field of health and medicine that had previously entered into a Material Transfer Agreement with the Company to allow INSERM to conduct research on the Company's proprietary compound LB-100 and/or its analogs for the treatment of depressive or stress disorders in humans. Pursuant to the Agreement, the Company has agreed to make certain milestone payments to INSERM aggregating up to $1,750,000 upon achievement of development milestones and up to $6,500,000 upon achievement of commercial milestones. The Company also agreed to pay INSERM certain commercial royalties on net sales of products attributed to the Agreement. The Company's initial plan was to complete the validation process to evaluate LB-100 for the treatment of depressive or stress disorders in humans within three years; however, the exploitation of this patent for the treatment of depressive and stress disorders in humans will require substantial additional capital and/or a joint venture or other type of business arrangement with a pharmaceutical company with substantially greater capital and business resources than those available to the Company. As there can be no assurances that the Company will be able to obtain the capital or business resources necessary to focus on the exploitation of this patent, it is uncertain as to when, if at all, the Company may reach any of the development or commercialization milestones under the Agreement. As of December 31, 2021 and 2020, no amounts were due under this agreement.

Effective August 20, 2018, the Company entered into an Exclusive License Agreement with Moffitt. Pursuant to the License Agreement, Moffitt granted the Company an exclusive license under certain patents owned by Moffitt (the "Licensed Patents") relating to the treatment of MDS and a non-exclusive license under inventions, concepts, processes, information, data, know-how, research results, clinical data, and the like (other than the Licensed Patents) necessary or useful for the practice of any claim under the Licensed Patents or the use, development, manufacture or sale of any product for the treatment of MDS which would otherwise infringe a valid claim under the Licensed Patents. The Company was obligated to pay Moffitt a non-refundable license issue fee of $25,000 after the first patient is entered into a Phase 1b/2 clinical trial to be managed and conducted by Moffitt. The clinical trial began at a single site in April 2019 and the first patient was entered into the clinical trial in July 2019. The Company is also obligated to pay Moffitt an annual license maintenance fee of $25,000 commencing on the first anniversary of the Effective Date and every anniversary thereafter until the Company commences payment of minimum royalty payments. The Company has also agreed to pay non-refundable milestone payments to Moffitt, which cannot be credited against earned royalties payable by the Company, based on reaching various clinical and commercial milestones aggregating $1,897,000, subject to reduction by 40% under certain circumstances relating to the status of Valid Claims, as such term is defined in the License Agreement. During the years ended December 31, 2021 and 2020, the Company recorded charges to operations of $24,999 and $25,001, respectively, in connection with its obligations under the License Agreement. As of December 31, 2021, no milestones had yet been attained.

The Company will be obligated to pay Moffitt earned royalties of 4% on worldwide cumulative net sales of royalty-bearing products, subject to reduction to 2% under certain circumstances, on a quarterly basis, with a minimum royalty payment of $50,000 in the first four years after sales commence, and $100,000 in year five and each year thereafter, subject to reduction by 40% under certain circumstances relating to the status of Valid Claims, as such term is defined in the License Agreement. The Company's obligation to pay earned royalties under the License Agreement commences on the date of the first sale of a royalty-bearing product, and shall automatically expire on a country-by-country basis on the date on which the last valid claim of the Licensed Patents expires, lapses or is declared invalid, and the obligation to pay any earned royalties under the License Agreement shall terminate on the date on which the last valid claim of the Licensed Patents expires, lapses, or is declared to be invalid in all countries.

Other Significant Agreements and Contracts

On December 24, 2013, the Company entered into an agreement with NDA Consulting Corp. for consultation and advice in the field of oncology research and drug development. As part of the agreement, NDA also agreed to cause its president, Dr. Daniel D. Von Hoff, M.D., to become a member of the Company's Scientific Advisory Committee. The term of the agreement was for one year. The agreement has been automatically renewed for additional one-year terms on its anniversary date since 2014.

Effective September 14, 2015, the Company entered into a Collaboration Agreement with BioPharmaWorks, pursuant to which the Company engaged BioPharmaWorks to perform certain services for the Company. Those services included, among other things: (a) assisting the Company to (i) commercialize its products and strengthen its patent portfolio, (ii) identify large pharmaceutical companies with potential interest in the Company's product pipeline, and (iii) prepare and deliver presentations concerning the Company's products; (b) at the request of the Board of Directors, serving as backup management for up to three months should the Company's Chief Executive Officer and scientific leader be temporarily unable to carry out his duties; (c) being available for consultation in drug discovery and development; and (d) identifying providers and overseeing tasks relating to clinical use and commercialization of new compounds.

BioPharmaWorks was founded in 2015 by former Pfizer scientists with extensive multi-disciplinary research and development and drug development experience. The Collaboration Agreement was for an initial term of two years and automatically renews for subsequent annual periods unless terminated by a party not less than 60 days prior to the expiration of the applicable period.

Effective August 12, 2020, the Company entered into a Master Service Agreement with the Foundation for Angelman Syndrome Therapy (FAST) to collaborate in supporting pre-clinical studies of the potential benefit of LB-100 in a mouse model of Angelman Syndrome (AS) as reported in The Proceedings of The National Academy of Science (Wang et al, June 3, 2019). The pre-clinical studies will be conducted at The University of California - Davis under the direction of Dr. David Segal, an internationally recognized leader in AS research. If the pre-clinical studies confirm that LB-100 reduces AS signs in rodent models, the Company has agreed to enter into discussions with FAST with respect to possible collaborations to most efficiently assess the benefit of LB-100 in patients with AS, which is a rare disease affecting an estimated one out of 12,000 to one out of 20,000 persons in the United States. The genetic cause of AS, reduced function of a specific maternal gene called Ube3, has been understood for some time, but the molecular abnormality resulting from the genetic lesion has now been shown to be increased concentrations of protein phosphatase 2A (PP2A), a molecular target of the Company's investigational compound, LB-100. The Company has agreed to provide FAST with a supply of LB-100 to be utilized in the conduct of this study, which is initially expected to be completed within three years. Conditioned on FAST's completion of this study, the Company has agreed to pay FAST five percent (5%) of all proceeds, as defined in the Master Service Agreement, received by the Company, up to a maximum of $250,000 from the exploitation of the study results.

The research team at the University of California, Davis recently completed their pre-clinical study of the potential benefit of LB-100 in a mouse model of AS, and the results are currently under review by FAST. The preliminary analysis indicates that the positive results previously reported by Chinese investigators were not confirmed in the US model. The Company is awaiting input from FAST as to whether it intends to continue to pursue pre-clinical studies of LB 100.

On October 8, 2021, the Company entered into a Development Collaboration Agreement with the Netherlands Cancer Institute, Amsterdam (NKI), one of the world's leading comprehensive cancer centers, and Oncode Institute, Utrecht, a major independent cancer research center, to identify the most promising drugs to be combined with LB-100, and potentially LB-100 analogues, to be used to treat a range of cancers, as well as to identify the specific molecular mechanisms underlying the identified combinations. The Company has agreed to fund the study and provide a sufficient supply of LB-100 to conduct the study. The study is expected to take approximately two years to conduct.

Potential Future Clinical Trials

Presented below is a clinical trial that we would currently consider conducting over the next few years. We expect that this potential clinical trial, and the details thereof, will change over time as we obtain more clinical information on LB-100. Our ability to conduct this clinical trial, and possibly other clinical trials, is subject to the availability of sufficient additional financial resources.

- A Phase 1b/2 randomized clinical trial in patients adding LB-100 to PD-1 inhibitors against one of several cancers in which PD-1 inhibitors alone have definite but modest activity.

The Phase 1b/2 clinical trial in LB-100 plus a PD-1 inhibitor in yet to be specified solid tumors would require additional financing in excess of that currently budgeted to fund a Phase 1b/2 clinical trial in myelodysplastic syndrome that began in April 2019, and/or partnering relationships with other pharmaceutical companies, in order for us to undertake and complete such clinical studies. From time to time, we engage discussions with various parties with respect to the financing of these clinical studies, although there can be no assurances that we will be able to obtain such financing and/or partnering relationships on acceptable terms or at all. Our longer-term objective is to secure one or more strategic partnerships with pharmaceutical companies with major programs in cancer research and drug development.

Intellectual Property

Our products will ultimately be based on our intellectual property and are expected to be covered by our patents. These patents now cover sole rights to the composition and synthesis of the LB-100 and LB-200 series of drugs, with coverage of the LB-200 series now limited to those patents issued in the United States. Joint patent applications with the NIH have been filed for the treatment of glioblastoma multiforme, medulloblastoma, and neuroblastoma. We have also filed patent applications for the use of certain homologs of both series of drugs for the treatment of neurodegenerative diseases such as Alzheimer's Disease and Parkinson's Disease, Amyotrophic Lateral Sclerosis (ALS, or Lou Gehrig's Disease), stroke, and traumatic brain injury, and patent applications for the use of homologs of the LB-200 series for the treatment of serious systemic fungal infections and for the treatment of common fungal infections of the skin and nails.

Patent applications for the LB-100 series (oxabicycloheptanes and heptenes) and the LB-200 series (histone deacetylase inhibitors; HDACi) have been filed in the United States and internationally under the Patent Cooperation Treaty. Patents for composition of matter and for several uses of both the LB-100 series and the LB-200 series have been issued in the United States, Mexico, Australia, Japan, China, Hong Kong, Canada, Germany, France, the United Kingdom, and by the European Patent Office and the Eurasian Patent Office. For the LB-200 series, only patents issued in the United States are being maintained.

The Company strives to protect and enhance the proprietary technology, inventions, and improvements that are commercially important to the development of its business, including seeking, maintaining, and defending its patent rights. The Company also relies on trade secrets relating to its proprietary pipeline of product candidates and on know-how and continuing technological innovation to develop and strengthen its pipeline. The Company intends to rely on regulatory protection afforded by regulatory agencies through data exclusivity, market exclusivity, and patent term extensions, where available.

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

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

A descriptive summary of the patent portfolio for the Company's most important clinical programs involving the development of LB-100 is presented below, followed by a detailed listing of each domestic and international patent that has been issued. Lixte Biotechnology, Inc. is the Company's wholly-owned Delaware subsidiary. The projected patent expiration dates noted below assume that that all required maintenance or annuity fees for the patents are timely paid and that a court or agency does not determine that the patents are invalid or unenforceable.

LB-100. The Company's lead compound LB-100 is covered by U.S. Patent Nos. 8,822,461 and 7,998,957, which are solely owned by Lixte Biotechnology, Inc. These patents are projected to expire in 2030 or 2028, exclusive of any available patent term extension. Counterpart non-U.S. patents are projected to expire in 2028. Pharmaceutical compositions of LB-100 are covered by U.S. Patent Nos. 10,532,050, 10,023,587 and 8,822,461, which are solely owned by Lixte Biotechnology, Inc. These patents and their non-U.S. counterparts are projected to expire in 2034 or 2028, exclusive of any available patent term extension.

LB-100 Combination Therapy with a Checkpoint Inhibitor. LB-100 combination therapy with a checkpoint inhibitor for treating gliomas is covered by pending U.S. and non-U.S. patent applications. These patent applications are jointly owned by Lixte Biotechnology, Inc. and The United States of America, as represented by the Secretary, Department of Health and Human Services. Patents issuing from these patent applications are projected to expire in 2037, exclusive of any patent term extension.

LB-100 Combination Therapy with Carboplatin, Etoposide or Atezolizumab. LB-100 combination therapy with carboplatin, etoposide or atezolizumab for treating small-cell lung cancer is covered by an international patent application that is solely owned by Lixte Biotechnology, Inc. Patents issuing from this patent application are projected to expire in 2041, exclusive of any patent term extension.

LB-100 Combination Therapy with Other Investigational Compounds. LB-100 combination therapy with one of several other investigational compounds for treating a wide-array of cancers is covered by a U.S. provisional patent application that is jointly owned by Lixte Biotechnology, Inc. and Stichting Het Nederlands Kanker Instituut – Antoni Van Leeuwenhoek Ziekenhuis. Patents issuing from counterpart nonprovisional applications are projected to expire in 2043, exclusive of any patent term extension.

LB-100 Therapeutic Methods. Administration of LB-100 for treating myelodysplastic syndrome is covered by U.S. Patent Nos. 10,434,100 and 10,071,094, which are jointly owned by Lixte Biotechnology, Inc. and H. Lee Moffitt Cancer Center and Research Institute, Inc. These patents and their non-U.S. counterparts are projected to expire in 2035, exclusive of any patent term extension. Administration of LB-100 for treating breast cancer, colon cancer, large cell lung cancer, adenocarcinoma of the lung, small cell lung cancer, stomach cancer, liver cancer, ovary adenocarcinoma, pancreas carcinoma, prostate carcinoma, promyelocytic leukemia, chronic myelocytic leukemia or acute lymphocytic leukemia, is covered by U.S. Patent No. 9,079,917, which is solely owned by Lixte Biotechnology, Inc. This patent and its non-U.S. counterparts are projected to expire in 2028, exclusive of any patent term extension.

LB-100 Prodrugs. The Company's LB-100 prodrugs are covered by U.S. Patent Nos. 10,618,908, 9,988,394, 8,822,461, 8,227,473 and 7,998,957, which are solely owned by Lixte Biotechnology, Inc. These patents and their non-U.S. counterparts are projected to expire in 2036, 2030 or 2028, exclusive of any patent term extension. Pharmaceutical compositions of LB-100 prodrugs are covered by U.S. Patent Nos. 11,236,102, 10,532,050, 10,023,587, 8,822,461, 8,227,473 and 7,998,957, which are solely owned by Lixte Biotechnology, Inc. These patents and their non-U.S. counterparts are projected to expire in 2034, 2030 or 2028, exclusive of any patent term extension.

Our portfolio of domestic and international patents issued is summarized below. We have additional domestic and international patents pending.

LB-100 Series of Compounds - Phosphatase Inhibitors – Composition and Use in Cancer Treatment

Oxabicycloheptanes and Oxabicycloheptenes, Their Preparation and Use

Patent	Priority Date or International Filing Date (non-U.S. applications)	Issue/Grant Date	Expiration Date
AM 023804	2/6/2008	7/29/2016	2/6/2028
AU 2008214299	2/6/2008	1/19/2014	2/6/2028
AZ 023804	2/6/2008	7/29/2016	2/6/2028
BR 0806365	2/6/2008	1/21/2020	2/6/2028
BY 023804	2/6/2008	7/29/2016	2/6/2028
CA 2,676,422	2/6/2008	10/16/2018	2/6/2028
CN 101662939	2/6/2008	11/25/2015	2/6/2028
CN 103788108	2/6/2008	4/12/2017	2/6/2028
EP 2124550	2/6/2008	4/19/2017	2/6/2028
EA 023804	2/6/2008	7/29/2016	2/6/2028
HK 1140375	2/6/2008	3/9/2018	2/6/2028
JP 5693850	2/6/2008	4/1/2015	2/6/2028
KG 023804	2/6/2008	7/29/2016	2/6/2028
KZ 023804	2/6/2008	7/29/2016	2/6/2028
MD 023804	2/6/2008	7/29/2016	2/6/2028
MX 309985	2/6/2008	5/28/2013	2/6/2028
RU 023804	2/6/2008	7/29/2016	2/6/2028
TJ 023804	2/6/2008	7/29/2016	2/6/2028
TM 023804	2/6/2008	7/29/2016	2/6/2028
US 7,998,957	2/6/2007	8/16/2011	2/20/2030
US 8,426,444	2/6/2007	4/23/2013	2/6/2028
US 8,227,473	8/1/2008	7/24/2012	3/11/2030
US 8,541,458	8/1/2008	9/24/2013	7/17/2029
US 8,822,461	2/6/2007	9/2/2014	2/6/2028
US 9,079,917	2/6/2007	7/14/2015	2/6/2028
US 10,023,587	2/6/2007	7/17/2018	2/6/2028
US 10,399,993	2/6/2007	9/3/2019	2/6/2028

LB-100 and LB-200 Series of Compounds – Use in Treatment of Multiple CNS Diseases

Neuroprotective Agents for the Prevention and Treatment of Neurodegenerative Diseases

Patent	Priority Date or International Filing Date (non-U.S. applications)	Issue/Grant Date	Expiration Date
US 8,058,268	8/1/2008	11/15/2011	12/31/2029
US 8,329,719	8/1/2008	12/11/2012	7/29/2029

Oxabicycloheptanes and Oxabicycloheptenes for the Treatment of Reperfusion Injury

Patent	Priority Date or International Filing Date (non-U.S. applications)	Issue/Grant Date	Expiration Date
CN 104619710	6/28/2013	9/22/2017	6/28/2033
EP 2870161	6/28/2013	8/8/2018	6/28/2033
DE 2870161	6/28/2013	8/8/2018	6/28/2033

FR 2870161	6/28/2013	8/8/2018	6/28/2033
GB 2870161	6/28/2013	8/8/2018	6/28/2033
HK 1209424	6/28/2013	10/11/2019	6/28/2033

Oxabicycloheptanes and Oxabicycloheptenes for the Treatment of Depressive and Stress Disorders

Patent	Priority Date or International Filing Date (non-U.S. applications)	Issue/Grant Date	Expiration Date
AU 2016219853	2/19/2016	5/16/2019	2/19/2036
EP 3258930	2/19/2016	12/9/2020	2/19/2036
DE 3258930	2/19/2016	12/9/2020	2/19/2036
FR 3258930	2/19/2016	12/9/2020	2/19/2036
GB 3258930	2/19/2016	12/9/2020	2/19/2036
US 9,833,450	2/19/2015	12/5/2017	2/19/2036
US 10,413,541	2/19/2015	9/17/2019	2/19/2036

HDAC Inhibitors

Patent	Priority Date or International Filing Date (non-U.S. applications)	Issue/Grant Date	Expiration Date
US 8,143,445	10/1/2007	3/27/2012	8/23/2029
US 8,455,688	10/1/2007	6/4/2013	10/1/2028

Oxabicycloheptanes and Oxabicycloheptenes for the Treatment of Diabetes

Patent	Priority Date or International Filing Date (non-U.S. applications)	Issue/Grant Date	Expiration Date
US 10,149,847	6/29/2012	12/11/2018	12/7/2033
US 10,668,062	6/29/2012	6/2/2020	6/28/2033

Formulations of Oxabicycloheptanes and Oxabicycloheptenes

Patent	Priority Date or International Filing Date (non-U.S. applications)	Issue/Grant Date	Expiration Date
AU 2014251087	4/8/2014	5/2/2019	4/8/2034
CN 105209036	4/8/2014	10/26/2018	4/8/2034
IL 241945	4/8/2014	4/30/2019	4/8/2034
US 10,532,050	4/9/2013	1/14/2020	7/5/2034

Process of Synthesizing 3-(4-Methylpiperazine-1-Carbonyl)-7-Oxabicyclo [2.2.1] Heptane-2-Carboxylic Acid

Patent	Priority Date or International Filing Date (non-U.S. applications)	Issue/Grant Date	Expiration Date
US 9,994,584	10/15/2014	6/12/2018	10/14/2035

Protein Phosphatase 2A Inhibitors for Treating Myelodysplastic Syndromes

Patent	Priority Date or International Filing Date (non-U.S. applications)	Issue/Grant Date	Expiration Date
JP 6453441	7/23/2015	1/16/2019	7/23/2035
US 10,071,094	7/24/2014	9/11/2018	7/23/2035
US 10,434,100	7/24/2014	10/8/2019	7/23/2035

Oxabicycloheptane Prodrugs

Patent	Priority Date or International Filing Date (non-U.S. applications)	Issue/Grant Date	Expiration Date
AU 2016263079	5/12/2016	8/15/2019	5/12/2036
EP 3294287	5/12/2016	4/8/2020	5/12/2036
IL 255516	5/12/2016	2/27/2020	5/12/2036
US 9,988,394	5/15/2015	6/5/2018	5/13/2036
US 10,364,252	5/15/2015	7/30/2019	5/13/2036
US 10,618,908	5/15/2015	4/14/2020	5/13/2036

The Market

Anti-Cancer Drugs

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 animal models. 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.

Marketing Plan

Our primary goal to date has been to take our primary compound, LB-100, through Phase 2 clinical trials. Because of the novelty and spectrum of activity of LB-100, we believe it is reasonably likely we may find a partner in the pharmaceutical industry with interest in this compound at some stage of its clinical development. However, we would prefer to delay the partnering/licensing decision until the potential value of our products are augmented by demonstrating there is no impediment to clinical evaluation and a therapeutic dose level is determined in clinical trials. Demonstration of clinical usefulness would be expected to substantially increase the value of our product.

Research and Development

Further development of lead compounds in addition to LB-100 will require pharmacokinetic/ pharmacodynamic characterization (i.e., how long a drug persists in the blood and how long the drug is active at the intended target) and large animal toxicologic evaluation under conditions meeting FDA requirements. Most anti-cancer drugs fail in development because of unacceptable toxicity. However, by analogy with mechanistically related compounds, there is good reason to believe that lead compounds in addition to LB-100 will be able to be given to humans safely by routes and at doses resulting in concentration of drug producing anti-cancer activity in animal models.

One of our most valuable resources is our scientific team, a coalition of various experts brought together through contracts and other collaborative arrangements. The team has expertise in cancer biology, proteomics (cancer biomarkers), medicinal and synthetic chemistry, pharmacology, clinical oncology and drug evaluation. In a relatively short period of time and at low cost, this group has developed lead compounds of two different classes of drugs that are positioned for development as new treatments for several types of cancer.

Product Development

We are subject to FDA regulations as it conducts clinical trials. Additionally, any product for which we obtain marketing approval, along with the manufacturing processes, post-approval clinical data and promotional activities for such product, will be subject to continual review and periodic inspections by the FDA and other regulatory bodies. Even if regulatory approval of a product is granted, the approval may be subject to limitations on the indicated uses for which the product may be marketed or contain requirements for costly post-marketing testing and surveillance to monitor the safety or efficacy of the product. Later discovery of previously unknown problems with our products, including unanticipated adverse events or adverse events of unanticipated severity or frequency, manufacturer or manufacturing processes, or failure to comply with regulatory requirements, may result in restrictions on such products or manufacturing processes, withdrawal of the products from the market, voluntary or mandatory recall, fines, suspension of regulatory approvals, product seizures, injunctions or the imposition of civil or criminal penalties.

Competition

The life sciences industry is highly competitive and subject to rapid and profound technological change. Our present and potential competitors include major pharmaceutical companies, as well as specialized biotechnology and life sciences firms in the United States and in other countries. Most of these companies have considerably greater financial, technical and marketing resources than we do. Additionally, mergers and acquisitions in the pharmaceutical and biotechnology industries may result in even more resources being concentrated in our competitors. Our existing or prospective competitors may develop processes or products that are more effective than ours or be more effective at implementing their technologies to develop commercial products faster. Our competitors may succeed in obtaining patent protection and/or receiving regulatory approval for commercializing products before we do. Developments by our competitors may render our product candidates obsolete or non-competitive.

We also experience competition from universities and other research institutions, and we are likely to compete with others in acquiring technology from those sources. There can be no assurance that other organizations will not develop technologies with significant advantages over those that we are seeking to develop. Any such development could harm our business.

We compete with universities and other research institutions engaged in research in these areas. Many of our competitors have greater technical and financial resources than we do.

Our ability to compete successfully is based on numerous factors, including:

- the cost-effectiveness of any product that we ultimately commercialize relative to competing products;
- the ease of use and ready availability of any product that we bring to market; and
- the relative speed with which we are able to bring any product resulting from its research to market in our target markets.

If we are unable to distinguish our products from competing products, or if competing products reach the market first, we may be unable to compete successfully with current or future competitors.

Employees and Human Capital Resources

As of March 11, 2022, we had three full-time officer/employees and one part-time officer/employee. The Company relies to a significant extent on outside consultants and advisors with various technical skills and expertise that the Company can draw on as necessary to conduct its research and development and clinical trial programs. We consider our relationship with our employees to be good. Our future performance depends significantly upon the continued service of our key personnel and our ability to attract highly skilled employees. We provide our employees with opportunities for equity ownership.

Facilities

As of March 11, 2022, we do not operate any facilities. We contract out research and development activities, drug production, and drug storage to various commercial laboratories, drug manufacturers and storage facilities.

Government Regulation

Our business is subject to the regulations of the FDA as it conducts clinical trials. Clinical trials are research studies to answer specific questions about new therapies or new ways of using known treatments. Clinical trials determine whether new drugs or treatments are both safe and effective and the FDA has determined that carefully conducted clinical trials are the fastest and safest way to find treatments that work in people.

The FDA also requires that an independent review body consider the benefits and risks of a clinical trial and grant approval for the proposed study including selecting of initial doses, plans for escalation of dose, plans for modification of dose if toxicity is encountered, plans for monitoring the wellbeing of individuals participating in the study, and for defining and measuring, to the extent possible, any untoward effects related to drug administration. Serious adverse effects, such as life-threatening toxicities and death, are immediately reportable to the review body and to the FDA. To minimize risk when studying a new drug, the initial dose is well below that expected to cause any toxicity. No more than three patients are entered at a given dose. In general, a dose is not escalated within an individual patient. Once safety is established by the absence of toxicity or low toxicity in a group of three patients, a planned higher dose is then evaluated in a subsequent group of three individuals and so on until dose-limiting toxicity is encountered. The dose level producing definite but acceptable toxicity is then selected as the dose level to be evaluated in Phase 2 trials. Thus, the goal of Phase 1 studies is to determine the appropriate dose level for evaluation of drug efficacy in patients with the same type of tumor at comparable stages of progression for which no beneficial treatment is established.

In addition to regulations imposed by the FDA, depending on our future activities, we may become subject to regulation under various federal and state statutes and regulations, such as the Occupational Safety and Health Act, the Environmental Protection Act, the Toxic Substances Control Act, the Research Conservation and Recovery Act, national restrictions on technology transfer, and import, export and customs regulations. From time to time, other federal agencies and congressional committees have indicated an interest in implementing further regulation of biotechnology applications. We are not able to predict whether any such regulations will be adopted or whether, if adopted, such regulations will apply to our business, or whether we or our collaborators would be able to comply with any applicable regulations.

In addition, as we intend to market our products in international markets, we may be required to obtain separate regulatory approvals from the European Union and many other foreign jurisdictions. Approval by the FDA does not ensure approval by regulatory authorities in other countries, and approval by one foreign regulatory authority does not ensure approval by regulatory authorities in other foreign countries or by the FDA. We may not be able to file for regulatory approvals and may not receive necessary approvals to commercialize our products in any market.

Legal Proceedings

We may be involved from time to time in ordinary litigation, negotiation, and settlement matters that will not have a material effect on our operations or finances. We are not currently party to any material legal proceedings, and we are not aware of any pending or threatened litigation against us.

ITEM 1A. RISK FACTORS

The following risk factors, together with the other information presented in this document, including the financial statements and the notes thereto, should be considered by investors.

Risks Related to Our Financial Resources and Capital Needs

We are engaged in early-stage research and as such might not be successful in our efforts to develop a portfolio of commercially viable products.

A key element of our strategy is to discover new product candidates and develop LB-100 as a monotherapy or combination therapy to treat cancer. We are seeking to do so through our internal research programs or strategic partnerships. A significant portion of the research or development that we are conducting involves new and unproven technologies. Research programs to identify new disease targets and product candidates or to develop them require substantial technical, financial and human resources whether or not any candidates or technologies are ultimately identified or proven successful. Our research programs might initially show promise in identifying potential product candidates, yet fail to yield product candidates for clinical development for the following reasons:

- the research methodology used might not be successful in identifying potential product candidates; however, we have identified several promising lead candidate compounds which have activity in animal models, one of which, LB-100, has completed a Phase 1 clinical trial; or
- product candidates for drugs might on further study be shown to have harmful side effects or other characteristics that indicate they are unlikely to be effective drugs.

If we are unable to discover suitable potential product candidates, develop additional delivery technologies through internal research programs or strategic partnerships, or in-license suitable products or delivery technologies on acceptable business terms, our business prospects will suffer. Even if we discover additional product candidates, and even though LB-100 has completed a Phase 1 clinical trial, subsequent clinical trials of LB-100 or new clinical trials of one or more additional drug candidates may show that these product candidates are unsafe or ineffective.

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 are a clinical-stage biopharmaceutical company that uses biomarker technology to identify enzyme targets associated with serious common diseases and then design novel compounds to attack those threats. We do not have any products approved by a regulatory authority and have not generated any revenue from collaboration or licensing agreements or product sales to date, and have incurred significant research, development and other expenses related to our ongoing operations and expect to continue to incur such expenses. As a result, we have not been profitable and have incurred significant operating losses since our inception. For the years ended December 31, 2021 and 2020, we reported a net loss of $6,728,396 and $3,264,882, respectively. As of December 31, 2021 and December 31, 2020, we had an accumulated deficit of $37,082,164 and $30,353,768, respectively.

We do not expect to generate revenues for many years, if at all. We expect to continue to incur significant expenses and operating losses for the foreseeable future. We anticipate these losses to increase as we continue to research, develop and seek regulatory approvals for one or more of our product candidates and any additional product candidates we might acquire, and potentially begin to commercialize product candidates that might achieve regulatory approval. We might also encounter unforeseen expenses, difficulties, complications, delays and other unknown factors that could adversely affect our business. The size of our future net losses will depend, in part, on the rate of future growth of our expenses and our ability to generate revenues. Our expenses will further increase as we:

- conduct clinical trials of our lead product candidate, LB-100;
- in-license or acquire rights to, and pursue development of, other products, product candidates or technologies;

- hire additional clinical, manufacturing, quality control, quality assurance and scientific personnel;
- seek marketing approval for any product candidates that successfully complete clinical trials;
- develop our outsourced manufacturing and commercial activities and establish sales, marketing and distribution capabilities, if we receive, or expect to receive, marketing approval for any product candidates;
- maintain, expand and protect our intellectual property portfolio; and
- add operational, financial and management information systems and personnel.

We need significant additional financing to fund our operations and complete the development and, if approved, the commercialization of our lead product candidate, LB-100. If we are unable to raise capital when needed, we could be forced to delay, reduce or eliminate our product development programs or commercialization efforts.

We expect that our existing cash resources as of December 31, 2021, combined with the proceeds from our registered direct equity offering completed in March 2021, 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 September 30, 2022. However, 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 quarter ending September 30, 2022. 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 and manufacturing 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, potentially acquiring new product candidates or technologies, conducting preclinical studies and clinical trials and potentially obtaining regulatory approvals and manufacturing products, as well as marketing and selling products approved for sale, if any.

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 to obtain data sufficient to seek marketing approval for our lead product candidate;
- the timing of, and the costs involved in, obtaining regulatory approvals for our lead drug candidate if our clinical trials are successful;
- the cost of commercialization activities for our lead product candidate, if it is approved for sale, including marketing, sales and distribution costs;
- the cost of manufacturing our lead product candidate for clinical trials in preparation for regulatory approval, including the cost and timing of process development, manufacturing scale-up and validation activities;
- 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.

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, or delay, limit, reduce or terminate our establishment of sales and marketing capabilities or other activities that may be necessary to commercialize our lead product candidate.

We currently have no source of revenues. We might never generate revenues or achieve profitability.

Currently, we do not generate any revenues from product sales or otherwise. Even if we are able to successfully achieve regulatory approval for our lead product candidate, we do not know when we will generate revenues or become profitable, if at all. Our ability to generate revenues from product sales and achieve profitability will depend on our ability to successfully commercialize products, including our lead product candidate, LB-100, and any other product candidates that we might develop, in-license or acquire in the future. Our ability to generate revenues and achieve profitability also depends on a number of additional factors, including our ability to:

- successfully complete development activities, including the necessary clinical trials;
- complete and submit New Drug Applications, or NDAs, to the FDA and obtain U.S. regulatory approval for indications for which there is a commercial market;
- complete and submit applications to foreign regulatory authorities;
- obtain regulatory approval in territories with viable market sizes;
- obtain coverage and adequate reimbursement from third parties, including government and private payors;
- set commercially viable prices for our intended product, if any;
- establish and maintain supply and manufacturing relationships with reliable third parties and/or build our own manufacturing facility and ensure adequate, legally and globally compliant manufacturing of bulk drug substances and drug products to maintain that supply;
- develop distribution processes for our lead product candidate;

- develop commercial quantities of our lead product candidate, once approved, at acceptable cost levels;
- obtain additional funding, if required to develop and commercialize our lead product candidate;
- develop a commercial organization capable of sales, marketing and distribution for any products we intend to sell ourselves, in the markets in which we choose to commercialize on our own;
- achieve market acceptance of one or more of our intended products;
- attract, hire and retain qualified personnel; and
- protect our rights in our intellectual property portfolio.

Our revenues for any product candidate for which regulatory approval is obtained will be dependent, in part, upon the size of the markets in the territories for which it gains regulatory approval, the accepted price for the product, the ability to get reimbursement at any price, and whether we own the commercial rights for that territory. If the number of our addressable-disease patients is not as significant as our estimates, the indication approved by regulatory authorities is narrower than we expect, or the reasonably accepted population for treatment is narrowed by competition, physician choice or treatment guidelines, we might not generate significant revenues from sales of such products, even if approved. In addition, we anticipate incurring significant costs associated with commercializing any approved product candidate. As a result, even if we generate revenues, we might not become profitable and might need to obtain additional funding to continue operations. If we fail to become profitable or are unable to sustain profitability on a continuing basis, then we might be unable to continue our operations at planned levels and might be forced to reduce our operations.

The Tax Cuts and Jobs Act could adversely affect our business and financial condition.

H.R. 1, "An Act to provide for reconciliation pursuant to title II and V of the concurrent resolution on the budget for fiscal year 2018," informally entitled the Tax Cuts and Jobs Act ("Tax Act") enacted on December 22, 2017, among other things, contains significant changes to corporate taxation, including reduction of the corporate tax rate from a top marginal rate of 35% to a single rate of 21%, limitation of the tax deduction for interest expense to 30% of adjusted taxable income (except for certain small businesses), limitation of the deduction for net operating losses carried forward from taxable years beginning after December 31, 2017 to 80% of current year taxable income and elimination of net operating loss carrybacks, one time taxation of offshore earnings at reduced rates regardless of whether they are repatriated, elimination of U.S. tax on foreign earnings (subject to certain important exceptions), providing immediate deductions for certain new investments instead of deductions for depreciation expense over time, and modifying or repealing many business deductions and credits (including reduction of tax credits under the Orphan Drug Act). Notwithstanding the reduction in the corporate income tax rate, the overall impact of the Tax Act is uncertain and our business and financial condition could be adversely affected. In addition, it is uncertain if and to what extent various states will conform to the Tax Act.

Our ability to use net operating losses to offset future taxable income might be subject to limitations.

As of December 31, 2021, we had federal net operating loss, or NOL, carryforwards of approximately $6,723,000. Our NOLs generated in tax years ending on or prior to December 31, 2017 are only permitted to be carried forward for 20 years under applicable U.S. tax laws, and will begin to expire, if not utilized, beginning in 2027. These NOL carryforwards could expire unused and be unavailable to offset future income tax liabilities. Under the Tax Act, federal NOLs incurred in tax years ending after December 31, 2017 may be carried forward indefinitely, but the deductibility of such federal NOLs is limited. It is uncertain if and to what extent various states will conform to the Tax Act, or whether any further regulatory changes may be adopted in the future that could minimize its applicability. In addition, under Section 382 of the Internal Revenue Code of 1986, as amended, and certain corresponding provisions of state law, if a corporation undergoes an "ownership change," which is generally defined as a greater than 50% change, by value, in the ownership of its equity over a three-year period, the corporation's ability to use its pre-change NOL carryforwards and other pre-change tax attributes to offset its post-change income might be limited.

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

Clinical-stage biopharmaceutical companies with product candidates in clinical development face a wide range of challenging activities which might entail substantial risk.

We are a clinical-stage biopharmaceutical company with a lead product candidate in clinical development. The success of our lead product candidate will depend on several factors, including the following:

- designing, conducting and successfully completing preclinical development activities, including preclinical efficacy and IND-enabling studies, for our lead product candidate or product candidates that we might, in the future, in-license or acquire;
- designing, conducting and completing clinical trials with positive results for our lead product candidate;
- receipt of regulatory approvals from applicable authorities;
- obtaining and maintaining patent and trade secret protection and regulatory exclusivity for our lead product candidate;
- making arrangements with third-party manufacturers, receiving regulatory approval of our manufacturing processes and our third-party manufacturers' facilities from applicable regulatory authorities and ensuring adequate supply of drug product;
- manufacturing our lead product candidate at an acceptable cost;
- effectively launching commercial sales of our lead product candidate, if approved, whether alone or in collaboration with others;
- achieving acceptance of our lead product candidate, if approved, by patients, the medical community and third-party payors;
- effectively competing with other therapies;
- if our lead product candidate is approved, obtaining and maintaining coverage and adequate reimbursement by third-party payors, including government payors, for our lead product candidate;
- complying with all applicable regulatory requirements, including FDA current Good Clinical Practices ("GCP"), current Good Manufacturing Practices ("cGMP"), and standards, rules and regulations governing promotional and other marketing activities;
- maintaining a continued acceptable safety profile of the lead product candidate during development and following approval.

If we do not achieve one or more of these factors in a timely manner or at all, we could experience significant delays or an inability to successfully develop and commercialize our lead product candidate, which could materially harm our business.

We might find it difficult to enroll patients in our clinical trials which could delay or prevent the start of clinical trials for our product candidate.

Identifying and qualifying patients to participate in clinical trials of our lead product candidate is essential to our success. The timing of our clinical trials depends in part on the rate at which we can recruit patients to participate in clinical trials of our lead product candidate, and we might experience delays in our clinical trials if we encounter difficulties in enrollment. If we experience delays in our clinical trials, the timeline for obtaining regulatory approval of our lead product candidate will most likely be delayed.

Many factors might affect our ability to identify, enroll and maintain qualified patients, including the following:

- eligibility criteria of our ongoing and planned clinical trials with specific characteristics appropriate for inclusion in our clinical trials;
- design of the clinical trial;
- size and nature of the patient population;
- patients' perceptions as to risks and benefits of the lead product candidate under study and the participation in a clinical trial generally in relation to other available therapies, including any new drugs that might be approved for the indications we are investigating;
- the availability and efficacy of competing therapies and clinical trials;
- pendency of other trials underway in the same patient population;
- willingness of physicians to participate in our planned clinical trials;
- severity of the disease under investigation;
- proximity of patients to clinical sites;
- patients who are noncompliant or do not otherwise complete the trials; and
- issues with contract research organizations (each being a "CRO") and/or with other vendors that handle our clinical trials.

We might not be able to initiate or continue to support clinical trials of LB-100, our lead product candidate, for one or more indications, or any future product candidates if we are unable to locate and enroll a sufficient number of eligible participants in these trials as required by the FDA or one or more other regulatory authorities. Even if we are able to enroll a sufficient number of patients in our clinical trials, if the pace of enrollment is slower than we expect, the development costs for our lead product candidate might increase and the completion of our trials might be delayed or our trials could become too expensive to complete.

If we experience delays in the completion of, or termination of, any clinical trials of our lead product candidate, the commercial prospects of our lead product candidate could be harmed, and our ability to generate product revenue from any of our product candidates could be delayed or prevented. In addition, any delays in completing our clinical trials would likely increase our overall costs, impair product candidate development and jeopardize our ability to obtain regulatory approval relative to our current plans. Any of these occurrences might harm our business, financial condition, and prospects significantly.

The results of preclinical studies or earlier clinical trials are not necessarily predictive of future results. Our lead product candidate in clinical trials, and any other product candidates that might advance into clinical trials, might not have favorable results in later clinical trials or receive regulatory approval.

Success in preclinical studies and early clinical trials does not ensure that later clinical trials will generate adequate data to demonstrate the efficacy and safety of an investigational drug. A number of companies in the pharmaceutical and biotechnology industries, including those with greater resources and experience than we have, have suffered significant setbacks in clinical trials, even after seeing promising results in earlier preclinical studies or clinical trials.

Despite the results reported in earlier preclinical studies or clinical trials for our lead product candidate, we do not know whether the clinical trials that we might conduct will demonstrate adequate efficacy and safety to result in regulatory approval to market our lead product candidate for a particular indication, in any particular jurisdiction. Efficacy data from prospectively designed trials might differ significantly from those obtained from retrospective subgroup analyses. If later-stage clinical trials do not produce favorable results, our ability to achieve regulatory approval for our lead product candidate might be adversely impacted. Even if we believe that we have adequate data to support an application for regulatory approval to market our lead product candidate or any future product candidates, the FDA or other regulatory authorities might not agree and might require that we conduct additional clinical trials.

Clinical drug development involves a lengthy and expensive process with an uncertain outcome.

Clinical testing is expensive and can take many years to complete, with the outcome inherently uncertain. Failure can occur at any time during the clinical trial process. Before obtaining approval from regulatory authorities for the sale of our lead product candidate, we must conduct extensive clinical trials to demonstrate the safety and efficacy of our lead product candidate in humans. Prior to initiating clinical trials, a sponsor must complete extensive preclinical testing of a product candidate, including, in most cases, preclinical efficacy experiments as well as IND-enabling toxicology studies. These experiments and studies might be time-consuming and expensive to complete. The necessary preclinical testing might not be completed successfully for a preclinical product candidate and a potentially promising product candidate might therefore never be tested in humans. Once it commences, clinical testing is expensive, difficult to design and implement, can take many years to complete and is uncertain as to outcome. A failure of one or more clinical trials can occur at any stage of testing. The outcome of preclinical testing and early clinical trials might not be predictive of the success of later clinical trials, and interim results of a clinical trial do not necessarily predict final results. Moreover, preclinical and clinical data are often susceptible to varying interpretations and analyses, and many companies that have believed their product candidates performed satisfactorily in preclinical studies and clinical trials have nonetheless failed to obtain marketing approval of their products. We might experience numerous unforeseen events during drug development that could delay or prevent our ability to receive marketing approval or commercialize our lead product candidate. In particular, clinical trials of our lead product candidate might produce inconclusive or negative results. We have limited data regarding the safety, tolerability and efficacy of our lead product candidate. Clinical trials also require the review and oversight of an institutional review board ("IRB"). An inability or delay in obtaining IRB approval could prevent or delay the initiation and completion of clinical trials, and the FDA might decide not to consider any data or information derived from a clinical investigation not subject to initial and continuing IRB review and approval.

We might experience delays in our ongoing or future clinical trials, and we do not know whether planned clinical trials will begin or enroll subjects on time, will need

to be redesigned or will be completed on schedule, if at all. There can be no assurance that the FDA will not put clinical trials of our lead product candidate on hold in the future. Clinical trials might be delayed, suspended or prematurely terminated for a variety of reasons, such as:

- delay or failure in reaching agreement with the FDA or a foreign regulatory authority on a clinical trial design that we are able to execute;
- delay or failure in obtaining authorization to commence a trial or inability to comply with conditions imposed by a regulatory authority regarding the scope or design of a trial;
- delay or failure in reaching agreement on acceptable terms with prospective CROs and clinical trial sites, the terms of which can be subject to extensive negotiation and may vary significantly among different CROs and trial sites;
- delay or failure in obtaining IRB approval or the approval of other reviewing entities, including comparable foreign regulatory authorities, to conduct a clinical trial at each site;
- withdrawal of clinical trial sites from our clinical trials or the ineligibility of a site to participate in our clinical trials;
- delay or failure in recruiting and enrolling suitable subjects to participate in a trial;
- delay or failure in subjects completing a trial or returning for post-treatment follow-up;
- clinical sites and investigators deviating from trial protocol, failing to conduct the trial in accordance with regulatory requirements, or dropping out of a trial;
- inability to identify and maintain a sufficient number of trial sites, many of which may already be engaged in other clinical trial programs, including some that may be for the same indication;
- failure of our third-party clinical trial managers, CROs, clinical trial sites, contracted laboratories or other third-party vendors to satisfy their contractual duties, meet expected deadlines or return trustworthy data;
- delay or failure in adding new trial sites;
- interim results or data that are ambiguous or negative or are inconsistent with earlier results or data;
- alteration of trial design necessitated by re-evaluation of design assumptions based upon observed data;
- feedback from the FDA, the IRB or a foreign regulatory authority, or results from earlier stage or concurrent preclinical studies and clinical trials, that might require modification to the protocol for a trial;
- a decision by the FDA, the IRB, a foreign regulatory authority, or us to suspend or terminate clinical trials at any time for safety issues or for any other reason;
- unacceptable risk-benefit profile, unforeseen safety issues or adverse side effects;
- failure to demonstrate a benefit from using a product candidate;
- difficulties in manufacturing or obtaining from one or more third parties sufficient quantities of a product candidate to start or to use in clinical trials;
- lack of adequate funding to continue a trial, including the incurrence of unforeseen costs due to enrollment delays, requirements to conduct additional studies or increased expenses associated with the services of our CROs and other third parties; or
- changes in governmental regulations or administrative actions or lack of adequate funding to continue a clinical trial.

If we experience delays in the completion or termination of any clinical trial of our lead product candidate, the approval and commercial prospects of our lead product candidate will be harmed, delaying our ability to generate product revenues from such product candidate and our costs will most likely increase. The required regulatory approvals may also be delayed, thereby jeopardizing our ability to commence product sales and generate revenues and the period of commercial exclusivity for our intended product may be shortened. Regulatory approval of our lead product candidate may be denied for the same reasons that caused the delay.

Risks associated with operating in foreign countries could materially adversely affect our product development.

We might conduct future studies in countries outside of the U.S. Consequently, we may be subject to risks related to operating in foreign countries. Risks associated with conducting operations in foreign countries include:

- differing regulatory requirements for drug approvals and regulation of approved drugs in foreign countries;
- more stringent privacy requirements for data to be supplied to our operations in the U.S., but generated outside the U.S., *e.g.*, General Data Protection Regulation in the European Union;
- unexpected changes in tariffs, trade barriers and regulatory requirements;
- economic weakness, including inflation, or political instability in particular foreign countries, economies or markets;
- compliance with tax, employment, immigration and labor laws for employees living or traveling abroad;
- foreign taxes, including withholding of payroll taxes;
- differing payor reimbursement regimes, governmental payors or patient self-pay systems and price controls;
- foreign currency fluctuations, which could result in increased operating expenses or reduced revenues, and other obligations incident to doing business or operating in another country;
- workforce uncertainty in countries where labor unrest is more common than in the U.S.;
- production shortages resulting from any events affecting raw material supply or manufacturing capabilities abroad; and

- business interruptions resulting from geopolitical actions or events, including civil or political unrest (such as the ongoing conflict between Ukraine and Russia), sanctions, war and terrorism.

Our current and future product candidates, the methods used to deliver them or their dosage levels may cause undesirable side effects or have other properties that could delay or prevent their regulatory approval, limit the commercial profile of an approved label or result in significant negative consequences following any regulatory approval.

Undesirable side effects caused by our current or future product candidates, their delivery methods or dosage levels could cause us, our collaborators or regulatory authorities to interrupt, delay or halt clinical trials and could result in a more restrictive label or the delay or denial of regulatory approval or termination of clinical trials by the FDA or other foreign regulatory authorities; or an IRB, that approves and, monitors biomedical research to protect the rights and welfare of human subjects. As a result of safety or toxicity issues that we might experience in our clinical trials, or negative or inconclusive results from the clinical trials of others for drug candidates that might be similar to our own, we might not receive approval to market our current lead product candidate or any product candidates we may pursue, which could prevent us from ever generating revenues or achieving profitability. Results of our trials could reveal an unacceptably high severity or incidence of side effects. In such an event, our trials or those or our collaborators could be suspended or terminated, and the FDA or foreign regulatory authorities could order us or our collaborators to cease further development of or deny approval of our current or any future product candidates for any or all targeted indications. Any drug-related side effects could also affect patient recruitment or the ability of enrolled subjects to complete clinical trials or result in potential product liability claims. Any of these occurrences could have a material adverse effect on our business, results of operations, financial condition, cash flows and future prospects.

Additionally, if our lead product candidate receives regulatory approval, and we or others later identify undesirable side effects caused by such product, a number of potentially significant negative consequences could result, including that:

- we may be forced to suspend marketing of such product;
- regulatory authorities might withdraw their approvals of such product;
- regulatory authorities might require additional warnings on the label that could diminish the usage or otherwise limit the commercial success of such product;
- we may be required to conduct post-marketing studies;
- we may be required to change the way the product is administered;
- we could be sued and held liable for harm caused to subjects or patients; and
- our reputation may suffer.

Any of these events could prevent us from achieving or maintaining market acceptance of our lead product candidate, if approved.

Our product development program might not uncover all possible adverse events that patients who take our lead product candidate may experience. The number of subjects exposed to our lead product candidate and the average exposure time in the clinical development program might be inadequate to detect rare adverse events or chance findings that might only be detected once the product is administered to more patients and for greater periods of time.

Clinical trials by their nature utilize a sample of the potential patient population. However, with a limited number of subjects and limited duration of exposure, we cannot be fully assured that rare and severe side effects of our lead product candidate will be uncovered. Such rare and severe side effects might only be uncovered with a significantly larger number of patients exposed to our lead product candidate. If such safety problems occur or are identified after our lead product candidate reaches the market, the FDA might require that we amend the labeling of the product or recall the product, or might even withdraw approval for the product.

Our future success is dependent on the regulatory approval of our lead product candidate.

Our business is dependent on our ability to obtain regulatory approval for our lead product candidate in a timely manner. We cannot commercialize our lead product candidate in the U.S. without first obtaining regulatory approval for the product from the FDA. Similarly, we cannot commercialize our lead product candidate outside of the U.S. without obtaining regulatory approval from one or more foreign regulatory authorities. Before obtaining regulatory approvals for the commercial sale of our lead product candidate for a target indication, we must demonstrate with substantial evidence gathered in preclinical studies and clinical trials, that the product candidate is safe and effective for use for that target indication and that the manufacturing facilities, processes and controls are adequate with respect to such product candidate.

The time required to obtain approval by the FDA and foreign regulatory authorities is unpredictable but typically takes many years following the commencement of preclinical studies and clinical trials and depends upon numerous factors, including the substantial discretion of the regulatory authorities. In addition, approval policies, regulations, or the type and amount of clinical data necessary to gain approval may change during the course of a product candidate's clinical development and may vary among jurisdictions.

Even if a product candidate were to successfully obtain approval from the FDA and one or more foreign regulatory authorities, any approval might contain significant limitations related to use restrictions for specified age groups, warnings, precautions or contraindications, or may be subject to burdensome post-approval study or risk management requirements. Also, any regulatory approval of our lead product candidate or any future product candidates we may pursue, once obtained, may be withdrawn.

Our lead product candidate and future product candidates could fail to receive regulatory approval from the FDA.

We have not obtained regulatory approval for our lead product candidate, and it is possible that our lead product candidate or any future product candidates will not obtain regulatory approval, for many reasons, including:

- disagreement with the regulatory authorities regarding the scope, design or implementation of our clinical trials;
- failure to demonstrate that a product candidate is safe and effective for our proposed indication;
- failure of clinical trials to meet the level of statistical significance required for approval;
- failure to demonstrate that a product candidate's clinical and other benefits outweigh its safety risks;

- disagreement with our interpretation of data from preclinical studies or clinical trials;
- the insufficiency of data collected from clinical trials of our lead product candidate to support the submission and filing of an NDA or other submission or to obtain regulatory approval;
- failure to obtain approval of our manufacturing processes or facilities of third-party manufacturers with whom we contract for clinical and commercial supplies or our own manufacturing facility; or
- changes in the approval policies or regulations that render our preclinical and clinical data insufficient for approval.

The FDA or a foreign regulatory authority might require more information, including additional preclinical or clinical data to support approval or additional studies, which might delay or prevent approval or our commercialization plans, or we might decide to abandon the development program. If we were to obtain approval, regulatory authorities might approve our lead product candidate and any future product candidates we might pursue for fewer or more limited indications than we request (including failing to approve the most commercially promising indications), might grant approval contingent on the performance of costly post-marketing clinical trials, or might approve a product candidate with a label that does not include the labeling claims necessary or desirable for the successful commercialization of that product candidate.

If we are unable to obtain regulatory approval for our lead product candidate in one or more jurisdictions, or if any approval contains significant limitations, we might not be able to obtain sufficient funding to continue the development of that product or generate revenues attributable to that product candidate.

Failure to obtain regulatory approval in international jurisdictions would prevent our lead product candidate from being marketed abroad.

In addition to regulations in the U.S., to market and sell our lead product candidate in the European Union, in the United Kingdom, in many Asian countries and in other jurisdictions, we must obtain separate regulatory approvals and comply with numerous and varying regulatory requirements. Approval by the FDA does not ensure approval by regulatory authorities in other countries or jurisdictions, and approval by one regulatory authority outside the U.S. does not ensure approval by regulatory authorities in other countries or jurisdictions or by the FDA. The regulatory approval process outside the U.S. generally includes all of the risks associated with obtaining FDA approval as well as risks attributable to the satisfaction of local regulations in foreign jurisdictions. The approval procedure varies among countries and can require additional data or involve additional testing. The time required to obtain foreign approval may differ substantially from that required to obtain FDA approval. We might not be able to obtain approvals from regulatory authorities outside the U.S. on a timely basis, if at all. Clinical trials accepted in one country might not be accepted by regulatory authorities in other countries. In addition, many countries outside the U.S. require that a product be approved for reimbursement before it can be approved for sale in that country. A product candidate that has been approved for sale in a particular country might not receive reimbursement approval in that country.

We might not be able to file for regulatory approvals and might not receive necessary approvals to commercialize our intended product in any market. If we are unable to obtain approval of any of our current product candidate or any future product candidates we might pursue by regulatory authorities in the European Union, United Kingdom, Asia or elsewhere, the commercial prospects of that product candidate might be significantly diminished, our business prospects could decline and this could materially adversely affect our business, results of operations and financial condition.

Even if our current primary product candidate received regulatory approval, it might still face future development and regulatory difficulties.

Even if we obtain regulatory approval for our lead product candidate, LB-100, that approval would be subject to ongoing requirements by the FDA and foreign regulatory authorities governing the manufacture, quality control, further development, labeling, packaging, storage, distribution, adverse event reporting, safety surveillance, import, export, advertising, promotion, recordkeeping and reporting of safety and other post-marketing information. These requirements can include submissions of safety and other post-marketing information and reports, registration, as well as continued compliance by us and/or our CMOs and CROs for any post-approval clinical trials that we or our collaborators might conduct. The safety profile of any product will continue to be closely monitored by the FDA and foreign regulatory authorities after approval. If the FDA or foreign regulatory authorities become aware of new safety information after approval of our lead product candidate, they might require labeling changes or establishment of a risk evaluation and mitigation strategy, impose significant restrictions on such product's indicated uses or marketing or impose ongoing requirements for potentially costly post-approval studies or post-market surveillance.

In addition, manufacturers of drug products and their facilities are subject to continual review and periodic inspections by the FDA and other regulatory authorities for compliance with cGMP, GCP, and other regulations. If we, a collaborator or a regulatory agency discover previously unknown problems with a product, such as adverse events of unanticipated severity or frequency, or problems with the facility where the product is manufactured, a regulatory agency might impose restrictions on that product, the manufacturing facility or us, including requiring recall or withdrawal of the product from the market or suspension of manufacturing. If we, our lead product candidate or the manufacturing facilities for our lead product candidate fail to comply with applicable regulatory requirements, a regulatory agency might:

- issue warning letters or untitled letters;
- mandate modifications to promotional materials or require us to provide corrective information to healthcare practitioners;
- require us to enter into a consent decree, which can include imposition of various fines, reimbursements for inspection costs, required due dates for specific actions and penalties for noncompliance;
- seek an injunction or impose civil or criminal penalties or monetary fines;
- suspend or withdraw regulatory approval;
- suspend any ongoing clinical trials;
- refuse to approve pending applications or supplements to applications filed by us or a collaborator;
- suspend or impose restrictions on operations, including costly new manufacturing requirements; or
- seize or detain products, refuse to permit the import or export of products, or require us to initiate a product recall.

The occurrence of any event or penalty described above might inhibit our ability to successfully commercialize our intended product and generate revenues.

Advertising and promotion of any product candidate that obtains approval in the U.S. is heavily scrutinized by the FDA, the Department of Justice, the Office of Inspector General of Health and Human Services, state attorneys general, members of Congress and the public. A company can make only those claims relating to safety and efficacy, purity and potency that are approved by the FDA and in accordance with the provisions of the approved label. Additionally, advertising and promotion of any product

candidate that obtains approval outside of the U.S. is heavily scrutinized by foreign regulatory authorities. Violations, including actual or alleged promotion of our intended product for unapproved or off-label uses, are subject to enforcement letters, inquiries and investigations, and civil and criminal sanctions by the FDA, as well as prosecution under the federal False Claims Act. Any actual or alleged failure to comply with labeling and promotion requirements can have a negative impact on our business.

Risks Related to Our Dependence on Third Parties

We depend on certain key scientific personnel for our success who do not work full time for us. The loss of any such personnel could adversely affect our business, financial condition and results of operations.

Our success depends on the continued availability and contributions of our founder and Chief Executive Officer, Dr. John S. Kovach. Dr. Kovach is 85 years old and is being treated for recurrent asymptomatic prostate cancer. The loss of services of Dr. Kovach could delay or reduce our product development and commercialization efforts and would require that we hire a qualified replacement to fill the position of the Chief Executive Officer. Furthermore, recruiting and retaining qualified scientific personnel to perform future research and development work is critical to our success. The loss of members of our scientific personnel, or our inability to attract or retain other qualified personnel or advisors, could significantly weaken our management, harm our ability to compete effectively and harm our business. The competition for qualified personnel in the pharmaceutical field is intense and, as a result, we might be unable to attract and retain qualified personnel necessary for the development of our business.

During September 2015, we entered into a Collaboration Agreement with BioPharmaWorks, pursuant to which we engaged BioPharmaWorks to perform certain services for us. Those services include, among other things: (a) assisting us to (i) commercialize our intended products and strengthen our patent portfolio, (ii) identify pharmaceutical companies with potential interest in our product pipeline, and (iii) prepare and deliver presentations concerning our product candidates; (b) at the request of the Board of Directors, serving as backup management for up to three months should our Chief Executive Officer and scientific leader be temporarily unable to carry out his duties; (c) being available for consultation in drug discovery and development; and (d) identifying providers and overseeing tasks relating to clinical use and commercialization of new compounds. BioPharmaWorks was founded in 2015 by former Pfizer scientists with extensive multi-disciplinary research and development and drug development experience. The Collaboration Agreement automatically renews annually unless either party elects to terminate it. Services under this Collaboration Agreement have been periodically suspended and resumed; effective March 1, 2019, we and BioPharmaWorks agreed to resume services under this Collaboration Agreement, and the Collaboration Agreement is currently in effect.

Additionally, we have hired Dr. James S. Miser as Chief Medical Officer. For the foreseeable future, Dr. Miser will be working with us on a half-time basis. We believe that this Collaboration Agreement with BioPharmaWorks and the hiring of Dr. Miser mitigate, to a certain extent, our reliance on the services of Dr. Kovach, and would allow us the time to replace Dr. Kovach in the event that such a need arose.

We expect to rely heavily on third parties for the conduct of clinical trials of our product candidates. If these clinical trials are not successful, or if we or our collaborators are not able to obtain the necessary regulatory approvals, we will not be able to commercialize our product candidates.

In order to obtain regulatory approval for the commercial sale of our product candidates, we or our collaborators will be required to complete extensive preclinical studies as well as clinical trials in humans to demonstrate to the FDA and foreign regulatory authorities that our product candidates are safe and effective.

Dr. Kovach is experienced in the design and conduct of early clinical cancer trials, having been the lead investigator for a National Cancer Institute Phase 1 clinical trial contract for ten years at the Mayo Clinic, Rochester, Minnesota. However, we have no experience in conducting clinical trials and expect to rely heavily on collaborative partners and CROs for their performance and management of clinical trials of our product candidates.

Our intended products under development might not be effective in treating any of our targeted disorders or might prove to have undesirable or unintended side effects, toxicities or other characteristics that might prevent or limit their commercial use. Institutional review boards or regulators, including the FDA, might hold, suspend or terminate our clinical research or the clinical trials of our product candidates for various reasons, including non-compliance with regulatory requirements or if, in their opinion, the participating subjects are being exposed to unacceptable health risks. Additionally, failure of third parties conducting or overseeing the operation of the clinical trials to perform their contractual or regulatory obligations in a timely fashion could delay the clinical trials. Failure of clinical trials can occur at any stage. Any of these events would adversely affect our ability to market a product candidate.

The development process necessary to obtain regulatory approval is lengthy, complex and costly. If we or our collaborative partners do not obtain necessary regulatory approvals, then our business would not be successful, and the market price of our common stock could decline substantially.

To the extent that we, or our collaborative partners, are able to successfully advance a product candidate through the clinic, we, or such partner, will be required to obtain regulatory approval prior to marketing and selling such product. The process of obtaining FDA and other required regulatory approvals is costly and lengthy. The time required for FDA and other approvals is uncertain and can typically take several or many years, depending on the complexity and novelty of the product.

Any regulatory approval to market a product might be subject to limitations on the indicated uses for which we, or our collaborative partners, may market the product. These limitations might restrict the size of the market for the product and affect reimbursement by third-party payors. In addition, regulatory agencies might not grant approvals on a timely basis or might revoke or significantly modify previously granted approvals.

We, or our collaborative partners, also are subject to numerous foreign regulatory requirements governing the manufacturing and marketing of our potential future products outside of the United States. The approval procedure varies among countries, additional testing might be required in some jurisdictions, and the time required to obtain foreign approvals often differs from that required to obtain FDA approvals. Moreover, approval by the FDA does not ensure approval by regulatory authorities in other countries, and vice versa.

As a result of these factors, we, or our collaborative partners, might not successfully complete clinical trials in the time periods estimated, if at all. Moreover, if we, or our collaborative partners, incur unanticipated costs and/or delays in development programs or if we fail to successfully develop and commercialize products based upon our technologies, we might not be able to generate significant operating revenues or sustainable profitability, as a result of which our stock price could decline substantially.

Business interruptions could adversely affect future operations, revenues, and financial conditions, and might increase our costs and expenses.

Our operations, and those of our directors, advisors, contractors, consultants, CROs, and collaborators, could be adversely affected by earthquakes, floods, hurricanes, typhoons, extreme weather conditions, fires, water shortages, power failures, business systems failures, medical epidemics and other natural and man-made disaster or business interruptions. Our phones, electronic devices and computer systems and those of our directors, advisors, contractors, consultants, CROs, and collaborators are vulnerable to damages, theft and accidental loss, negligence, unauthorized access, terrorism, war, electronic and telecommunications failures, and other natural and man-made disasters. Operating as a virtual company, our employees conduct business outside of our headquarters and leased or owned facilities. These locations might be subject to additional security and other risk factors due to the limited control of our employees. If such an event as described above were to occur in the future, it might cause interruptions in our operations, delay research and development programs, clinical trials, regulatory activities, manufacturing and quality assurance activities, sales and marketing activities, hiring, training of employees and persons within associated third parties, and other business activities. For example, the loss of clinical trial data from completed or future clinical trials could result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the data.

Likewise, we will rely on third parties to manufacture our product candidates and conduct clinical trials, and similar events as those described in the prior paragraph relating to their business systems, equipment and facilities could also have a material adverse effect on our business. To the extent that any disruption or security breach were to result in a loss of, or damage to, our data or applications, or misappropriation or disclosure of confidential or proprietary information, we could incur liability and the further development and commercialization of our lead product candidate could be delayed or altogether terminated.

Our failure to find third party collaborators to assist or share in the costs of product development could materially harm our business, financial condition or results of operations.

Our strategy for the development and commercialization of our proprietary product candidates might include the formation of collaborative arrangements with third parties. We have entered into a number of agreements with third parties as described below under "Business," including a clinical trial research agreement with H. Lee Moffitt Cancer Center and Research Institute, Inc. ("Moffitt"); a collaboration agreement with the Spanish Sarcoma Group; a cooperative research and development agreement with the National Cancer Institute; a clinical research support agreement with City of Hope National Medical Center; an agreement with Theradex Systems, Inc.; a patent assignment and exploitation agreement with Inserm Transfert SA; an exclusive license agreement with Moffitt, a material cooperative research and development agreement with the National Institutes of Health, a collaboration agreement with BioPharmaWorks; and a consulting agreement with NDA Consulting Corp. Existing and future collaborators have significant discretion in determining the efforts and resources they apply and might not perform their obligations as expected. Potential third-party collaborators include biopharmaceutical, pharmaceutical and biotechnology companies, academic institutions, government agencies and other entities. Third-party collaborators may assist us in:

- funding research, preclinical development, clinical trials and manufacturing;
- seeking and obtaining regulatory approvals; and
- successfully commercializing any future product candidates.

If we are not able to establish further collaboration agreements, we might be required to undertake product development and commercialization at our own expense. Such an undertaking might limit the number of product candidates that we will be able to develop, significantly increase our capital requirements and place additional strain on our internal resources. Our failure to enter into additional collaborations could materially harm our business, financial condition and results of operations.

In addition, our dependence on licensing, collaboration and other agreements with third parties might subject us to a number of risks. If we fail to comply with our obligations under these agreements, of if one or more third parties allege that we fail to comply, then one or more third parties might terminate the agreements. In this event, we might not be able to develop, manufacture or market our product candidates. This would materially adversely affect our business prospects.

These agreements might not be on terms that prove favorable to us and might require us to relinquish certain rights in our product candidates. To the extent we agree to work exclusively with one collaborator in a particular territory, research area, or therapeutic field of use, our opportunities to collaborate with other entities could be curtailed. Lengthy negotiations with potential new collaborators might lead to delays in the research, development or commercialization of product candidates. The decision by our collaborators to pursue alternative technologies or the failure of our collaborators to develop or commercialize successfully any product candidate to which they have obtained rights from us could materially harm our business, financial condition and results of operations.

In addition, our agreements might not be assignable by us without the consent of the respective other party or parties, which might limit or delay our ability to consummate transactions, adversely impact the value of those transactions, or limit our ability to pursue research, development or other activities.

We might be subject to claims by third parties asserting that our employees, consultants, collaborators contractors or we have misappropriated their intellectual property, or claiming ownership of what we regard as our own intellectual property.

Our employees, consultants, collaborators or contractors have been previously employed at universities or third-party pharmaceutical companies, including our actual or possible competitors, and received confidential and proprietary information from them. Although we try to ensure that our employees, consultants, collaborators or contractors do not use the proprietary information or know-how of others in their work for us, we may be subject to claims that these employees, consultants, collaborators or contractors, or we, have used or disclosed intellectual property, including trade secrets or other proprietary information, of any former employer. We might also be subject to claims that former employers or other third parties have an ownership interest in our patents. Litigation may be necessary to defend against these claims. We might not be successful in defending these claims, and if we fail in defending any such claims, in addition to paying monetary damages, we could lose valuable intellectual property rights, such as exclusive ownership of, or right to use, valuable intellectual property. Even if we are successful, litigation could result in substantial cost and reputational loss and be a distraction to our business.

In addition, while it is our policy to require our employees, consultants, collaborators and contractors who may be involved in the development of intellectual property to execute agreements assigning such intellectual property to us, we might be unsuccessful in executing such an agreement with each party who in fact develops intellectual property that we regard as our own. Such assignment agreements might not be self-executing or may be breached, and we might be forced to bring claims against third parties, or defend claims that third parties might bring against us, to determine the ownership of what we regard as our intellectual property.

Risks Related to Our Intellectual Property

We cannot be certain we will be able to obtain patent protection to protect our product candidates and technology.

Our patents and patent applications are owned solely by our subsidiary Lixte Biotechnology, Inc., or jointly by Lixte Biotechnology, Inc., and one of our collaborators.

The patent prosecution process is expensive and time-consuming, and we might not be able to file or prosecute all necessary or desirable patent applications at a reasonable cost or in a timely manner. It is also possible that we will fail to identify patentable aspects of our research or development before it is too late to obtain patent protection. Therefore, these patents and applications might not be prosecuted and enforced in a manner consistent with the best interests of our business.

The patent position of pharmaceutical companies generally is highly uncertain, involves complex legal and factual questions and has in recent years been the subject of much litigation. In addition, the laws of foreign countries might not protect our rights to the same extent as the laws of the United States. Publications of discoveries in the scientific literature often lag behind the actual discoveries, and patent applications in the United States and other jurisdictions are typically not published until after filing, or in some cases not at all. Therefore, we cannot know with certainty whether we were the first to make the inventions claimed in our solely owned or jointly owned patents or pending patent applications, or that we were the first inventors to file for patent protection of such inventions. As a result, the issuance, scope, validity, enforceability and commercial value of our patent rights are highly uncertain. Our pending and future patent applications might not result in patents being issued that protect our technology or products, in whole or in part, or that effectively prevent others from commercializing competitive technologies and products. Changes in the patent laws or their interpretation by courts or patent offices might diminish the value of our patents or patent applications, or narrow their scope.

The issuance of a patent is not conclusive as to its inventorship, scope, term, validity or enforceability, and our solely or jointly owned patents might be challenged in a U.S. or non-U.S. court or patent office. Such challenges might result in loss of exclusivity or in patent claims being narrowed, invalidated or held unenforceable, in whole or in

part, which could limit our ability to stop others from using or commercializing similar or identical technology and products, or limit the duration of the patent protection of our technology and products. Given the amount of time required for research, development, testing or regulatory review of product candidates, patents protecting such candidates might expire before or shortly after such candidates are approved or commercialized. As a result, our solely or jointly owned patents might not provide us with sufficient rights to exclude others from commercializing intended products similar or identical to ours.

We cannot be certain that all patents applied for will be issued. If a third party has also filed a patent application relating to an invention claimed by us, solely or jointly with one of our collaborators, we might be required to participate in an interference or derivation proceeding declared or instituted by the United States Patent and Trademark Office, which could result in substantial uncertainties and cost for us, even if the eventual outcome is favorable to us. The degree of future protection for our proprietary rights is uncertain. For example:

- we, solely or jointly with our collaborators, might not have been the first to make the inventions covered by our pending or future patent applications;
- we, solely or jointly with our collaborators, might not have been the first to file patent applications for these inventions;
- others might independently develop identical, similar or alternative technologies;
- it is possible that our patent applications will not result in an issued patent or patents, or that the scope of protection granted by any patents arising from our patent applications will be significantly narrower than expected;
- we might be unaware of prior art that renders one or more of our patent applications unpatentable or one or more of our patents invalid;
- a court might determine that we failed to disclose to a patent office prior art that we were aware of and that is material to patentability and, therefore, conclude that one or more of our patents are unenforceable;
- any patents under which we hold rights might not cover commercially viable products, might not provide us with any competitive advantages or might be challenged by one or more third parties as being not infringed, being invalid, or being unenforceable under United States or foreign laws;
- a court or patent office might determine that two or more of our patents claim patentably indistinct subject matter, which could adversely affect one or more of the patents' the term, validity or enforceability;
- a court or patent office might determine that one or more patents issued to us in the future or under which we hold rights are invalid or unenforceable; or
- we might develop additional proprietary technologies that are not patentable and which might not be adequately protected through trade secrets or know-how.

In addition, we solely or jointly own patents or patent applications in jurisdictions having, or that might in the future have, geopolitical disputes, including over sovereignty. We cannot guarantee that patents granted in these jurisdictions will be enforceable. An inability to enforce patents in these jurisdictions could have a material adverse effect on our business.

If we do not obtain patent term extension in the United States under the Hatch-Waxman Act or in foreign countries under similar legislation, our business might be materially harmed.

In the United States, the term of a patent that covers an FDA-approved drug, its method for use or method for manufacture, can be eligible for patent term extension. U.S. law provides a patent term extension of up to five years beyond the expiration of the patent for time during which the drug is under regulatory review. Patent term extension cannot extend the term of a patent beyond a total of 14 years from the date of regulatory approval; only one patent can be extended for the same regulatory review period; and the scope of a patent's enforceability during a patent term extension is limited to the scope of FDA approval. There is no guarantee that the relevant agencies, including the United States Patent and Trademark Office ("USPTO"), will agree with our assessment of whether such extensions should be granted, and even if granted, the term of these extensions. We might not be granted patent term extension in the United States or in any foreign country because of, for example, expiration of our patents before obtaining regulatory approval, failing to exercise due diligence during the testing phase or regulatory review process, failing to apply within applicable deadlines, failing to apply prior to expiration of relevant patents or otherwise failing to satisfy applicable requirements. Moreover, the length of a patent term extension, as well as the scope of patent protection during any such extension, afforded by the governmental authority could be less than we request. If we are unable to obtain any patent term extension or if the term of any such extension is less than we request, our competitors might obtain approval of competing products following the expiration of our patent rights, and our business, financial condition, results of operations and prospects could be materially harmed.

It is possible that we will not obtain patent term extension under the Hatch-Waxman Act for a U.S. patent covering any of our product candidates that we may identify even where that patent is eligible for patent term extension, or if we obtain such an extension, it may be for a shorter period than we had sought.

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

We have entered into, and might in the future enter into, one or more intellectual property license agreements that are important to our business. These license agreements might impose various diligence, milestone payment, royalty and other obligations on us. For example, we might be required to use commercially reasonable efforts to engage in various development and commercialization activities with respect to licensed products, and might need to satisfy specified milestone and royalty payment obligations. If we fail to comply with any obligations under our agreements with any of these licensors, we might be subject to termination of the license agreement in whole or in part, increased financial obligations to our licensors or loss of exclusivity in a particular field or territory, in which case our ability to develop or commercialize products covered by the license agreement will be impaired.

In addition, disputes might arise regarding intellectual property subject to a license agreement, including:

- the scope of rights granted under the license agreement and other interpretation-related issues;
- whether our technology, product candidates or processes infringe intellectual property rights that are owned by the licensor, but that are not subject to the licensing agreement;
- our diligence obligations under the license agreement and the activities that satisfy those obligations;
- whether we are required to sublicense to a third party rights that the license grants to us, but that we do not commercially pursue; and
- the ownership of inventions, data and know-how resulting from joint creation or use of intellectual property by our licensors and us.

If disputes over intellectual property that we have licensed, or might in the future license, prevent or impair our ability to maintain our licensing arrangements on acceptable terms, we may be unable to successfully develop or commercialize the affected product candidates.

We might need to obtain licenses from third parties to advance our research or allow commercialization of our product candidates. We may fail to obtain any of these licenses at a commercially reasonable cost or on commercially reasonable terms, if at all. Other companies might have a competitive advantage over us due to their larger size or cash resources or greater clinical development and commercialization capabilities. We might be unable to further develop or commercialize one or more of our product candidates, which could harm our business significantly.

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

Our success will depend in part on our ability to operate without infringing the proprietary rights of third parties. We cannot guarantee that our intended products or our product candidates, or manufacture or use of our intended products or our product candidates, will not infringe third-party patents. Furthermore, a third party might claim that we are using without permission one or more inventions covered by the third party's patent rights and might go to court to stop us from engaging in our normal operations and activities, including making, offering to sell or selling our product candidates. Still further a third party might go to court seeking judgment that our patents are invalid or unenforceable. These lawsuits are costly and could affect our results of operations and divert the attention of managerial and scientific personnel. Some of these third parties might be better capitalized and have more resources than us. There is a risk that a court would decide that we are infringing the third party's patents and would order us to stop the activities covered by the patents. In that event, we might not have a viable way around the patent and might need to halt commercialization of the relevant product candidate. In addition, there is a risk that a court will order us to pay the other party damages for having violated the other party's patents. There is also a risk that a court would decide that one or more of our patents are invalid or unenforceable. In addition, we might be obligated to indemnify our licensors and collaborators against intellectual property infringement claims brought by third parties, which could require us to expend additional resources. The pharmaceutical and biotechnology industries have produced a proliferation of patents, and it is not always clear to industry participants, including us, which patents cover various types of products or methods of use. The coverage of patents is subject to interpretation by the courts, and the interpretation is not always uniform.

We cannot guarantee that we have identified all third-party patents or pending patent applications that are or might be necessary for the commercialization of our intended products and technologies in any jurisdiction. Patent applications in the United States and elsewhere are not published until approximately 18 months after the earliest filing for which priority is claimed, with such earliest filing date being commonly referred to as the priority date. Therefore, patent applications covering our technologies and intended products could have been filed by others without our knowledge.

Additionally, pending patent applications that have been published can, subject to certain limitations, be later amended in a manner that could cover our technologies or intended products. The scope of a patent claim is determined by the interpretation of the law, the words of a patent claim, the written disclosure in a patent and the patent's prosecution history. Our interpretation of the relevance or the scope of a patent or a pending patent application may be incorrect, which may negatively impact our ability to market our intended products. We might incorrectly determine that our technologies or intended products are not covered by a third-party patent or might incorrectly predict whether a third party's pending patent application will issue with claims of relevant scope. Our determination of the expiration date of any patent in the United States or abroad that we consider relevant might be incorrect, and we might incorrectly conclude that a third-party patent does not cover our technology or intended products, is invalid or is unenforceable. Our inability to identify or correctly interpret relevant patents might negatively impact our ability to develop or market our technologies or intended products. If we fail to identify or correctly interpret relevant patents, we might be subject to infringement claims. We cannot guarantee that we will be able to successfully settle or otherwise resolve such infringement claims. If we fail in any such dispute, in addition to being liable for damages, we might be temporarily or permanently enjoined or otherwise prohibited from commercializing any of technologies or intended products that are held to be infringing. We might, if possible, also be forced to redesign intended products or product formulations so that we no longer infringe the third-party intellectual property rights. Any of these events, even if we were ultimately to prevail, could require us to divert substantial financial and management resources that we would otherwise be able to devote to our business.

As the pharmaceutical or biotechnology industry expands and more patents are issued, the risk increases that our product candidates or intended products give rise to claims of infringement of the patent rights of others. There may be third-party patents of which we are currently unaware with claims to materials, formulations, methods of manufacture or methods for treatment related to the use or manufacture of our product candidates. If we are sued for patent infringement, we would need to demonstrate that our products or methods either do not infringe the patent claims of the relevant patent or that the patent claims are invalid or unenforceable, negotiate and obtain a license under reasonable terms to us or discontinue performing the allegedly infringing activities. We might not be able to do any of these. Proving invalidity is difficult. For example, in the United States, proving invalidity requires a showing of clear and convincing evidence to overcome the presumption of validity enjoyed by issued patents. Even if we are successful in these proceedings, we might incur substantial costs and divert management's time and attention in pursuing these proceedings, which could have a material adverse effect on us. If we are unable to avoid infringing the patent rights of others, we might be required to seek a license, which might not be available, and then we will have to defend an infringement action, challenge the validity of the patents in the USPTO or in court, or discontinue performing the allegedly infringing activities. Patent litigation is costly and time consuming. We might not have sufficient resources to bring these actions to a successful conclusion. In addition, if we do not obtain a license, develop or obtain non-infringing technology, fail to defend an infringement action successfully or fail to have infringed patents declared invalid or unenforceable, we might incur substantial monetary damages, encounter significant delays in bringing our product candidates to market and be precluded from manufacturing or selling our product candidates.

We cannot be certain that others have not filed patent applications for technology covered by our pending applications, that we were the first to invent the technology or that we were the first to file patent applications covering our technology, because:

- some patent applications in the United States are maintained in secrecy until the patents are issued;
- patent applications in the United States are typically not published until 18 months after their earliest claimed priority date; and
- publications in the scientific literature often lag behind actual discoveries.

Our competitors might have filed, and might in the future file, patent applications covering technology similar or identical to ours. Any such patent applications might dominate our patent applications, which could further require us to obtain rights to issued patents covering such technologies. If another party has filed US patent applications that cover inventions similar or identical to ours and claim priority to any applications filed prior to the priority dates of our applications, we might have to participate in an interference proceeding declared or a derivation proceed instituted by the USPTO to determine priority of invention in the United States. The costs of these proceedings could be substantial, and it is possible that such efforts would be unsuccessful if the other party had independently arrived at the same or similar inventions before us, possibly resulting in a loss of our U.S. patent position with respect to such inventions. Other countries might have similar laws that permit secrecy of patent applications. Either way, the third party's patents or patent applications might be entitled to priority over our applications in such jurisdictions.

Some of our competitors might be able to sustain the costs of a patent challenge more effectively than we can because they have substantially greater resources. In addition, uncertainties regarding the outcome of the challenge could have a material adverse effect on our ability to raise the funds necessary to continue our operations.

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

As is common in the biotechnology and pharmaceutical industries, we employ, and might employ in the future, individuals who were previously employed at other biotechnology or pharmaceutical companies, including our competitors or potential competitors. Although we try to ensure that our employees, consultants and independent contractors do not use the proprietary information or know-how of others in their work for us, we might be subject to claims that we or our employees, consultants or independent contractors have inadvertently or otherwise used or disclosed trade secrets or other proprietary information of their former employers. Litigation might be necessary to defend against these claims. If we fail in defending any such claims, in addition to paying monetary damages, we could lose valuable intellectual property rights or personnel, which could adversely impact our business. Even if we are successful in defending against these claims, litigation could result in substantial costs and be a distraction to management.

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

We might be subject to competition despite the existence of intellectual property we license or own. We can give no assurances that our intellectual property claims will be sufficient to prevent third parties from designing around patents we own or license and developing and commercializing competitive products. The existence of competitive products that avoid our intellectual property could materially adversely affect our operating results and financial condition. Furthermore, any actual or perceived limitations, in our intellectual property might lessen the interest of third parties to partner, collaborate or otherwise transact with us, if third parties perceive a higher than acceptable risk to commercialization of our intended products or future products.

Our approach includes filing patent applications covering combination therapy with known, studied and/or marketed drugs. Although the protection afforded by our patent applications might be significant, when looking at our patents' ability to block competition, the protection offered by our patents might be, to some extent, more limited than protection provided by patents claiming a composition of matter that is entirely new and previously unknown. If a competitor were able to successfully design around any combination therapy patents we have or might have in the future, our business and competitive advantage could be significantly affected.

We might elect to sue a third party, or otherwise make a claim, alleging infringement or other violation of patents, trademarks, trade dress, copyrights, trade secrets, domain names or other intellectual property rights that we either own or license. We might alternatively elect to sue a third party, or otherwise make a claim, alleging that we don't infringe a third party's patents or that the third party's patents are invalid or unenforceable. Any claims that we assert against a third party could provoke the third party to assert one or more counterclaims against us, for example, alleging that we infringe their patents. In addition, in a patent infringement proceeding, a court might decide that a patent of ours is invalid or unenforceable, in whole or in part; construe the patent's claims narrowly; or refuse to stop the other party from using the technology at issue. Any litigation proceeding could put one or more of our patents at risk of being invalidated, held unenforceable or interpreted narrowly. Even if we prevail in a lawsuit, a court might not award remedies that sufficiently compensate us for our losses.

If we do not prevail in either type of litigation, we might be subject to:

- paying monetary damages related to the legal expenses of the third party;
- facing additional competition that might have a significant adverse effect on our intended-product pricing, market share, business operations, financial condition, and the commercial viability of our intended products; and
- restructuring our company or delaying or terminating select business opportunities, including, but not limited to, research and development, clinical trials, and commercialization activities, due to a potential deterioration of our financial condition or market competitiveness.

A third party might also challenge the validity, enforceability or scope of the intellectual property rights that we license or own, and the result of these challenges might narrow the scope or claims of or invalidate patents that are integral to our product candidates in the future. There can be no assurance that we will be able to successfully defend patents we own in an action against third parties due to the unpredictability of litigation and the high costs associated with intellectual property litigation, among other factors.

The laws of some jurisdictions do not protect intellectual property rights to the same extent as the laws or rules and regulations of the United States, and many companies have encountered significant difficulties in protecting and defending such rights in non-U.S. jurisdictions. The legal systems of some countries are less supportive of enforcement of patents, trade secrets and other intellectual property protection, than the United States. This could make it difficult for us to enforce our patents or market competing products outside the United States, in violation of our proprietary rights generally. Proceedings to enforce our patent rights in non-U.S. jurisdictions, whether or not successful, could result in substantial costs and divert our efforts and attention from other aspects of our business, could put our patents at risk of being invalidated or interpreted narrowly and our patent applications at risk of not issuing, and could provoke third parties to assert claims against us. We might not prevail in any lawsuits that we initiate, and the damages or other remedies awarded, if any, might not be commercially meaningful. Accordingly, our efforts to enforce our intellectual property rights in all jurisdictions where we have the rights might be inadequate to obtain a significant commercial advantage from the intellectual property that we develop or license. Furthermore, while we seek to protect our intellectual property rights in significant markets, we cannot ensure that we will be able to initiate or maintain similar efforts in all jurisdictions in which we might wish to market our intended products or our product candidates. Accordingly, our efforts to protect our intellectual property rights in such countries might be inadequate, which might have an adverse effect on our ability to successfully commercialize our product candidates in all of our expected significant foreign markets. If we or our licensors encounter difficulties in protecting, or are otherwise precluded from effectively protecting, the intellectual property rights important for our business in such jurisdictions, the value of these rights might be diminished, and we might face additional competition from others in those jurisdictions.

Changes to patent law, for example the Leahy-Smith America Invests Act, AIA or Leahy-Smith Act, of 2011 and the Patent Reform Act of 2009 and other future article of legislation in the U.S., might substantially change the regulations and procedures surrounding patent applications, issuance of patents, prosecution of patents, challenges to patent validity, and patent enforcement. We can give no assurances that our patents or those of our licensor(s) can be defended or will protect us against future intellectual property challenges, particularly as they pertain to changes in patent law and future patent law interpretations.

In addition, enforcing and maintaining our intellectual property protection depends on compliance with various procedural, document-submission, fee-payment and other requirements imposed by the U.S. Patent and Trademark Office and courts, and foreign government patent agencies and courts, and our patent protection could be reduced or eliminated for non-compliance with these requirements.

Filing, prosecuting and defending patents covering our product candidates in all countries throughout the world would be prohibitively expensive, and our intellectual property rights in some jurisdictions outside the United States can be less extensive than those in the United States. And filing, prosecuting and defending patents even in only those jurisdictions in which we develop or commercialize our product candidates might be prohibitively expensive or impractical. Competitors might use our technologies in jurisdictions where we have not obtained patent protection to develop their own products or technologies and, further, may export otherwise infringing products or technologies to territories where we and have patent protection, but where enforcement is not as strong as that in the United States. These third-party products or technologies might compete with our product candidates, and our intellectual property rights may not be effective or sufficient to prevent third parties from competing.

In addition, we might decide to abandon national or regional patent applications while they are still pending or to abandon granted patents. This might invite or encourage third parties to develop their products or technologies in jurisdictions where we abandon patent applications or patents.

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

We also rely on proprietary trade secrets and unpatented know-how to protect our research and development activities, particularly when we do not believe that patent protection is appropriate or available. However, trade secrets are difficult to protect. We will attempt to protect our trade secrets and unpatented know-how by requiring our employees, consultants, collaborators, and advisors to execute a confidentiality and non-use agreement. We cannot guarantee that these agreements will provide meaningful protection; that these agreements will not be breached, by, e.g., a misappropriating or disclosing our confidential information; that we will have an adequate remedy for any such breach; or that our trade secrets will not otherwise become known or independently developed by a third party. Our trade secrets, and those of our present or future collaborators that we utilize by agreement, might become known or might be independently discovered by others, which could adversely affect the competitive position of our product candidates.

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

We might be unaware of or unfamiliar with prior art and/or interpretations of prior art that could potentially impact the validity or scope of our patents or pending patent applications, or patent applications that we will file. We might have elected, or elect now or in the future, not to maintain or pursue intellectual property rights that, at some point in time, might be considered relevant to or enforceable against a competitor.

We take efforts and enter into agreements with employees, consultants, collaborators, and advisors to confirm ownership of and chain of title in intellectual property rights. However, an inventorship or ownership dispute could arise that might permit one or more third parties to practice our intellectual property rights, including possible efforts to enforce rights against us.

We might not have rights under some patents or patent applications that cover technologies that we use in our research, drug targets that we select, product candidates and particular uses thereof that we seek to develop and commercialize, as well as synthesis of our product candidates. Third parties might own or control these patents and patent applications in the United States and elsewhere. These third parties could bring claims against us or our collaborators that would cause us to incur substantial expenses and, if successful against us, could cause us to pay substantial damages. Further, if a patent infringement suit were brought against us or our collaborators, we or they could be forced to stop or delay research, development, manufacturing or sales of the product or product candidate that is the subject of the suit. We or our collaborators therefore might choose to seek, or be required to seek, a license from the third-party and would most likely be required to pay license fees or royalties or both. These licenses might not be available on acceptable terms, or at all. Even if we or our collaborators were able to obtain a license, the rights might be nonexclusive, which would give our competitors access to the same intellectual property. Ultimately, we could be prevented from commercializing a product or product candidate, or forced to cease some aspect of our business operations, as a result of patent infringement claims, which could harm our business.

Periodic maintenance fees on issued U.S. patents are due to be paid to the USPTO, and periodic maintenance fees on issued non-U.S. patents and pending non-U.S. patent applications are due to be paid to non-U.S. patent offices. The patent offices require compliance with many procedural, documentary, fee payment and other requirements during the patent application process and after a patent issues or grants. While an inadvertent lapse can in some cases be cured by payment of a late fee or by other means in accordance with the applicable rules, there are situations in which non-compliance, for example, caused by geopolitical events such as civil or political unrest (including the ongoing conflict between Ukraine and Russia), can result in abandonment or lapse of the patent or patent application, resulting in partial or complete loss of a patent or patent rights in the relevant jurisdiction. Non-compliance events that could result in abandonment or lapse of a patent or patent application include, but are not limited to, failure to respond to patent office actions within prescribed time limits, non-payment of fees and failure to properly legalize and submit formal documents. In such an event, our competitors might be able to enter the market, which would have a material adverse effect on our business.

The USPTO and various non-U.S. government agencies require compliance with certain foreign filing requirements during the patent application process. For example, in some countries, including the United States, a foreign filing license is required before certain patent applications are filed outside that country. The foreign filing license requirements can vary by country. In some cases, a foreign filing license may be obtained retroactively in accordance with the applicable rules. There are situations, however, in which non-compliance can result in abandonment of a pending patent application or can be grounds for revoking or invalidating an issued patent, resulting in the loss of patent rights in the relevant jurisdiction. In such an event, potential competitors might be able to enter the relevant markets with similar or identical products or technology, which could have a material adverse effect on our business, financial condition, results of operations, and prospects.

There has been substantial litigation and other legal proceedings regarding patent and other intellectual property rights in the pharmaceutical and biotechnology industries. Although we are not currently a party to any patent litigation or any other adversarial proceeding, including any interference or derivation proceeding declared or instituted before the United States Patent and Trademark Office, regarding intellectual property rights with respect to our intended products, our product candidates and our technology, it is possible that we might become one in the future. We are not currently aware of any actual or reasonably foreseeable third-party infringement claim involving our product candidates. The cost to us of any patent litigation or other proceeding, even if resolved in our favor, could be substantial. The outcome of patent litigation is subject to uncertainties that cannot be adequately quantified in advance, including the dispute forum, demeanor and credibility of witnesses and the identity of the adverse party, especially in pharmaceutical and biotechnology related patent cases that might turn on the testimony of experts as to technical facts upon which experts might reasonably disagree. Some of our competitors might be able to sustain the costs of such litigation or proceedings more effectively than we can because of their substantially greater financial resources. If a patent or other proceeding is resolved against us, we might be enjoined from researching, developing, manufacturing or commercializing our intended products or our product candidates without a license from the other party and we might be held liable for significant damages. We might not be able to obtain any required license on commercially acceptable terms or at all.

Uncertainties resulting from the initiation and continuation of patent litigation or other proceedings could harm our ability to compete in the marketplace. Patent litigation or other proceedings might also absorb significant management time.

If we are unable to protect our intellectual property rights, our competitors might develop and market products with similar or identical features that might reduce demand for our potential products.

The following factors are important to our success:

- receiving patent protection for our product candidates;
- preventing others from infringing our intellectual property rights; and
- maintaining our patent rights and trade secrets.

We will be able to protect our intellectual property rights in patents and trade secrets from unauthorized use by third parties only to the extent that such intellectual property rights are covered by valid and enforceable patents or are effectively maintained as trade secrets and we enforce these rights.

Because issues of patentability involve complex legal and factual questions, the issuance, scope or enforceability of patents cannot be predicted with certainty. Patents can be challenged, invalidated, found unenforceable, or circumvented. United States patents and patent applications can be subject to interference or derivation proceedings.

United States patents can also be subject to post grant proceedings, including re-examination, derivation, *Inter Partes* Review and Post Grant Review, in the United States Patent and Trademark Office. Foreign patents can be subject to opposition or comparable proceedings in corresponding foreign patent offices. Any of these challenges might result in loss of the patent, rejection of the patent application or loss or reduction in the scope of one or more of the claims of the patent or patent application. In addition, these proceedings can be costly. Thus, any patents that we own or license from others might not provide any protection against competitors. Furthermore, an adverse decision in an interference or derivation proceeding can result in a third-party receiving the patent rights sought by us, which in turn could affect our ability to market a potential product to which that patent filing was directed. Our pending patent applications, those that we might file in the future, or those that we might license from third parties might not result in patents being issued. If issued, they might not provide us with proprietary protection or competitive advantages against competitors with similar or identical technology. Furthermore, others might independently develop similar technologies or duplicate any technology that we have developed. Some countries have compulsory licensing laws under which a patent owner might be compelled to grant licenses to third parties. For example, compulsory licenses might be required in cases such as where the patent owner has failed to "work" the invention in that country or where a third-party has patented improvements. In addition, some countries might limit the enforceability of patents against government agencies or government contractors. In these countries, we might have limited infringement remedies, which could materially diminish the value of our patents. Moreover, the legal systems of some countries are less supportive of enforcement of patents, trade secrets and other intellectual property protection, than the United States, which might make it difficult to stop infringement in these countries.

In addition, our ability to enforce our patent rights depends on our ability to detect infringement. It is difficult to detect infringers who do not advertise or otherwise promote the compounds that are used in their products. Any litigation to enforce or defend our patent rights, even if we prevail, could be costly and time-consuming and would divert the attention of management and key personnel from business operations.

We will also rely on trade secrets, know-how and technology, which are not protected by patents, to maintain our competitive position. We will seek to protect this information by entering into confidentiality agreements with parties that have access to it, such as strategic partners, collaborators, employees, contractors and consultants. Any of these parties might breach these agreements and misappropriate or disclose our confidential information or our competitors might learn of the information in some other way. If any trade secret, know-how or other technology not protected by a patent were disclosed to, or independently developed by, a competitor, our business, financial condition and results of operations could be materially adversely affected.

Risks Related to Commercialization of Our Current Product Candidate and Future Product Candidates

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

Even if we obtain regulatory approval for our lead product candidate or any future product candidates, the products might not gain market acceptance among physicians, healthcare payors, patients or the medical community, including cancer treatment centers. Market acceptance of any product candidates for which we receive approval depends on a number of factors, including:

- the efficacy and safety of such product candidates as demonstrated in clinical trials;
- the clinical indications and patient populations for which the product candidate is approved;
- acceptance by physicians, major cancer treatment centers and patients of the drug as a safe and effective treatment;
- the adoption of novel immunotherapies by physicians, hospitals and third-party payors;
- the potential and perceived advantages of product candidates over alternative treatments;
- the safety of product candidates seen in a broader patient group, including our use outside the approved indications;
- any restrictions on use together with other medications;
- the prevalence and severity of any side effects;
- product labeling or product insert requirements of the FDA or other regulatory authorities;
- the timing of market introduction of our intended product as well as competitive products;
- the development of manufacturing and distribution processes for commercial scale manufacturing for our lead product candidate and any future product candidates;
- the cost of treatment in relation to alternative treatments;
- the availability of coverage and adequate reimbursement from third-party payors and government authorities;
- relative convenience and ease of administration; and
- the effectiveness of our sales and marketing efforts and those of our collaborators.

If our lead product candidate and any future product candidates are approved but fail to achieve market acceptance among physicians, patients, healthcare payors or cancer treatment centers, we will not be able to generate significant revenues, which would compromise our ability to become profitable.

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

Our ability to commercialize any product successfully will depend, in part, on the extent to which coverage and adequate reimbursement for such product and related treatments will be available from third-party payors, including government health administration authorities, private health insurers and other organizations.

Third-party payors determine which medications they will cover and establish reimbursement levels. A primary trend in the healthcare industry is cost containment. Third-party payors have attempted to control costs by limiting coverage and the amount of reimbursement for particular medications. Increasingly, third-party payors are requiring that drug companies provide them with predetermined discounts from list prices and are challenging the prices charged for medical products. Third-party payors might also seek additional clinical evidence, beyond the data required to obtain regulatory approval, demonstrating clinical benefit and value in specific patient populations before covering our intended product for those patients. We cannot be sure that coverage and adequate reimbursement will be available for any product that we commercialize and, if

coverage is available, what the level of reimbursement will be. Coverage and reimbursement might impact the demand for, or the price of, any product candidate for which we obtain regulatory approval. If reimbursement is not available or is available only at limited levels, we might not be able to successfully commercialize any product candidate for which we obtain regulatory approval.

There might be significant delays in obtaining coverage and reimbursement for newly approved drugs, and coverage might be more limited than the purposes for which the drug is approved by the FDA or comparable foreign regulatory authorities. Moreover, eligibility for coverage and reimbursement does not imply that any drug will be paid for in all cases or at a rate that covers our costs, including research, development, manufacture, sale and distribution. Interim reimbursement levels for new drugs, if applicable, might also not be sufficient to cover our costs and might only be temporary. Reimbursement rates might vary according to the use of the drug and the clinical setting in which it is used, might be based on reimbursement levels already set for lower cost drugs and might be incorporated into existing payments for other services. Net prices for drugs might be reduced by mandatory discounts or rebates required by third-party payors and by any future relaxation of laws that presently restrict imports of drugs from countries where they might be sold at lower prices than in the U.S. No uniform policy for coverage and reimbursement exists in the U.S., and coverage and reimbursement can differ significantly from payor to payor. Third-party payors can rely upon Medicare coverage policy and payment limitations in setting their own reimbursement policies, but also have their own methods and approval process apart from Medicare determinations. Our inability to promptly obtain coverage and profitable reimbursement rates from both government-funded and private payors for any approved product that we develop could have a material adverse effect on our operating results, ability to raise capital needed to commercialize our intended product and overall financial condition.

Healthcare legislative measures aimed at reducing healthcare costs might have a material adverse effect on our business and results of operations.

Third-party payors, whether domestic or foreign, or governmental or commercial, are developing increasingly sophisticated methods of controlling healthcare costs. In both the U.S. and certain international jurisdictions, there have been a number of legislative and regulatory changes to the health care system that could impact our ability to sell our intended product profitably. In particular, in 2010, the Affordable Care Act ("ACA") was enacted, which, among other things, subjected biologic products to potential competition by lower-cost biosimilars, addressed a new methodology by which rebates owed by manufacturers under the Medicaid Drug Rebate Program are calculated for drugs that are inhaled, infused, instilled, implanted or injected, increased the minimum Medicaid rebates owed by most manufacturers under the Medicaid Drug Rebate Program, extended the Medicaid Drug Rebate Program to utilization of prescriptions of individuals enrolled in Medicaid managed care organizations, subjected manufacturers to new annual fees and taxes for certain branded prescription drugs, and provided incentives to programs that increase the federal government's comparative effectiveness research. Since its enactment, there have been judicial and Congressional challenges to certain aspects of the ACA, as well as recent efforts by the current U.S. administration to repeal or repeal and replace certain aspects of the ACA. On December 14, 2018, a U.S. District Court Judge in the Northern District of Texas, or the Texas District Court Judge, ruled that the individual mandate is a critical and inseverable feature of the ACA, and therefore, because it was repealed as a part of the Tax Act, the remaining provisions of the ACA are invalid as well. While the Texas District Court Judge, as well as the Trump Administration and CMS, have stated that the ruling will have no immediate effect, it is unclear how this decision, subsequent appeals and other efforts to repeal and replace the ACA will impact the ACA. Until there is more certainty concerning the future of the ACA, it will be difficult to predict its full impact and influence on our business.

In addition, other legislative changes have been proposed and adopted in the U.S. since the ACA was enacted. In August 2011, the Budget Control Act of 2011, among other things, created measures for spending reductions by Congress. A Joint Select Committee on Deficit Reduction, tasked with recommending a targeted deficit reduction of at least $1.2 trillion for the years 2013 through 2021, was unable to reach required goals, thereby triggering the legislation's automatic reduction to several government programs. This includes aggregate reductions of Medicare payments to providers of 2% per fiscal year, which went into effect in 2013, and will remain in effect through 2027 unless additional Congressional action is taken. The American Taxpayer Relief Act of 2012 further reduced Medicare payments to several providers, including hospitals and cancer treatment centers, and increased the statute of limitations period for the government to recover overpayments to providers from three to five years.

There have been, and likely will continue to be, legislative and regulatory proposals at the foreign, federal and state levels directed at containing or lowering the cost of healthcare. We cannot predict the initiatives that might be adopted in the future. The continuing efforts of the government, insurance companies, managed care organizations and other payors of healthcare services to contain or reduce costs of healthcare and/or impose price controls might adversely affect:

- the demand for our lead product candidate, if we obtain regulatory approval;
- our ability to receive or set a price that we believe is fair for our intended product;
- our ability to generate revenue and achieve or maintain profitability;
- the level of taxes that we are required to pay; and
- the availability of capital.

We expect that the ACA, as well as other healthcare reform measures that might be adopted in the future, might result in additional reductions in Medicare and other healthcare funding, more rigorous coverage criteria, lower reimbursement and new payment methodologies. This could lower the price that we receive for any approved product. Any denial in coverage or reduction in reimbursement from Medicare or other government-funded programs might result in a similar denial or reduction in payments from private payors, which might prevent us from being able to generate sufficient revenue, attain profitability or commercialize our product candidate, if approved.

Price controls might be imposed in foreign markets, which might adversely affect our future profitability.

In some countries, the pricing of prescription drugs is subject to governmental control. In these countries, pricing negotiations with governmental authorities can take considerable time after receipt of regulatory approval for a product. In addition, there can be considerable pressure by governments and other stakeholders on prices and reimbursement levels, including as part of cost containment measures. Political, economic and regulatory developments might further complicate pricing negotiations, and pricing negotiations might continue after reimbursement has been obtained. Reference pricing used by various European Union member states and parallel distribution, or arbitrage between low-priced and high-priced member states, can further reduce prices.

In some countries, we or our collaborators might be required to conduct a clinical trial or other studies that compare the cost-effectiveness of our product candidate to other available therapies in order to obtain or maintain reimbursement or pricing approval. Publication of discounts by third-party payors or authorities might lead to further pressure on the prices or reimbursement levels within the country of publication and other countries. If reimbursement of our intended product is unavailable or limited in scope or amount, or if pricing is set at unsatisfactory levels, our business could be adversely affected.

Risks Related to Healthcare Compliance Regulations

Our relationships with customers and third-party payors will be subject to applicable anti-kickback, fraud and abuse and other healthcare laws and regulations, which could expose us to criminal sanctions, civil penalties, contractual damages, reputational harm and diminished profits and future earnings. If we or they are unable to comply with these provisions, we might become subject to civil and criminal investigations and proceedings that could have a material adverse effect on our business, financial condition and prospects.

Healthcare providers, physicians and third-party payors will play a primary role in the recommendation and prescription of any product candidates for which we obtain regulatory approval. Our current and future arrangements with healthcare providers, healthcare entities, third-party payors and customers might expose us to broadly applicable fraud and abuse and other healthcare laws and regulations that might constrain the business or financial arrangements and relationships through which we research, develop and will market, sell and distribute our intended product. As a pharmaceutical company, even though we do not and will not control referrals of healthcare services or bill directly to Medicare, Medicaid or other third-party payors, federal and state healthcare laws and regulations pertaining to fraud and abuse and patients' rights are applicable to our business. Restrictions under applicable federal and state healthcare laws and regulations that might affect our ability to operate include the following:

- the federal healthcare Anti-Kickback Statute which prohibits, among other things, individuals and entities from knowingly and willfully soliciting, offering, receiving or providing remuneration, directly or indirectly, overtly or covertly, in cash or in kind, to induce or reward, or in return for, either the referral of an individual for, or the purchase, order or recommendation of, any good or service, for which payment might be made under a federal healthcare program such as Medicare and Medicaid;

- federal civil and criminal false claims laws, including the federal False Claims Act that can be enforced through civil whistleblower or qui tam actions, and civil monetary penalty laws, prohibit individuals or entities from knowingly presenting, or causing to be presented, to the federal government, including the Medicare and Medicaid programs, claims for payment or approval that are false or fraudulent or making a false statement to avoid, decrease or conceal an obligation to pay money to the federal government;

- the federal Health Insurance Portability and Accountability Act of 1996 ("HIPAA") which imposes criminal and civil liability for executing a scheme to defraud any healthcare benefit program and also created federal criminal laws that prohibit knowingly and willfully falsifying, concealing or covering up a material fact or making any materially false statements in connection with the delivery of or payment for healthcare benefits, items or services, as amended by the Health Information Technology for Economic and Clinical Health Act of 2009 ("HITECH") which imposes obligations, including mandatory contractual terms, with respect to safeguarding the privacy, security and transmission of individually identifiable health information on entities subject to the law, such as certain healthcare providers, health plans, and healthcare clearinghouses, known as covered entities, and their respective business associates that perform services for them that involve the creation, use, maintenance or disclosure of, individually identifiable health information;

- the federal physician sunshine requirements under the ACA which requires certain manufacturers of drugs, devices, biologics and medical supplies, with certain exceptions, to report annually to HHS information related to payments and other transfers of value to physicians, other healthcare providers, and teaching hospitals, and ownership and investment interests held by physicians and other healthcare providers and their immediate family members and applicable group purchasing organizations;

- analogous state and foreign laws and regulations, such as state anti-kickback and false claims laws, which might apply to sales or marketing arrangements and claims involving healthcare items or services reimbursed by non-governmental third-party payors, including private insurers; some state laws which require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government and might require drug manufacturers to report information related to payments and other transfers of value to physicians and other healthcare providers, marketing expenditures or pricing information; and certain state and local laws which require the registration of pharmaceutical sales representatives; and

- state and foreign laws govern the privacy and security of health information in specified circumstances, many of which differ from each other in significant ways and often are not pre-empted by HIPAA, thus complicating compliance efforts.

Efforts to ensure that our business arrangements with third parties will comply with applicable healthcare laws and regulations will involve substantial costs. It is possible that governmental authorities will conclude that our business practices might not comply with current or future statutes, regulations or case law involving applicable fraud and abuse or other healthcare laws and regulations. If our operations are found to be in violation of any of these laws or any other governmental regulations that might apply to us, we might be subject to significant civil, criminal and administrative penalties, damages, fines, imprisonment, disgorgement, exclusion from government funded healthcare programs, such as Medicare and Medicaid, integrity oversight and reporting obligations, and the curtailment or restructuring of our operations. If any physicians or other healthcare providers or entities with whom we expect to do business are found to not be in compliance with applicable laws, they might be subject to criminal, civil or administrative sanctions, including exclusions from government funded healthcare programs.

Our employees might engage in misconduct or other improper activities, including noncompliance with regulatory standards and requirements, which could cause significant liability for us and harm our reputation.

We are exposed to the risk of employee fraud or other misconduct, including intentional failures to comply with FDA regulations or similar regulations of comparable foreign regulatory authorities, provide accurate information to the FDA or comparable foreign regulatory authorities, comply with manufacturing standards we have established, comply with federal and state healthcare fraud and abuse laws and regulations and similar laws and regulations established and enforced by comparable foreign regulatory authorities, report financial information or data accurately or disclose unauthorized activities to us. Employee misconduct could also involve the improper use of information obtained in the course of clinical trials, which could result in regulatory sanctions and serious harm to our reputation. It is not always possible to identify and deter employee misconduct, and the precautions we take to detect and prevent this activity might not be effective in controlling unknown or unmanaged risks or losses or in protecting us from governmental investigations or other actions or lawsuits stemming from a failure to be in compliance with such laws or regulations. If any such actions are instituted against us, and we are not successful in defending ourselves or asserting our rights, those actions could have a significant impact on our business and results of operations, including the imposition of significant civil, criminal and administrative penalties, damages, fines, imprisonment, exclusion from government funded healthcare programs, such as Medicare and Medicaid, and integrity oversight and reporting obligations.

Product liability lawsuits against us could cause us to incur substantial liabilities and to limit commercialization of any products that we might develop.

We face an inherent risk of product liability exposure related to the testing of our lead product candidate or future product candidates in human clinical trials and will face an even greater risk if we commercially sell any products that we might develop. Product liability claims might be brought against us by subjects enrolled in our clinical trials, patients, healthcare providers or others using, administering or selling our intended product. If we cannot successfully defend ourselves against claims that our lead product candidate or product caused injuries, we could incur substantial liabilities. Regardless of merit or eventual outcome, liability claims might result in:

- decreased demand for any product candidates or products that we might develop;

- termination of clinical trial sites or entire clinical trial programs;

- injury to our reputation and significant negative media attention;

- withdrawal of clinical trial participants;

- significant costs to defend the related litigation;

- substantial monetary awards to trial subjects or patients;
- loss of revenue;
- diversion of management and scientific resources from our business operations; and
- the inability to commercialize any products that we might develop.

Prior to engaging in future clinical trials, we intend to obtain product liability insurance coverage at a level that we believe is customary for similarly situated companies and adequate to provide us with insurance coverage for foreseeable risks; however, we might be unable to obtain such coverage at a reasonable cost, if at all. If we are able to obtain product liability insurance, we might not be able to maintain insurance coverage at a reasonable cost or in an amount adequate to satisfy any liability that might arise and such insurance might not be adequate to cover all liabilities that we might incur. Furthermore, we intend to expand our insurance coverage for products to include the sale of commercial products if we obtain regulatory approval for our lead product candidate in development, but we might be unable to obtain commercially reasonable product liability insurance for any products that receive regulatory approval. Large judgments have been awarded in class action lawsuits based on drugs that had unanticipated side effects. A successful product liability claim or series of claims brought against us, particularly if judgments exceed our insurance coverage, could decrease our cash and adversely affect our business.

Risks Related to our Business Operations

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

We will face competition from numerous pharmaceutical and biotechnology enterprises, as well as from academic institutions, government agencies and private and public research institutions for our lead product candidate. Our commercial opportunities will be reduced or eliminated if our competitors develop and commercialize products that are safer, more effective, have fewer side effects or are less expensive than any products that we might develop. Competition could result in reduced sales and pricing pressure on our lead product candidate, if approved, which in turn would reduce our ability to generate meaningful revenues and have a negative impact on our results of operations. In addition, significant delays in the development of our lead product candidate could allow our competitors to bring products to market before we do and impair our ability to commercialize our lead product candidate. The biotechnology industry, including the cancer immunotherapy market, is intensely competitive and involves a high degree of risk. We compete with other companies that have far greater experience and financial, research and technical resources than us. Potential competitors in the U.S. and worldwide are numerous and include pharmaceutical and biotechnology companies, educational institutions and research foundations, many of which have substantially greater capital resources, marketing experience, research and development staffs and facilities than ours. Some of our competitors might develop and commercialize products that compete directly with those incorporating our technology or might introduce products to market earlier than our intended product or on a more cost-effective basis. Our competitors compete with us in recruiting and retaining qualified scientific and management personnel as well as in acquiring technologies complementary to our technology. We might face competition with respect to product efficacy and safety, ease of use and adaptability to various modes of administration, acceptance by physicians, the timing and scope of regulatory approvals, availability of resources, reimbursement coverage, price and patent position, including the potentially dominant patent positions of others. An inability to successfully complete our product development or commercializing our lead product candidate could result in our having limited prospects for establishing market share or generating revenue.

Many of our competitors or potential competitors have significantly greater established presence in the market, financial resources and expertise in research and development, manufacturing, preclinical testing, conducting clinical trials, obtaining regulatory approvals and marketing approved products than we do, and as a result might have a competitive advantage over us. Mergers and acquisitions in the pharmaceutical and biotechnology industries might result in even more resources being concentrated among a smaller number of our competitors. Smaller or early-stage companies might also prove to be significant competitors, particularly through collaborative arrangements with large and established companies. These third parties compete with us in recruiting and retaining qualified scientific and management personnel, establishing clinical trial sites and patient registration for clinical trials, as well as in acquiring technologies and technology licenses complementary to our programs or potentially advantageous to our business.

As a result of these factors, these competitors might obtain regulatory approval of their products before we are able to obtain patent protection or other intellectual property rights, which will limit our ability to develop or commercialize our lead product candidate. Our competitors might also develop drugs that are safer, more effective, more widely used and cheaper than ours, and might also be more successful than us in manufacturing and marketing their products. These appreciable advantages could render our lead product candidate obsolete or non-competitive before we can recover the expenses of development and commercialization.

Our business might be adversely affected by the ongoing coronavirus pandemic.

The outbreak of the novel coronavirus (SARS-CoV-2) has evolved into a global pandemic. The coronavirus has spread to many regions of the world. The extent to which the coronavirus impacts our business and operating results will depend on future developments that are highly uncertain and cannot be accurately predicted, including new information that might emerge concerning the coronavirus and the actions to contain the coronavirus or treat its impact, among others.

As a result of the continuing spread of the coronavirus and emergence of new variants, our business operations could be delayed or interrupted. For instance, our clinical trials might be affected by the pandemic. Site initiation, participant recruitment and enrollment, participant dosing, distribution of clinical trial materials, study monitoring and data analysis might be paused or delayed due to changes in hospital or university policies, federal, state or local regulations, prioritization of hospital resources toward pandemic efforts, or other reasons related to the pandemic. If the coronavirus continues to spread, some participants and clinical investigators might not be able to comply with clinical trial protocols. For example, quarantines or other travel limitations (whether voluntary or required) might impede participant movement, affect sponsor access to study sites, or interrupt healthcare services, and we might be unable to conduct our clinical trials. Further, if the spread of the coronavirus pandemic continues and our operations are adversely impacted, we risk a delay, default and/or non-performance under existing agreements which might increase our costs. These cost increases might not be fully recoverable or adequately covered by insurance.

Infections and deaths related to the pandemic might disrupt the United States healthcare and healthcare regulatory systems. Such disruptions could divert healthcare resources away from, or materially delay FDA review and/or approval with respect to, our clinical trials. It is unknown how long these disruptions could continue, were they to occur. Any elongation or de-prioritization of our clinical trials or delay in regulatory review resulting from such disruptions could materially affect the development and study of our product candidates.

We currently utilize third parties to, among other things, manufacture raw materials. If either any third-party parties in the supply chain for materials used in the production of our product candidates are adversely impacted by restrictions resulting from the coronavirus outbreak, our supply chain might be disrupted, limiting our ability to manufacture our product candidates for our clinical trials and research and development operations.

As a result of the shelter-in-place order and other mandated local travel restrictions, our employees conducting research and development or manufacturing activities might not be able to access their laboratory or manufacturing space which might result in our core activities being significantly limited or curtailed, possibly for an extended

period of time.

The spread of the coronavirus, which has caused a broad impact globally, including travel restrictions and quarantine policies put into place by businesses and governments, might have a material adverse effect on our business. While the potential economic impact brought by and the duration of the pandemic might be difficult to assess or predict, it has already caused, and is likely to result in further, significant disruption of global financial markets, which might reduce our ability to access capital either at all or on favorable terms. In addition, a recession, depression or other sustained adverse market event resulting from the spread of the coronavirus could materially and adversely affect our business and the value of our common stock.

The ultimate impact of the current pandemic, or any other health epidemic, is highly uncertain and subject to change. We do not yet know the full extent of potential delays or impacts on our business, our clinical trials, our research programs, healthcare systems or the global economy as a whole. However, these effects could have a material impact on our operations, and we will continue to monitor the situation closely.

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

We rely to a large extent upon sophisticated information technology systems to operate our business. In the ordinary course of business, we collect, store and transmit large amounts of confidential information (including, but not limited to, personal information and intellectual property). The size and complexity of our information technology and information security systems, and those of our third-party vendors with whom we might contract, make such systems potentially vulnerable to service interruptions or to security breaches from inadvertent or intentional actions by our employees or vendors, or from malicious attacks by third parties. Such attacks are of ever-increasing levels of sophistication and are made by groups and individuals with a wide range of motives (including, but not limited to, industrial espionage and market manipulation) and expertise. While we intend to invest in the protection of data and information technology, there can be no assurance that our efforts will prevent service interruptions or security breaches.

Our internal computer systems, and those of our CROs, our CMOs, and other business vendors on which we might rely, are vulnerable to damage from computer viruses, unauthorized access, natural disasters, fire, terrorism, war and telecommunication and electrical failures. We exercise little or no control over these third parties, which increases our vulnerability to problems with their systems. If such an event were to occur and cause interruptions in our operations, it could result in a material disruption of our drug development programs. Any interruption or breach in our systems could adversely affect our business operations and/or result in the loss of critical or sensitive confidential information or intellectual property, and could result in financial, legal, business and reputational harm to us or allow third parties to gain material, inside information that they use to trade in our securities. For example, the loss of clinical trial data from completed or ongoing clinical trials could result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the data. To the extent that any disruption or security breach results in a loss of or damage to our data or applications, or misappropriation or disclosure of confidential or proprietary information, we could incur liability, the further development of our lead and future product candidates could be delayed and our business could be otherwise adversely affected.

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

As of March 11, 2022, we had three full-time officer/employees and one part-time officer/employee. The Company relies to a significant extent on outside consultants and advisors with various technical skills and expertise that the Company can draw on as necessary to conduct its research and development and clinical trial programs. We might need to grow the size of our organization in order to support our continued development and potential commercialization of our lead product candidate. As our development and commercialization plans and strategies continue to develop, our need for additional managerial, operational, manufacturing, sales, marketing, financial and other resources might increase. Our management, personnel and systems currently in place might not be adequate to support this future growth. Future growth would impose significant added responsibilities on members of management, including:

- managing our clinical trials effectively;
- identifying, recruiting, maintaining, motivating and integrating additional employees;
- managing our internal development efforts effectively while complying with our contractual obligations to licensors, licensees, contractors and other third parties;
- improving our managerial, development, operational, information technology, and finance systems; and
- expanding our facilities.

If our operations expand, we will likely also need to manage additional relationships with various strategic partners, suppliers and other third parties. Our future financial performance and our ability to commercialize our lead product candidate and to compete effectively will depend, in part, on our ability to manage any future growth effectively, as well as our ability to develop a sales and marketing force when appropriate for our company. To that end, we must be able to manage our development efforts and preclinical studies and clinical trials effectively and hire, train and integrate additional management, research and development, manufacturing, administrative and sales and marketing personnel. The failure to accomplish any of these tasks could prevent us from successfully growing our company.

Inadequate funding for the FDA, the SEC and other government agencies could hinder their ability to hire and retain key leadership and other personnel, prevent new products and services from being developed or commercialized in a timely manner or otherwise prevent those agencies from performing normal business functions on which the operation of our business might rely, which could negatively impact our business.

The ability of the FDA to review and approve new products can be affected by a variety of factors, including government budget and funding levels, ability to hire and retain key personnel and accept the payment of user fees, and statutory, regulatory, and policy changes. Average review times at the agency have fluctuated in recent years as a result. In addition, government funding of the SEC and other government agencies on which our operations might rely, including those that fund research and development activities is subject to the political process, which is inherently fluid and unpredictable.

Disruptions at the FDA and other agencies might also slow the time necessary for new drugs to be reviewed and/or approved by necessary government agencies, which would adversely affect our business. For example, over the last several years, including beginning on December 22, 2018, the U.S. government has shut down several times and certain regulatory agencies, such as the FDA and the SEC, have had to furlough critical FDA, SEC and other government employees and stop critical activities. If a prolonged government shutdown occurs, it could significantly impact the ability of the FDA to timely review and process our regulatory submissions, which could have a material adverse effect on our business. Further, in our operations as a public company, future government shutdowns could impact our ability to access the public markets and obtain necessary capital in order to properly capitalize and continue our operations.

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 our November 2020 public 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 $5.70 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.

There is a limited market for the Warrants to purchase shares of our common stock.

Although the Warrants are currently trading on The Nasdaq Capital Market, there can be no assurance that there will be an active trading market for the Warrants. Without an active trading market, the liquidity of the Warrants will be limited.

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.

The price of our common stock or Warrants might fluctuate substantially.

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

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

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

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

The Company's failure to meet the continued listing standards of Nasdaq could result in a delisting of its common stock.

In order to meet the continued listing standards of the Nasdaq Capital Market ("Nasdaq"), the Company is required to meet various requirements, including that it has stockholders' equity of at least $2,500,000 and that its common stock have a minimum closing bid price of $1.00 per share.

If we fail to satisfy the continued listing standards of Nasdaq in the future, Nasdaq may take steps to delist our common stock. Such a delisting would likely have a negative effect on the price of our common stock and would impair your ability to buy or sell our common stock when you wish to do so. A delisting would adversely affect the liquidity, trading volume and likely the price of our common stock, causing the value of an investment in us to decrease, would adversely affect our ability to raise capital, and would have an adverse effect on our business, financial condition and results of operations.

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.

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 current downturn related to the current 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.

Because certain of our stockholders control a significant number of shares of our common stock, they might have effective control over actions requiring stockholder approval.

Our directors, executive officers and principal stockholders, and their respective affiliates, currently beneficially own approximately 23% of our outstanding shares of common stock, based on 13,746,593 shares of common stock currently issued and outstanding. This percentage decreases to approximately 22% in the event that the shares of our Series A Preferred Stock are converted into shares of common stock. As a result, these stockholders, acting together, would have the ability to control the outcome of matters submitted to our stockholders for approval, including the election of directors and any merger, consolidation or sale of all or substantially all of our assets. In addition, these stockholders, acting together, would have the ability to control the management and affairs of our company. Accordingly, this concentration of ownership might harm the market price of our common stock by:

- delaying, deferring or preventing a change in corporate control;
- impeding a merger, consolidation, takeover or other business combination involving us; or
- discouraging a potential acquirer from making a tender offer or otherwise attempting to obtain control of us.

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.

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. As of March 11, 2022, 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 U.S. 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 U.S. 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.

ITEM 1B. UNRESOLVED STAFF COMMENTS

None.

ITEM 2. PROPERTIES

None.

ITEM 3. LEGAL PROCEEDINGS

The Company is not a party to any threatened or pending legal proceedings.

ITEM 4. MINE SAFETY DISCLOSURES

Not applicable.

PART II

ITEM 5. MARKET FOR REGISTRANT'S COMMON EQUITY, RELATED STOCKHOLDER MATTERS AND ISSUER PURCHASES OF EQUITY SECURITIES

Effective November 25, 2020, the Company's common stock and Warrants began to trade on The Nasdaq Capital Market under the symbols "LIXT" and "LIXTW", respectively. Prior to November 30, 2020, the Company's common stock traded on the OTCQB. The stock market in general has experienced extreme stock price fluctuations in the past few years. In some cases, these fluctuations have been unrelated to the operating performance of the affected companies. Many companies have experienced dramatic volatility in the market prices of their common stock. The Company believes that a number of factors, both within and outside its control, could cause the price of the Company's common stock to fluctuate, perhaps substantially.

The following table sets forth the range of reported closing prices of the Company's common stock during the periods presented. Such quotations reflect prices between dealers in securities and do not include any retail mark-up, markdown or commissions, and may not necessarily represent actual transactions.

All share and per share amounts and information presented herein have been retroactively adjusted for all periods presented to reflect the 1-for-6 reverse stock split effected November 18, 2020.

	Low	High
Year Ended December 31, 2020		
First Quarter	$ 3.90	$ 6.00
Second Quarter	$ 4.80	$ 6.00
Third Quarter	$ 5.10	$ 7.20
Fourth Quarter	$ 3.09	$ 7.02

	Low	High
Year Ended December 31, 2021		
First Quarter	$ 3.05	$ 5.58
Second Quarter	$ 2.38	$ 3.37
Third Quarter	$ 2.00	$ 3.25
Fourth Quarter	$ 1.15	$ 2.08

Holders

As of March 11, 2022, the Company had 46 stockholders of record holding 13,746,593 shares of the Company's common stock outstanding, including 9,132,118 shares of common stock held by an indeterminate number of beneficial owners of securities whose shares are held in the names of various depository accounts, brokerage firms and clearing agencies.

Dividends

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.

Securities Authorized For Issuance Under Equity Incentive Plans

Set forth in the table below is information regarding awards made through compensation plans or arrangements through December 31, 2021, the most recently completed fiscal year.

Plan Category	Number of securities to be issued upon exercise of outstanding options, warrants and rights (1)	Weighted average price of outstanding options, warrants and rights (2)	Number of securities remaining available for future issuance compensation plans (excluding securities reflected in column 2) (3)
Equity Compensation Plans Approved by Security Holders	N/A	$ N/A	N/A
Equity Compensation Plans Not Approved by Security Holders	2,666,667	$ 3.74	933,333(1)

(1) The 2,133,333 shares that remain available are pursuant to the Company's 2020 Stock Incentive Plan, which was adopted on July 14, 2020 (see "ITEM 11. EXECUTIVE COMPENSATION").

ITEM 6. SELECTED FINANCIAL DATA

Not applicable.

ITEM 7. MANAGEMENT'S DISCUSSION AND ANALYSIS OF FINANCIAL CONDITION AND RESULTS OF OPERATIONS

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 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 the Company believes have broad therapeutic potential not only for cancer but also for other debilitating and life-threatening diseases. The Company has developed two classes of drugs for the treatment of cancer, consisting of protein phosphatase inhibitors (PTase-i), designated by us as the LB-100 series of compounds, and histone deacetylase inhibitors (HDACi), designated by us as the LB-200 series of compounds.

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

Recent Developments

The following is a summary of recent developments, including information contained in recent news releases issued by the Company:

January 12, 2022 - The Company reported that its recent collaboration with the Netherlands Cancer Institute (NKI), Amsterdam, one of the world's leading comprehensive cancer centers, and Stichting Oncode Institute (Oncode Institute), Utrecht, a major independent cancer research center, has led to an initial joint patent application covering LB-100 combination therapy with one of several other investigational compounds. The Company, NKI and Oncode Institute believe that the combination therapy would provide unexpectedly strong synergistic anti-cancer effects in cancer patients. The Company previously announced its entry into a collaboration with the NKI and the Oncode Institute to identify the most promising drugs to be used in combination with the Company's LB-100 or with one of the Company's LB-100 analogues to treat a range of cancers, as well as to identify the specific molecular mechanisms underlying the identified combinations.

Going Concern

At December 31, 2021, the Company had cash of $4,823,745 available to fund its operations. Because the Company is currently engaged in Phase 2 clinical trials, it is expected that it will take a significant amount of time and resources to develop any product or intellectual property capable of generating sustainable revenues. Accordingly, the Company's business is unlikely to generate any sustainable operating revenues in the next several years and may never do so. Even if the Company is able to generate revenues through licensing its technologies or through product sales, there can be no assurance that the Company will be able to achieve positive earnings and operating cash flows.

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. The Company has financed its working capital requirements primarily through the recurring sale of its equity securities.

As a result, management has concluded that there is substantial doubt about the Company's ability to continue as a going concern. The Company's independent registered public accounting firm, in its report on the Company's consolidated financial statements for the year ended December 31, 2021, has also expressed substantial doubt about the Company's ability to continue as a going concern. The Company's consolidated financial statements do not include any adjustments that might result from the outcome of this uncertainty.

Recent Accounting Pronouncements

In December 2019, the Financial Accounting Standards Board (the "FASB") issued Accounting Standards Update ("ASU") 2019-12, Income Taxes (Topic 740): Simplifying the Accounting for Income Taxes ("ASU 2019-12"). ASU 2019-12 simplifies the accounting for income taxes by removing certain exceptions and enhances and simplifies various aspects of the income tax accounting guidance in ASC 740. The Company adopted ASU 2019-12 effective January 1, 2021. The adoption of ASU 2019-12 did not have any impact on the Company's consolidated financial statement presentation or disclosures.

In August 2020, the FASB issued ASU 2020-06, Debt — Debt with Conversion and Other Options (Subtopic 470-20) and Derivatives and Hedging—Contracts in Entity's Own Equity (Subtopic 815-40): Accounting for Convertible Instruments and Contracts in an Entity's Own Equity ("ASU 2020-06"). ASU 2020-06 simplifies the accounting for convertible debt by eliminating the beneficial conversion and cash conversion accounting models. Upon adoption of ASU 2020-06, convertible debt proceeds, unless issued with a substantial premium or an embedded conversion feature that is not clearly and closely related to the host contract, will no longer be allocated between debt and equity components. This modification will reduce the issue discount and result in less non-cash interest expense in financial statements. ASU 2020-06 also updates the earnings per share calculation and requires entities to assume share settlement when the convertible debt can be settled in cash or shares. For contracts in an entity's own equity, the type of contracts primarily affected by ASU 2020-06 are freestanding and embedded features that are accounted for as derivatives under the current guidance due to a failure to meet the settlement assessment by removing the requirements to (i) consider whether the contract would be settled in registered shares, (ii) consider whether collateral is required to be posted, and (iii) assess shareholder rights. ASU 2020-06 is effective for fiscal years beginning after December 15, 2023. Early adoption is permitted, but no earlier than fiscal years beginning after December 15, 2020, and only if adopted as of the beginning of such fiscal year. The Company adopted ASU 2020-06 effective January 1, 2021. The adoption of ASU 2020-06 did not have any impact on the Company's consolidated financial statement presentation or disclosures.

In May 2021, the FASB issued ASU 2021-04, Earnings Per Share (Topic 260), Debt — Modifications and Extinguishments (Subtopic 470-50), Compensation — Stock Compensation (Topic 718), and Derivatives and Hedging — Contracts in Entity's Own Equity (Subtopic 815-40): Issuer's Accounting for Certain Modifications or Exchanges of Freestanding Equity-Classified Written Call Options ("ASU 2021-04"). ASU 2021-04 provides guidance as to how an issuer should account for a modification of the terms or conditions or an exchange of a freestanding equity-classified written call option (i.e., a warrant) that remains classified after modification or exchange as an exchange of the original instrument for a new instrument. An issuer should measure the effect of a modification or exchange as the difference between the fair value of the modified or exchanged warrant and the fair value of that warrant immediately before modification or exchange and then apply a recognition model that comprises four categories of transactions and the corresponding accounting treatment for each category (equity issuance, debt origination, debt modification, and modifications unrelated to equity issuance and debt origination or modification). ASU 2021-04 is effective for all entities for fiscal years beginning after December 15, 2021, including interim periods within those fiscal years. An entity should apply the guidance provided in ASU 2021-04 prospectively to modifications or exchanges occurring on or after the effective date. Early adoption is permitted for all entities, including adoption in an interim period. If an entity elects to early adopt ASU 2021-04 in an interim period, the guidance should be applied as of the beginning of the fiscal year that includes that interim period. The adoption of ASU 2021-04 is not expected to have any impact on the Company's consolidated financial statement presentation or disclosures.

Management does not believe that any other recently issued, but not yet effective, authoritative guidance, if currently adopted, would have a material impact on the Company's financial statement presentation or disclosures.

Concentration of Risk

The Company periodically contracts with vendors and consultants to provide services related to the Company's operations. Charges incurred for these services can be for a specific time period (typically one year) or for a specific project or task. Costs and expenses incurred that represented 10% or more of general and administrative costs or research and development costs for the years ended December 31, 2021 and 2020 are described as follows.

General and administrative costs for the years ended December 31, 2021 and 2020 include combined charges from two legal firms for general licensing and patent prosecution costs relating to the Company's intellectual properties representing 14.6% and 27.1%, respectively, of total general and administrative costs. General and administrative costs for the years ended December 31, 2021 and 2020 also included charges for the fair value of stock options granted to directors and corporate officers representing 44.2% and 23.5%, respectively, of total general and administrative costs for those periods.

Research and development costs for the year ended December 31, 2021 include charges from three vendors and consultants representing 30.3%, 21.8%, and 14.4%, respectively, of total research and development costs for that period. Research and development costs for the year ended December 31, 2020 include charges from a consultant, and the value associated with extending stock options previously granted to that consultant, representing 65.6% of total research and development costs, and charges from a vendor representing 13.7% of total research and development costs.

Critical Accounting Policies and Estimates

The preparation of the Company's consolidated financial statements in conformity with generally accepted accounting principles in the United States ("GAAP") requires management to make estimates and assumptions that affect the reported amounts of assets and liabilities at the date of the financial statements and the reported amounts of expenses during the reporting period. Some of those judgments can be subjective and complex, and therefore, actual results could differ materially from those estimates under different assumptions or conditions. Management bases its estimates on historical experience and on various assumptions that are believed to be reasonable in relation to the financial statements taken as a whole under the circumstances, the results of which form the basis for making judgments about the carrying values of assets and liabilities that are not readily apparent from other sources. Management regularly evaluates the key factors and assumptions used to develop the estimates utilizing currently available information, changes in facts and circumstances, historical experience and reasonable assumptions. After such evaluations, if deemed appropriate, those estimates are adjusted accordingly. Actual results could differ from those estimates. Significant estimates include those related to assumptions used in accruals for potential liabilities, valuing equity instruments issued for services, and the realization of deferred tax assets.

The following critical accounting policies affect the more significant judgements and estimates used in the preparation of the Company's consolidated financial statements.

Research and Development

Research and development costs consist primarily of fees paid to consultants and contractors, and other expenses relating to the acquisition, design, development and clinical trials with respect to the Company's compounds and product candidates. Research and development costs also include the costs to produce the compounds used in research and clinical trials, which are charged to operations as incurred.

Research and development costs are generally charged to operations ratably over the life of the underlying contracts, unless the achievement of milestones, the completion of contracted work, the termination of an agreement, or other information indicates that a different expensing schedule is more appropriate. However, payments for research and development costs that are contractually defined as non-refundable are charged to operations as incurred.

Obligations incurred with respect to mandatory scheduled payments under research agreements with milestone provisions are recognized as charges to research and development costs in the Company's consolidated statement of operations based on the achievement of such milestones, as specified in the agreement. Obligations incurred with respect to mandatory scheduled payments under research agreements without milestone provisions are accounted for when due, are recognized ratably over the appropriate period, as specified in the agreement, and are recorded as liabilities in the Company's consolidated balance sheet, with a corresponding charge to research and development costs in the Company's consolidated statement of operations.

Payments made pursuant to research and development contracts are initially recorded as advances on research and development contract services in the Company's consolidated balance sheet and are then charged to research and development costs in the Company's consolidated statement of operations as those contract services are performed. Expenses incurred under research and development contracts in excess of amounts advanced are recorded as research and development contract liabilities in the Company's consolidated balance sheet, with a corresponding charge to research and development costs in the Company's consolidated statement of operations. The Company reviews the status of its research and development contracts on a quarterly basis.

Patent and Licensing Legal and Filing Fees and Costs

Due to the significant uncertainty associated with the successful development of one or more commercially viable products based on the Company's research efforts and related patent applications, all patent and licensing legal and filing fees and costs are charged to operations as incurred. Patent and licensing legal and filing fees and costs are included in general and administrative costs in the Company's consolidated statements of operations.

During the years ended December 31, 2021 and 2020, patent and licensing legal and filing fees and costs related to the development and protection of its intellectual property were $729,171 and $553,173, respectively, an increase of $175,998 (31.8%) in 2021 as compared to 2020.

In late 2021, the Company engaged a new patent law firm, highly regarded for its expertise in biotechnology, and requested a comprehensive analysis of the Company's extensive patent portfolio in order to maximize intellectual property protection, both domestically and internationally. In addition, several patents were filed recently, reflecting potentially new uses of the Company's unique lead clinical compound LB-100 in cancer therapy. These activities resulted in the increase in patent and licensing legal and filing fees and costs in 2021 as compared to 2020. The Company expects that patent and licensing legal and filing fees and costs will remain relatively stable in 2022, as the Company expects to focus primarily on obtaining clinical data validating its novel approach to cancer treatment.

A descriptive summary of the patent portfolio for the Company's most important clinical programs involving the development of LB-100, as well as a detailed listing of each domestic and international patent that has been issued, is presented at "ITEM 1. BUSINESS – Intellectual Property".

Stock-Based Compensation

The Company periodically issues common stock and stock options to officers, directors, employees, Scientific Advisory Committee members, contractors and consultants for services rendered. Options vest and expire according to terms established at the issuance date of each grant. Stock grants, which are generally time vested, are measured at the grant date fair value and charged to operations ratably over the vesting period.

The Company accounts for stock-based payments to officers, directors, employees, Scientific Advisory Committee members contractors and consultants by measuring the cost of services received in exchange for equity awards utilizing the grant date fair value of the awards, with the cost recognized as compensation expense on the straight-line basis in the Company's financial statements over the vesting period of the awards.

The fair value of stock options granted as stock-based compensation is determined utilizing the Black-Scholes option-pricing model, and is affected by several variables, the most significant of which are the expected life of the stock option, the exercise price of the stock option as compared to the fair market value of the common stock on the grant date, and the estimated volatility of the common stock. Unless sufficient historical exercise data is available, the expected life of the stock option is calculated as the mid-point between the vesting period and the contractual term (the "simplified method"). The estimated volatility is based on the historical volatility of the Company's common stock, calculated utilizing a look-back period approximately equal to the contractual life of the stock option being granted. The risk-free interest rate is based on the U.S. Treasury yield curve in effect at the time of grant. The fair market value of the common stock is determined by reference to the quoted market price of the Company's common stock on the grant date. The expected dividend yield is based on the Company's expectation of dividend payouts and is assumed to be zero.

The Company recognizes the fair value of stock-based compensation awards in general and administrative costs and in research and development costs, as appropriate, in the Company's consolidated statements of operations. The Company issues new shares of common stock to satisfy stock option exercises.

Summary of Business Activities and Plans

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 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 the Company believes have broad therapeutic potential not only for cancer but also for other debilitating and life-threatening diseases.

The Company has developed two series of pharmacologically active drugs, the LB-100 series and the LB-200 series. The Company believes 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 animal models. 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, the Company's compounds will improve therapeutic benefit without enhancing toxicity in humans.

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.

The Company has 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, the Company's primary focus is on the clinical development of LB-100.

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, the Company has demonstrated that its 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 the Company's focus on the clinical development of LB-100 and analogs for cancer therapy as described below in more detail, the Company have decided not to actively pursue the pre-clinical development of our LB-200 series of compounds at this time. At this time, the Company 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 the Company. 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 the Company has 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.

The Company 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, the Company was 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.

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

Impact of the Novel Coronavirus (Covid-19) on the Company's Business Activities

The global outbreak of the novel coronavirus (Covid-19) has led to disruptions in general economic activities worldwide, as businesses and governments have taken broad actions to mitigate this public health crisis. In light of the uncertain and continually evolving situation relating to the spread of Covid-19, this pandemic could pose a risk to the Company. The extent to which the coronavirus may impact the Company's business activities will depend on future developments, which are highly uncertain and cannot be predicted at this time. The Company intends to continue to monitor the situation and may adjust its current business plans as more information and guidance become available.

The coronavirus pandemic presents a challenge to medical facilities worldwide. As the Company's clinical trials are conducted on an outpatient basis, it is not currently possible to predict the full impact of this developing health crisis on such clinical trials, which could include delays in and increased costs of such clinical trials. Current indications from the clinical research organizations conducting the clinical trials for the Company are that such clinical trials are being delayed or extended for several months or more as a result of the coronavirus pandemic.

Over the near term, there is also significant and continuing uncertainty as to the effect that the coronavirus may have on the capital markets in general and on the amount and type of financing available to the Company in particular.

The Company is continuing to monitor the situation and will adjust its current business and financing plans as more information and guidance become available.

Results of Operations

At December 31, 2021, the Company had not yet commenced any revenue-generating operations, does not have any positive cash flows from operations, and is dependent on its ability to raise equity capital to fund its operating requirements.

The Company's consolidated statements of operations as discussed herein are presented below.

	Years Ended December 31,	
	2021	**2020**
Revenues	$ —	$ —
Costs and expenses:		
General and administrative costs:		
Compensation to related parties	2,931,280	765,085
Patent and licensing legal and filing fees and costs	729,171	553,173
Other	1,323,218	724,506
Research and development costs	1,736,776	1,223,676
Total costs and expenses	6,720,445	3,266,440
Loss from operations	(6,720,445)	(3,266,440)
Interest income	626	4,342
Interest expense	(7,414)	(3,674)
Foreign currency gain (loss)	(1,163)	890
Net loss	$ (6,728,396)	$ (3,264,882)
Net loss per common share – basic and diluted	$ (0.50)	$ (0.29)
Weighted average common shares outstanding – basic and diluted	13,473,839	11,277,126

Years Ended December 31, 2021 and 2020

Revenues. The Company did not have any revenues for the years ended December 31, 2021 and 2020.

General and Administrative Costs. For the year ended December 31, 2021, general and administrative costs were $4,983,669, which consisted of the fair value of vested stock options issued to directors and officers of $2,201,280, patent and licensing legal and filing fees and costs of $729,171, other consulting and professional fees of $610,846, insurance expense of $385,312, officer's salary and related costs of $781,254, cash-based director and committee fees of $92,833, licensing fees of $24,999, shareholder reporting costs of $42,792, listing fees of $58,000, filing fees of $18,114, taxes and licenses of $16,200, and other operating costs of $22,868.

For the year ended December 31, 2020, general and administrative costs were $2,042,764, which consisted of the fair value of vested stock options issued to directors and officers of $480,634, patent and licensing legal and filing fees and costs of $553,173, other consulting and professional fees of $503,983, insurance expense of $142,575, officer's salary and related costs of $268,457, licensing fees of $25,001, shareholder reporting costs of $11,801, listing fees of $12,000, filing fees of $10,616, taxes and licenses of $19,032, and other operating costs of $15,492.

General and administrative costs increased by $2,940,905, or 144.0%, in 2021 as compared to 2020, primarily as a result of an increase in the fair value of vested stock options issued to directors and officers of $1,720,646, an increase in patent and licensing legal and filing fees and costs of $175,998, an increase in other consulting and professional fees of $106,863, an increase in insurance expense of $242,737, an increase in officer's salary and related costs of $512,797, and an increase in cash-based director and committee fees $92,833.

Research and Development Costs. For the year ended December 31, 2021, research and development costs were $1,736,776, which consisted of the fair value of vested stock options issued to a consultant of $397,642, contractor costs incurred in connection with the synthesis work done to develop a new supply of LB-100 of $624,187, clinical and related oversight costs of $456,921, and pre-clinical research focused on development of additional novel anti-cancer compounds to add to the Company's clinical pipeline of $258,026.

For the year ended December 31, 2020, research and development costs were $1,223,676, which consisted of the fair value of vested stock options issued to a consultant of $670,715, contractor costs incurred in connection with the synthesis work done to develop a new supply of LB-100 of $167,120, clinical and related oversight costs of $115,941, and pre-clinical research focused on development of additional novel anti-cancer compounds to add to the Company's clinical pipeline of $269,900.

Research and development costs increased by $513,100, or 41.9% in 2021 as compared to 2020, primarily as a result of an increase in contractor costs incurred in

connection with the synthesis work done to develop a new supply of LB-100 of $457,067, an increase in clinical and related oversight costs of $340,980, which included an upfront payment to City of Hope of $240,508 upon execution of the Clinical Research Support Agreement in January 2021, offset by a decrease in the fair value of vested stock options issued to a consultant of $273,073. The absence of costs associated with ongoing clinical trials during the years ended December 31, 2021 and 2020 reflects the slow accrual of patients into such clinical trials.

Interest Income. For the year ended December 31, 2021, the Company had interest income of $626, as compared to interest income of $4,342 for the year ended December 31, 2020, as a result of a reduction in the Company's cash resources previously invested in short-term federally insured certificates of deposit.

Interest Expense. For the year ended December 31, 2021, the Company had interest expense of $7,414, as compared to interest expense of $3,674 for the year ended December 31, 2020, related to the financing of its directors and officers liability insurance policy premium.

Foreign Currency Loss. For the year ended December 31, 2021, the Company had a loss from foreign currency transactions of $1,163 as compared to a gain of $890 for the year ended December 31, 2020.

Net Loss. For the year ended December 31, 2021, the Company incurred a net loss of $6,728,396, as compared to a net loss of $3,264,882 for the year ended December 31, 2020.

Liquidity and Capital Resources – December 31, 2021

The Company's consolidated statements of cash flows as discussed herein are presented below.

	Years Ended December 31,	
	2021	2020
Net cash used in operating activities	$ (4,142,915)	$ (2,131,414)
Net cash provided by (used in) investing activities	—	—
Net cash provided by financing activities	3,897,394	4,601,816
Net increase (decrease) in cash	$ (245,521)	$ 2,470,402

At December 31, 2021, the Company had working capital of $4,790,338, as compared to working capital of $5,011,951 at December 31, 2020, reflecting a decrease in working capital of $221,613 for the year ended December 31, 2021. The decrease in working capital during the year ended December 31, 2021 was the result of the net cash proceeds of $3,689,761 from the Company's March 2021 direct equity offering, proceeds of $17,100 from the exercise of warrants, and proceeds of $201,000 from the exercise of stock options that were utilized to pay offering costs of $10,467 and to fund the Company's research and development activities and ongoing operating expenses, including the Company's clinical trial program and maintaining and developing its patent portfolio. At December 31, 2021, the Company had cash of $4,823,745 available to fund its operations.

The Company's ability to continue as a going concern is dependent upon its ability to raise additional equity capital to fund its research and development activities and to ultimately achieve sustainable operating revenues and profitability. The amount and timing of future cash requirements depends on the pace and design of the Company's clinical trial program, which, in turn, depends on the availability of operating capital to fund such activities.

Effective November 30, 2020, the Company listed on The Nasdaq Capital Market in conjunction with the completion of its public offering of units of common stock and warrants that generated net cash proceeds of $4,591,349. Subsequently, effective March 2, 2021, the Company completed a sale of common stock under a registered direct equity offering that generated net cash proceeds of $3,689,761.

Based on current operating plans, the Company estimates that it will need to raise additional capital to fund its operations, including its various clinical trial commitments, during the quarter ending September 30, 2022. In addition, the Company's operating plans may change as a result of many factors which are currently unknown to the Company, including possible additional clinical trials, and the Company may need additional funds sooner than currently planned.

As market conditions present uncertainty as to the Company's ability to secure additional funds, there can be no assurances that the Company will be able to secure additional financing on acceptable terms, as and when necessary, to continue to conduct operations. There is also significant uncertainty as to the effect that the coronavirus pandemic may have on the Company's clinical trial schedule and the amount and type of financing available to the Company in the future.

If cash resources are insufficient to satisfy the Company's ongoing cash requirements, the Company would be required to scale back or discontinue its clinical trial program, as well as its licensing and patent prosecution efforts and its technology and product development efforts, or obtain funds, if available, through strategic alliances or joint ventures that could require the Company to relinquish rights to and/or control of LB-100, or to discontinue operations

Operating Activities. For the year ended December 31, 2021, operating activities utilized cash of $4,142,915, as compared to utilizing cash of $2,131,414 for the year ended December 31, 2020, to fund the Company's ongoing research and development activities and to fund its other ongoing operating expenses, including maintaining and developing its patent portfolio.

Investing Activities. For the years ended December 31, 2021 and 2020, the Company had no investing activities.

Financing Activities. For the year ended December 31, 2021, financing activities consisted of the gross proceeds from the sales of common stock in the Company's direct equity offering of $4,192,478, reduced by offering costs of $502,717, $17,100 from the exercise of common stock warrants, and $201,000 from the exercise of common stock options. The Company also paid offering costs of $10,467 during the year ended December 31, 2021. For the year December 31, 2020, financing activities consisted of the gross proceeds from the sales of units and warrants in the Company's public offering of $5,701,800, offset by the payment of offering costs of $1,099,984.

Principal Commitments

At December 31, 2021, the Company's contractual commitments pursuant to clinical trial agreements, clinical trial monitoring agreements, and agreements for the production of LB-100 for clinical use, as described below, aggregated $8,646,000, which are currently scheduled to be incurred through December 31, 2025. The Company's ability to conduct and fund these contractual commitments is subject to the timely availability of sufficient capital to fund such expenditures, as well as any changes in the allocation or reallocation of such funds to the Company's current or future clinical trial programs. The Company expects that the full amount of these expenditures will be incurred only if such clinical trial programs are conducted as originally designed and their respective enrollments and duration are not modified or reduced. Clinical trial programs, such as the types that the Company is engaged in, can be highly variable and can frequently involve a series of changes and modifications over time as clinical data is obtained and analyzed, and are frequently modified, suspended or terminated before the clinical trial endpoint. Accordingly, such contractual commitments as discussed herein should be considered as estimates only based on current clinical assumptions and conditions, and are typically subject to significant revisions over time. Additional information with respect to the conduct of the Company's clinical trial programs is provide at "ITEM 1A. RISK FACTORS - Risks Related to the Development and Regulatory Approval of Our Product Candidates".

Clinical Trial Agreements

Moffitt. Effective August 20, 2018, the Company 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 the Company 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 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 ("IND") 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. An interim analysis will be done after the first 21 patients are entered. If there are 3 or more responders but fewer than 7, an additional 20 patients will be entered. If at any point there are 7 or more responders, this will be sufficient evidence to support continued development of LB-100 for the treatment of low and intermediate-1 risk MDS. Recruitment has been slow and the Covid-19 pandemic has further reduced recruitment of patients into the protocol. At the current rate of accrual, the clinical trial is expected to be completed by June 30, 2025. However, with additional funds, the Company would consider adding two additional MDS centers to the Phase 2 portion of the study to accelerate patient accrual.

During the years ended December 31, 2021 and 2020, the Company incurred costs of $18,443 and $41,142, respectively, pursuant to this agreement, which have been included in research and development costs in the Company's consolidated statements of operations. As of December 31, 2021, total costs of $104,677 have been incurred pursuant to this agreement. The Company's aggregate commitment pursuant to this agreement, less amounts previously paid to date, totaled approximately $601,000 as of December 31, 2021, which is expected to be incurred through December 31, 2025.

GEIS. Effective July 31, 2019, the Company entered into a Collaboration Agreement for an Investigator-Initiated Clinical Trial with the Spanish Sarcoma Group (Grupo Español de Investigación en Sarcomas or "GEIS"), Madrid, Spain, to carry out a study entitled "Randomized phase I/II trial of LB-100 plus doxorubicin vs. doxorubicin alone in first line of advanced soft tissue sarcoma". The purpose of this clinical trial is to obtain information with respect to the efficacy and safety of LB-100 combined with doxorubicin in soft tissue sarcomas. Doxorubicin is the global standard for initial treatment of advanced soft tissue sarcomas ("ASTS"). Doxorubicin alone has been the mainstay of first line treatment of ASTS for over 40 years, with little 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.

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

The Company had previously expected that this clinical trial would commence during the quarter ended June 30, 2020. However, during July 2020, the Spanish regulatory authority advised the Company that although it had approved the scientific and ethical basis of the protocol, it required that the Company manufacture new inventory of LB-100 under current Spanish pharmaceutical manufacturing standards. These standards were adopted subsequent to the production of the Company's existing LB-100 inventory.

A new batch of LB 100 has been prepared and is now undergoing the multitude of analytical studies of the formulated product necessary to gain approval for use in the European Union. Regulatory reviews by the European Union have been delayed, as a result of which the final review of the clinical product by Spanish regulatory authorities will also be delayed. Accordingly, the clinical trial is now estimated to begin during the quarter ending June 30, 2022 and be completed by June 30, 2025.

The interim analysis of this clinical trial could indicate either inferiority or superiority of LB-100 plus doxorubicin as compared to doxorubicin alone. A positive study would have the potential to change the standard therapy for this disease after four decades of failure to improve the marginal benefit of doxorubicin alone.

The Company's agreement with GEIS provides for various payments based on achieving specific milestones over the term of the agreement. Through December 31, 2021, the Company has paid GEIS an aggregate of $67,582 towards the second milestone payment for current work being done under this agreement.

During the years ended December 31, 2021 and 2020, the Company incurred costs of $24,171 and $43,411, respectively, pursuant to this agreement, which have been included in research and development costs in the Company's consolidated statements of operations. As of December 31, 2021, total costs of $155,053 have been incurred pursuant to this agreement. The Company's aggregate commitment pursuant to this agreement, less amounts previously paid to date, totaled approximately $4,250,000 as of December 31, 2021, which is expected to be incurred through December 31, 2025.

In order to manufacture a new inventory supply of LB-100 for the GEIS clinical trial, the Company has engaged a number of vendors to carry out the multiple tasks needed to make and gain approval of a new clinical product for investigational study in Spain. These tasks include the synthesis under good manufacturing practices (GMP) of the active pharmacologic ingredient (API), with documentation of each of the steps involved by an independent auditor. The API is then transferred to a vendor that prepares the clinical drug product, also under GMP conditions documented by an independent auditor. The clinical drug product is then sent to a vendor to test for purity and sterility, provide appropriate labels, store the drug, and distribute the drug to the clinical centers for use in the clinical trials. A formal application documenting all steps taken to prepare the clinical drug product for clinical use must be submitted to the appropriate regulatory authorities for review and approval before being used in a clinical trial.

On November 2, 2021, the Company entered into a Development Agreement with Famar Health Care Services Madrid SA ("Famar") to prepare a new batch of clinical LB-100 for use in clinical trials to be conducted in the European Union. During the year ended December 31, 2021, the Company incurred costs of $119,860, pursuant to this agreement, which has been included in research and development costs in the Company's consolidated statements of operations. The Company's aggregate commitment pursuant to this agreement, less amounts previously paid to date, totaled approximately $180,000 as of December 31, 2021, which is expected to be incurred through June 30, 2024.

As of December 31, 2021, the Company estimates that this program to provide new inventory of the clinical drug product for the Spanish sarcoma study, and potentially for subsequent multiple trials within the European Union, including the costs incurred and to be incurred with Famar as described above, will cost approximately

$1,076,000. The Company's aggregate commitments under this program, less amounts previously paid to date, totaled approximately $318,000 as of December 31, 2021, which are expected to be incurred through December 31, 2024. As the production of the new inventory of the clinical drug product is being conducted in Europe and is paid for in Euros, final costs are subject to foreign currency fluctuations between the United States Dollar and the Euro.

City of Hope. Effective January 18, 2021, the Company executed a Clinical Research Support Agreement with the City of Hope National Medical Center, an NCI-designated comprehensive cancer center, and City of Hope Medical Foundation (collectively, "City of Hope"), to carry out a Phase 1b clinical trial of LB-100, the Company's first-in-class protein phosphatase inhibitor, combined with a standard regimen for treatment of untreated extensive- stage disease small cell lung cancer (ED-SCLC). LB-100 will be given in combination with carboplatin, etoposide and atezolizumab, an FDA-approved but marginally effective regimen, to previously untreated ED-SCLC patients. The dose of LB-100 will be escalated with the standard fixed doses of the 3-drug regimen to reach a recommended Phase 2 dose (RP2D). Patient entry will be expanded so that a total of 12 patients will be evaluable at the RP2D to confirm the safety of the LB-100 combination and to look for potential therapeutic activity as assessed by objective response rate, duration of overall response, progression-free-survival and overall survival.

The clinical trial was initiated on March 9, 2021, with patient accrual expected to take approximately two years to complete. If LB-100 does potentiate the benefit of the standard regimen, some evidence could be noted at 12 months into the clinical trial, but an assessment of potential increased activity is likely to require at least 24 months. The Company is currently seeking to add two additional centers to increase the rate of accrual. The Company expects this clinical trial to be completed by June 30, 2024.

During the year ended December 31, 2021, the Company incurred costs, and total costs, of $378,511, pursuant to this agreement. The Company's aggregate commitment pursuant to this agreement, less amounts previously paid to date, totaled approximately $2,433,000 as of December 31, 2021, which is expected to be incurred through December 31, 2024, based upon a target of 42 enrollees. If a significant number of patients fail during the dose-escalation process, an increase of up to 12 patients would likely be necessary, at an estimated additional cost of approximately $800,000. The Company currently expects that enrollment in this clinical trial will range from approximately 18 to 30 enrollees, with 24 enrollees as the most likely number. Should fewer than 42 enrollees be required, the Company has agreed to compensate City of Hope on a per enrollee basis.

National Cancer Institute Pharmacologic Clinical Trial. In May 2019, the National Cancer Institute (NCI) initiated a glioblastoma (GBM) pharmacologic clinical trial. During the fourth quarter of 2019, the 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 Cooperative Research and Development Agreement, with the Company being required to provide the LB-100 clinical compound.

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

The NCI study is designed to determine the extent to which LB-100 enters recurrent malignant gliomas. Patients having surgery to remove one or more tumors will receive one dose of LB-100 prior to surgery and have blood and tumor tissue analyzed to determine the amount of LB-100 present and to determine whether the cells in the tumors show the biochemical changes expected to be present if LB-100 reaches its molecular target. The goal is to obtain data in up to eight patients. As a result of the innovative design of the NCI study, data from so few patients should be sufficient to provide a sound rationale for conducting a larger clinical trial to determine the effectiveness of adding LB-100 to the standard treatment regimen for GBMs.

The neurosurgical unit at the NCI, which had been closed due to the Covid-19 epidemic, has reopened, and patient accrual has resumed. Patient entry remains at two, with the goal to enter eight patients before analyzing results. There is an urgent need to improve therapy for this type of aggressive brain tumor. If the NCI study shows that LB-100 does penetrate the brain, a clinical study of LB-100 in combination with standard therapy for GBM, the drug temozolomide and radiation, both of which have been well documented in pre-clinical studies to be significantly enhanced by LB-100, would be of significant interest to neuro-oncologists frustrated by decades of limited advances in therapy for this common brain tumor in adults.

Clinical Trial Monitoring Agreements

Moffitt. On September 12, 2018, the Company finalized a work order agreement with Theradex Systems, Inc. ("Theradex"), an international contract research organization ("CRO"), to monitor the Phase 1b/2 clinical trial being managed and conducted by Moffitt. The clinical trial began in April 2019 and the first patient was entered into the clinical trial in July 2019. At the current rate of accrual, the clinical trial is expected to be completed by June 30, 2025.

Costs under this work order agreement are estimated to be approximately $954,000, with such payments expected to be divided approximately 94% to Theradex for services and approximately 6% for payments for pass-through costs. The costs of the Phase 1b/2 clinical trial being paid to or through Theradex are being recorded and charged to operations based on the periodic documentation provided by the CRO. During the years ended December 31, 2021 and 2020, the Company incurred costs of $9,750 and $18,663, respectively, pursuant to this work order. As of December 31, 2021, total costs of $91,885 have been incurred pursuant to this work order agreement. The Company's aggregate commitment pursuant to this clinical trial monitoring agreement, less amounts previously paid to date, totaled approximately $868,000 as of December 31, 2021, which is expected to be incurred through June 30, 2025.

City of Hope. On February 5, 2021, the Company signed a new work order agreement with Theradex to monitor the City of Hope investigator-initiated clinical trial in small cell lung cancer in accordance with FDA requirements for oversight by the sponsoring party. During the year ended December 31, 2021, the Company incurred costs of $24,626, pursuant to this work order. As of December 31, 2021, total costs of $24,626 have been incurred pursuant to this work order agreement. The Company's aggregate commitment pursuant to this clinical trial monitoring agreement, less amounts previously paid to date, totaled approximately $314,000 as of December 31, 2021, which is expected to be incurred through June 30, 2025.

Patent and License Agreements

On March 22, 2018, the Company entered into a Patent Assignment and Exploitation Agreement with INSERM TRANSFERT SA, acting as delegatee of the French National Institute of Health and Medical Research, for the assignment to the Company of INSERM'S interest in United States Patent No. 9,833,450 entitled "Oxabicyloheptanes and Oxabicycloheptenes for the Treatment of Depressive and Stress Disorders", which was filed with the United States Patent and Trademark Office in the name of INSERM and the Company as co-owners on February 19, 2015 and granted on May 12, 2017, and related patent applications and filings. INSERM is a French public institution dedicated to research in the field of health and medicine that had previously entered into a Material Transfer Agreement with the Company to allow INSERM to conduct research on the Company's proprietary compound LB-100 and/or its analogs for the treatment of depressive or stress disorders in humans. Pursuant to the Agreement, the Company has agreed to make certain milestone payments to INSERM aggregating up to $1,750,000 upon achievement of development milestones and up to $6,500,000 upon achievement of commercial milestones. The Company also agreed to pay INSERM certain commercial royalties on net sales of products attributed to the Agreement. The Company's initial plan was to complete the validation process to evaluate LB-100 for the treatment of depressive or stress disorders in humans within three years; however, the exploitation of this patent for the treatment of depressive and stress disorders in humans will require substantial additional capital and/or a joint venture or other type of business arrangement with a pharmaceutical company with substantially greater capital and business resources than those available to the Company. As there can be no assurances that the Company will be able to obtain the capital or business resources necessary to focus on the exploitation of this patent, it is uncertain as to when, if at all, the Company may

reach any of the development or commercialization milestones under the Agreement. As of December 31, 2021 and 2020, no amounts were due under this agreement.

Effective August 20, 2018, the Company entered into an Exclusive License Agreement with Moffitt. Pursuant to the License Agreement, Moffitt granted the Company an exclusive license under certain patents owned by Moffitt (the "Licensed Patents") relating to the treatment of MDS and a non-exclusive license under inventions, concepts, processes, information, data, know-how, research results, clinical data, and the like (other than the Licensed Patents) necessary or useful for the practice of any claim under the Licensed Patents or the use, development, manufacture or sale of any product for the treatment of MDS which would otherwise infringe a valid claim under the Licensed Patents. The Company was obligated to pay Moffitt a non-refundable license issue fee of $25,000 after the first patient is entered into a Phase 1b/2 clinical trial to be managed and conducted by Moffitt. The clinical trial began at a single site in April 2019 and the first patient was entered into the clinical trial in July 2019. The Company is also obligated to pay Moffitt an annual license maintenance fee of $25,000 commencing on the first anniversary of the Effective Date and every anniversary thereafter until the Company commences payment of minimum royalty payments. The Company has also agreed to pay non-refundable milestone payments to Moffitt, which cannot be credited against earned royalties payable by the Company, based on reaching various clinical and commercial milestones aggregating $1,897,000, subject to reduction by 40% under certain circumstances relating to the status of Valid Claims, as such term is defined in the License Agreement. During the year ended December 31, 2021 and 2020, the Company recorded charges to operations of $24,999 and $25,001, respectively, in connection with its obligations under the License Agreement. As of December 31, 2021, no milestones had yet been attained.

The Company will be obligated to pay Moffitt earned royalties of 4% on worldwide cumulative net sales of royalty-bearing products, subject to reduction to 2% under certain circumstances, on a quarterly basis, with a minimum royalty payment of $50,000 in the first four years after sales commence, and $100,000 in year five and each year thereafter, subject to reduction by 40% under certain circumstances relating to the status of Valid Claims, as such term is defined in the License Agreement. The Company's obligation to pay earned royalties under the License Agreement commences on the date of the first sale of a royalty-bearing product, and shall automatically expire on a country-by-country basis on the date on which the last valid claim of the Licensed Patents expires, lapses or is declared invalid, and the obligation to pay any earned royalties under the License Agreement shall terminate on the date on which the last valid claim of the Licensed Patents expires, lapses, or is declared to be invalid in all countries.

Employment Agreements with Officers

During July and August 2020, the Company entered into one-year employment agreements with its executive officers, consisting of Dr. John S. Kovach, Eric J. Forman, Dr. James S. Miser, and Robert N. Weingarten, which provided for aggregate annual compensation of $640,000, payable monthly. The employment agreements are automatically renewable for additional one-year periods unless terminated by either party upon 60 days written notice prior to the end of the applicable one-year period, or by death, or by termination for cause. These employment agreements were automatically renewed for an additional one-year period in July and August 2021.

On April 9, 2021, the Board of Directors increased the annual compensation of Eric J. Forman, the Company's Chief Administrative Officer, Dr. James S. Miser, the Company's Chief Medical Officer, and Robert N. Weingarten, the Company's Chief Financial Officer, under the employment agreements such that the total aggregate annual compensation of all officers increased to $775,000, effective May 1, 2021.

Other Significant Agreements and Contracts

On December 24, 2013, the Company entered into an agreement with NDA Consulting Corp. for consultation and advice in the field of oncology research and drug development. As part of the agreement, NDA also agreed to cause its president, Dr. Daniel D. Von Hoff, M.D., to become a member of the Company's Scientific Advisory Committee. The term of the agreement was for one year and provided for a quarterly cash fee of $4,000. The agreement has been automatically renewed for additional one-year terms on its anniversary date since 2014. Consulting and advisory fees charged to operations pursuant to this agreement were $16,000 and $16,000 for the years ended December 31, 2021 and 2020, respectively, which were included in research and development costs in the consolidated statements of operations.

Effective September 14, 2015, the Company entered into a Collaboration Agreement with BioPharmaWorks, pursuant to which the Company engaged BioPharmaWorks to perform certain services for the Company. Those services included, among other things: (a) assisting the Company to (i) commercialize its products and strengthen its patent portfolio, (ii) identify large pharmaceutical companies with potential interest in the Company's product pipeline, and (iii) prepare and deliver presentations concerning the Company's products; (b) at the request of the Board of Directors, serving as backup management for up to three months should the Company's Chief Executive Officer and scientific leader be temporarily unable to carry out his duties; (c) being available for consultation in drug discovery and development; and (d) identifying providers and overseeing tasks relating to clinical use and commercialization of new compounds.

BioPharmaWorks was founded in 2015 by former Pfizer scientists with extensive multi-disciplinary research and development and drug development experience. The Collaboration Agreement was for an initial term of two years and automatically renews for subsequent annual periods unless terminated by a party not less than 60 days prior to the expiration of the applicable period. In connection with the Collaboration Agreement, the Company agreed to pay BioPharmaWorks a monthly fee of $10,000, subject to the right of the Company to pay a negotiated hourly rate in lieu of the monthly payment and agreed to issue to BioPharmaWorks certain equity-based compensation. The Company recorded charges to operations pursuant to this Collaboration Agreement of $120,000 and $120,000 for the years ended December 31, 2021 and 2020, respectively, which were included in research and development costs in the consolidated statements of operations.

Effective August 12, 2020, the Company entered into a Master Service Agreement with the Foundation for Angelman Syndrome Therapy (FAST) to collaborate in supporting pre-clinical studies of the potential benefit of LB-100 in a mouse model of Angelman Syndrome (AS) as reported in The Proceedings of The National Academy of Science (Wang et al, June 3, 2019). The pre-clinical studies will be conducted at The University of California - Davis under the direction of Dr. David Segal, an internationally recognized leader in AS research. If the pre-clinical studies confirm that LB-100 reduces AS signs in rodent models, the Company has agreed to enter into discussions with FAST with respect to possible collaborations to most efficiently assess the benefit of LB-100 in patients with AS, which is a rare disease affecting an estimated one out of 12,000 to one out of 20,000 persons in the United States. The genetic cause of AS, reduced function of a specific maternal gene called Ube3, has been understood for some time, but the molecular abnormality resulting from the genetic lesion has now been shown to be increased concentrations of protein phosphatase 2A (PP2A), a molecular target of the Company's investigational compound, LB-100. The Company has agreed to provide FAST with a supply of LB-100 to be utilized in the conduct of this study, which is initially expected to be completed within three years. Conditioned on FAST's completion of this study, the Company has agreed to pay FAST five percent (5%) of all proceeds, as defined in the Master Service Agreement, received by the Company, up to a maximum of $250,000 from the exploitation of the study results.

The research team at the University of California, Davis recently completed their pre-clinical study of the potential benefit of LB-100 in a mouse model of AS, and the results are currently under review by FAST. The preliminary analysis indicates that the positive results previously reported by Chinese investigators were not confirmed in the US model. The Company is awaiting input from FAST as to whether it intends to continue to pursue pre-clinical studies of LB 100.

On October 8, 2021, the Company entered into a Development Collaboration Agreement with the Netherlands Cancer Institute, Amsterdam (NKI), one of the world's leading comprehensive cancer centers, and Oncode Institute, Utrecht, a major independent cancer research center, to identify the most promising drugs to be combined with LB-100, and potentially LB-100 analogues, to be used to treat a range of cancers, as well as to identify the specific molecular mechanisms underlying the identified combinations. The Company has agreed to fund the study and provide a sufficient supply of LB-100 to conduct the study. The study is expected to take approximately two years to conduct. During the year ended December 31, 2021, the Company incurred charges in the amount of $55,248, with respect to this agreement, which amount is included in research and development0 costs in the Company's consolidated statements of operations.

Off-Balance Sheet Arrangements

At December 31, 2021, the Company did not have any transactions, obligations or relationships that could be considered off-balance sheet arrangements.

Trends, Events and Uncertainties

Research and development of new pharmaceutical compounds is, by its nature, unpredictable. Although we will undertake research and development efforts with commercially reasonable diligence, there can be no assurance that our cash position will be sufficient to enable us to develop our pharmaceutical compounds to the extent needed to create future sales to sustain operations as contemplated herein.

There can be no assurances that one or more of our pharmaceutical compounds will obtain the regulatory approvals and market acceptance to achieve sustainable revenues sufficient to support our operations. Even if we are able to generate revenues, there can be no assurances that we will be able to achieve operating profitability or positive operating cash flows. There can be no assurances that we will be able to secure additional financing, to the extent required, on acceptable terms or at all. If cash resources are insufficient to satisfy our ongoing cash requirements, we would be required to reduce or discontinue our research and development programs, or attempt to obtain funds, if available (although there can be no assurances), through strategic alliances that may require us to relinquish rights to certain of our pharmaceutical compounds, or to curtail or discontinue our operations entirely.

Other than as discussed above, we are not currently aware of any trends, events or uncertainties that are likely to have a material effect on our financial condition in the near term, although it is possible that new trends or events may develop in the future that could have a material effect on our financial condition.

ITEM 7A. QUANTITATIVE AND QUALITATIVE DISCLOSURES ABOUT MARKET RISK

Not applicable.

ITEM 8. FINANCIAL STATEMENTS AND SUPPLEMENTARY DATA

The Company's consolidated financial statements and notes thereto and the related report of its independent registered public accounting firm are attached to this Annual Report on Form 10-K beginning on page F-1.

ITEM 9. CHANGES IN AND DISAGREEMENTS WITH ACCOUNTANTS ON ACCOUNTING AND FINANCIAL DISCLOSURE

Not applicable.

ITEM 9A. CONTROLS AND PROCEDURES

Evaluation of Disclosure Controls and Procedures

The Company's management is responsible for establishing and maintaining a system of disclosure controls and procedures (as defined in Rule 13a-15(e) and 15d-15(e) under the Securities Exchange Act of 1934, as amended (the "Exchange Act")) that is designed to ensure that information required to be disclosed by the Company in the reports that it files or submits under the Exchange Act is recorded, processed, summarized, and reported, within the time periods specified in the rules and forms. Disclosure controls and procedures include, without limitation, controls and procedures designed to ensure that information required to be disclosed by an issuer in the reports that it files or submits under the Exchange Act is accumulated and communicated to the issuer's management, including its principal executive officer(s) and principal financial officer(s), or persons performing similar functions, as appropriate to allow timely decisions regarding required disclosure.

In accordance with Exchange Act Rules 13a-15 and 15d-15, an evaluation was completed under the supervision and with the participation of the Company's management, including its Chief Executive Officer and Chief Financial Officer, of the effectiveness of the design and operation of the Company's disclosure controls and procedures as of the fiscal year ended December 31, 2021, the end of the most recent fiscal year covered by this report. Based on that evaluation, the Company's management concluded that the Company's disclosure controls and procedures were effective in providing reasonable assurance that information required to be disclosed in the Company's reports filed or submitted under the Exchange Act was recorded, processed, summarized, and reported within the time periods specified in the rules and forms of the Securities and Exchange Commission ("SEC").

Management's Annual Report on Internal Control Over Financial Reporting

The Company's management, including its Chief Executive Officer and Chief Financial Officer, is responsible for establishing and maintaining adequate internal control over financial reporting (as defined in Rule 13a-15(f) and 15d-15(f) under the Exchange Act). Internal control over financial reporting is a process, including policies and procedures, designed to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external reporting purposes in accordance with U.S. generally accepted accounting principles. The Company's internal control over financial reporting is designed to ensure that material information regarding the Company's operations is made available to management and the Board of Directors to provide them reasonable assurance that the published financial statements are fairly presented.

The Company's management assessed the Company's internal control over financial reporting based on the Internal Control—Integrated Framework (2013 Framework) issued by the Committee of Sponsoring Organizations of the Treadway Commission ("COSO"). The Company's system of internal control over financial reporting is designed to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with U.S. generally accepted accounting principles.

Because of its inherent limitations, internal control over financial reporting may not prevent or detect misstatements. Therefore, even those systems determined to be effective can provide only reasonable assurance of achieving their control objectives. Furthermore, smaller reporting companies face additional limitations. Smaller reporting companies employ fewer individuals and find it more difficult to properly segregate duties. Smaller reporting companies tend to utilize general accounting software packages that lack a rigorous set of software controls.

A material weakness is a deficiency, or a combination of deficiencies, in internal control over financial reporting such that there is a reasonable possibility that a material misstatement of the Company's annual or interim financial statements will not be prevented or deterred on a timely basis.

Based on the Company's evaluation under the framework in COSO, the Company's management, with the participation of the Chief Executive Officer and Chief Financial Officer, concluded that the Company's internal control over financial reporting was effective as of December 31, 2021.

Management believes that the consolidated financial statements included in this report fairly present, in all material respects, the Company's financial condition, results

of operations and cash flows as of and for the period ended December 31, 2021.

Auditor's Report on Internal Control Over Financing Reporting

This report does not include an attestation report of the Company's independent registered public accounting firm regarding internal control over financial reporting. Management's report was not subject to attestation by the Company's independent registered public accounting firm pursuant to rules of the SEC that permit the Company to provide only management's report in this report.

Changes in Internal Control Over Financial Reporting

The Company's management, including its Chief Executive Officer and Chief Financial Officer, has determined that no change in the Company's internal control over financial reporting (as that term is defined in Rules 13(a)-15(f) and 15(d)-15(f) of the Securities Exchange Act of 1934) occurred during or subsequent to the period ended December 31, 2021 that has materially affected, or is reasonably likely to materially affect, the Company's internal control over financial reporting.

ITEM 9B. OTHER INFORMATION

None.

ITEM 9C. DISCLOSURE REGARDING FOREIGN JURISDICTIONS THAT PREVENT INSPECTIONS

Not applicable.

PART III

ITEM 10. DIRECTORS, EXECUTIVE OFFICERS AND CORPORATE GOVERNANCE

Directors and Executive Officers

The following table and text set forth the names of all of our directors and executive officers as of March 11, 2021. The Board of Directors is comprised of only one class. All of the directors will serve until the next annual meeting of stockholders and until their successors are elected and qualified, or until their earlier death, retirement, resignation or removal. The brief descriptions of the business experience of each director and executive officers and an indication of directorships held by each director in other companies subject to the reporting requirements under the Federal securities laws are provided herein below. Also provided are the biographies of the members of the Scientific Advisory Committee and our consultants.

Our directors and executive officers are as follows:

Name	Age	Position(s) Held with the Company
Dr. John S. Kovach	85	President, Chief Executive Officer, Chief Scientific Officer, and Chairman of the Board of Directors
Dr. James S. Miser	74	Chief Medical Officer
Robert N. Weingarten	69	Vice President and Chief Financial Officer
Eric J. Forman	42	Chief Administrative Officer
Dr. Philip F. Palmedo	87	Director
Dr. Stephen J. Forman	73	Director
Gil N Schwartzberg	79	Director
Regina Brown	58	Director
Dr. Yun Yen	65	Director

Biographies of Directors and Executive Officers

Dr. John S. Kovach

Dr. John S. Kovach founded the Company in August 2005 and is our President, Chief Executive Officer, Chief Scientific Officer and Chairman of our Board of Directors. He received a B.A. (cum laude) from Princeton University and an M.D. (AOA) from the College of Physicians & Surgeons, Columbia University. Dr. Kovach trained in Internal Medicine and Hematology at Presbyterian Hospital, Columbia University, and spent six years in the laboratory of Chemical Biology at the National Institute of Arthritis and Metabolic Diseases studying control of gene expression in bacterial systems.

Dr. Kovach was recruited to the State University of New York at Stony Brook ("SUNY – Stony Brook") in Stony Brook, New York in 2000 to found the Long Island Cancer Center (now named the Stony Brook University Cancer Center). From 1994 to 2000, Dr. Kovach was Executive Vice President for Medical and Scientific Affairs at the City of Hope National Medical Center in Los Angeles, California. His responsibilities included oversight of all basic and clinical research initiatives at the City of Hope. During that time, Dr. Kovach was also Director of the Beckman Research Center at City of Hope and a member of the Arnold and Mabel Beckman Scientific Advisory Board in Newport Beach, California.

From 1976 to 1994, Dr. Kovach was a consultant in oncology and director of the Cancer Pharmacology Division at the Mayo Clinic in Rochester, Minnesota. During this time, he directed the early clinical trials program for evaluation of new anti-cancer drugs as principal investigator of contracts from the National Cancer Institute. From 1986 to 1994, he was also Chair of the Department of Oncology and Director of the NCI-designated Mayo Comprehensive Cancer Center. During that time, Dr. Kovach, working with a molecular geneticist, Steve Sommer, M.D., Ph.D., published extensively on patterns of acquired mutations in human cancer cells as markers of environmental mutagens and as potential indicators of breast cancer patient prognosis. Dr. Kovach has published over 100 articles on the pharmacology, toxicity and effectiveness of anti-cancer treatments and on the molecular epidemiology of breast cancer.

Effective February 23, 2017, Dr. Kovach retired from his part-time (50%) academic position at SUNY – Stony Brook, as a result of which he has been devoting 100% of his time to our business activities since that date.

Dr. James S. Miser

James S. Miser, M.D., was appointed as Chief Medical Officer effective August 1, 2020. Dr. Miser is a pediatric hematologist/oncologist, internationally recognized as an expert in the study and treatment of childhood cancers. His outstanding career includes leadership positions as Clinical Director, Department of Pediatrics, Division of

Pediatric Hematology/Oncology, Children's Hospital and Medical Center and Associate Member, Fred Hutchinson Cancer Research Center, Seattle, Washington; Chairman, Division of Pediatrics, Director, Department of Pediatric Hematology/Oncology, President and Chief Executive Officer, and Chief Medical Officer, all at City of Hope National Medical Center, Duarte, California. Since 2009, he has been a member of the Active Staff, Department of Pediatrics at City of Hope, most recently part-time, and Chair Professor, College of Medical Sciences and Technology, Taipei Medical University, Taipei, Taiwan.

Dr. Miser has extensive experience in the clinical development of new anti-cancer drugs for pediatric malignancies, leading many clinical trials at institutional and national cancer study groups. He is expert in the design and monitoring of clinical cancer trials and was a member of the Soft Tissue Sarcoma Strategy Group, and Member of the New Agents Executive and Steering Committee, Phase II Coordinator Children's Cancer Group and Chairman, Data Monitoring Committee, National Wilms Tumor Society. He has authored more than a 100 peer-reviewed articles dealing primarily with pediatric clinical cancer studies.

Robert N. Weingarten

Robert N. Weingarten was appointed as Vice President and Chief Financial Officer effective August 12, 2020. Mr. Weingarten is an experienced business consultant and advisor with a consulting practice focusing on accounting and SEC compliance issues. Since 1979, Mr. Weingarten has provided such financial consulting and advisory services, has acted as chief financial officer, and has served on the boards of directors of numerous public companies in various stages of development, operation or reorganization. Mr. Weingarten has experience in a variety of industries, including the pharmaceutical industry.

Mr. Weingarten has been a Director of Guardion Health Sciences, Inc. (Nasdaq Capital Market: GHSI) since June 2015 and Chairman of its Board of Directors since July 2020. Previously, Mr. Weingarten served as Lead Director on Guardion's Board of Directors from January 2017 to March 2020. From July 2017 to June 2018, Mr. Weingarten was the Chief Financial Officer of Alltemp, Inc. From April 2013 to February 2017, Mr. Weingarten served on the Board of Directors of RespireRx Pharmaceuticals Inc. and also served as its Vice President and Chief Financial Officer. Mr. Weingarten received a B.A. in Accounting from the University of Washington in 1974, a M.B.A. in Finance from the University of Southern California in 1975, and is a Certified Public Accountant (inactive) in the State of California.

Eric Forman, J.D.

Eric Forman has led our business development, initially as a consultant, since 2013. Effective October 1, 2020, Mr. Forman was appointed as our Chief Administrative Officer. In his capacity as a consultant, and in his role as Chief Administrative Officer, his responsibilities include overseeing all internal operations, the development of science/business collaborations, and the management of our growing intellectual property portfolio. Prior to his involvement with our Company, he served as Counsel and Senior Project Manager at Shore Group Associates, managing in-house legal, tax, and regulatory affairs and supervising client relations for financial software and mobile application development teams.

As an attorney, Mr. Forman has represented and advised both technology and biotechnology companies, entrepreneurs, non-profits, and start-ups, with a focus on intellectual property, licensing, corporate structure, and transactions.

Mr. Forman earned a B.A. Degree Cum Laude from Loyola Marymount University and a J.D. from the Benjamin N. Cardozo School of Law. He has an active law license and is a member of the New York State Bar Association.

Dr. Philip F. Palmedo

Philip F. Palmedo, Ph.D., is a physicist, entrepreneur and corporate manager. Dr. Palmedo was appointed to our Board of Directors on June 30, 2006. He founded and served as Chairman of the International Resources Group (IRG), an international consultancy in energy, natural resources and economic development. IRG was acquired by L3 Communications in 2008. Dr. Palmedo designed and was the first President of the Long Island Research Institute formed by Brookhaven National Laboratory, Cold Spring Harbor Laboratory, and SUNY – Stony Brook to facilitate the commercialization of technologies. In 1988, Dr. Palmedo joined in the formation of Kepler Financial Management, Ltd., a quantitative financial research and trading company. He was President and Managing Director until 1991, when Renaissance Technologies Corporation acquired the company.

Dr. Palmedo served on the boards of Asset Management Advisors, the Teton Trust Company, EHR Investments and C-Quest Capital, and is currently a member of the Board of Directors of Gyrodyne LLC. He also served on the Board of Trustees of Williams College and of the Stony Brook (University) Foundation, where he chaired the Foundation's Investment Committee.

Dr. Stephen J. Forman

Stephen J. Forman, M.D., is an internationally recognized expert in hematologic malignancies and bone marrow transplantation, and is a leader in pre-clinical and clinical cancer research. Dr. Forman was appointed to our Board of Directors on May 13, 2016. He is co-editor of Thomas' Hematopoietic Cell Transplantation, a definitive textbook for clinicians, scientists and health care professionals. Dr. Forman is the Francis and Kathleen McNamara Distinguished Chair in Hematology and Hematopoietic Cell Transplantation at the City of Hope Comprehensive Cancer Center, a position he has held since 1987.

In nearly 40 years at City of Hope, Dr. Forman has been instrumental in advancing the survival rates for patients suffering from cancers of the blood and immune system such as leukemia, lymphoma and myeloma.

As Director of the T Cell Immunotherapy Research Laboratory, his current research is focused on cancer immunotherapy, using the body's own immune system to attack cancer. Pharmacological enhancement of patients' immune responses to their cancers is of special interest to the Company, as the enzyme target of its lead clinical compound, LB-100, has been reported recently to be critical to immune function. Much of Dr. Forman's current work centers on T cells and their cancer-fighting potential.

Dr. Yun Yen

Yun Yen, M.D., Ph.D., F.A.C.P., is a physician, scientist, innovator, and philanthropist. Dr. Yen was appointed to our Board of Directors on August 4, 2018. He is widely regarded as an expert in ribonucleotide reductase, a critical target in cancer therapy and diagnostics. He is President Emeritus of Taipei Medical University (TMU) and Chair Professor of the Ph.D. Program for Cancer Biology and Drug Discovery. Prior to TMU, Dr. Yen was the Allen and Lee Chao Endowed Chair in Developmental Cancer Therapeutics, Chair of Molecular Pharmacology Department, Associate Director for Translational Research, and Co-Director of the Developmental Cancer Therapeutics Program at the City of Hope NCI-designated Comprehensive Cancer Center, Duarte California. He has published more than 300 peer-reviewed articles, holds over 60 patents, and has commercialized multiple methodologies involving nanoparticles, small and large molecule drugs, biomarkers, stem cells, and medical devices. Dr. Yen also founded philanthropic organizations aimed at serving the global cancer community and holds membership in numerous professional societies. He serves on the boards of Fulgent Genetics and Tanvex BioPharma Inc.

Gil N Schwartzberg, JD, ScD (hon), was appointed to our Board of Directors on April 9, 2021, and has been a consultant to the Company since its inception. Mr. Schwartzberg was the Chairman of the Board, President and Chief Executive Officer of the City of Hope National Medical Center, one of the nation's leading biomedical research and treatment facilities and a National Cancer Institute (NCI) Comprehensive Cancer Center. Following his departure, the Graduate School of Biological Science of The Beckman Research Institute at the City of Hope awarded Mr. Schwartzberg the degree of Doctor of Science, honoring his work in the advancement of science through programmatic development and the growth of the Graduate School. This was the first ScD. degree awarded by the Beckman Graduate School., which received its full academic accreditation during Mr. Schwartzberg's tenure as the school's president. Mr. Schwartzberg was the only person in the hundred-plus-year history of City of Hope to have served as both Chairman of the Board of Directors and as Chief Executive Officer. Mr. Schwartzberg is now City of Hope Chairman Emeritus for life.

Prior to his joining the City of Hope, Mr. Schwartzberg was Vice Chairman of the Board of Sterling Bank of Los Angeles, of which he was a founder, and where he served for many years as the Chairman of the Loan Committee until the bank's sale. Additionally, he was a founding shareholder of Skechers USA, Inc. (NYSE: SKX). He is currently a consultant to Skechers and both trustee and co-trustee of trusts that hold the controlling interest in the Skechers USA, Inc.

Mr. Schwartzberg earned a Juris Doctorate awarded magna cum laude. He practiced law, specializing in business structure and transactions, and remains a member in good standing of the California Bar Association. He is the author of two books. *Warning Toxic Business Mistakes and How to Avoid Making Them* and *Jane Austen's Persuasion Annotated, a Royal Navy Reading Companion*.

Regina Brown, CPA

Regina Brown was appointed to our Board of Directors effective May 11, 2021. Ms. Brown has been a practicing accountant for over thirty years. Currently, her practice has a wide range of clients, varying in size, industry and geographic locations. They include large national corporations listed on the New York Stock Exchange, as well as Southern California businesses. Other clients consist of professionals, wholesalers and high net worth individuals. Many of her clients have international and cross-border operations.

As a consequence of her depth of experience, she regularly assists other professionals with their client's issues and performs tax research and analysis in connection with litigation and other matters including marital dissolution, tax and accounting with respect to mergers and acquisitions, implementation of internal controls, and extensive work in the area of trusts and estates. In addition, international tax matters and compliance are also a significant part of her practice. Ms. Brown is a member in good standing of the California Society of CPAs and the American Institute of Certified Public Accountants and has appeared as a speaker before both organizations.

SCIENTIFIC ADVISORY COMMITTEE

The Scientific Advisory Committee was established to advise our management in three areas: human molecular pathology; the clinical management of human brain tumors; and medicinal chemistry. Our objective is to meet with the committee as a group annually. The committee has been apprised of our general objectives and several of the specific challenges and leads for developing improved therapies for human brain tumors. Members of the committee do not serve in any management capacity with us. The committee currently consists of the following member:

Dr. Daniel D. Von Hoff

Dr. Daniel D. Von Hoff, M.D., is currently Physician in Chief, Distinguished Professor and Director of the Clinical Translational Research Division at the Translational Genomics Research Institute in Phoenix, Arizona. He is also Chief Scientific Officer for US Oncology and for Scottsdale Healthcare's Clinical Research Institute. He holds an appointment as Professor of Medicine, Mayo Clinic, Scottsdale, Arizona. Dr. Von Hoff is a Fellow of the American College of Physicians.

Dr. Von Hoff's major interest is in the development of new anticancer agents, both in the clinic and in the laboratory. He and his colleagues were involved in the beginning of the development of many of the agents that are now used routinely, including mitoxantrone, fludarabine, paclitaxel, docetaxel, gemcitabine, irinotecan, nelarabine, capecitabine and lapatinib. At present, he and his colleagues are concentrating on the development of molecularly targeted therapies, particularly for patients with advanced pancreatic cancer.

Dr. Von Hoff has published more than 620 papers, 137 book chapters and over 1,050 abstracts. Dr. Von Hoff received the 2010 David A. Karnofsky Memorial Award from the American Society of Clinical Oncology for his outstanding contributions to cancer research leading to significant improvement in patient care.

Dr. Von Hoff was appointed to President Bush's National Cancer Advisory Board from 2004 to 2010. Dr. Von Hoff is the past President of the American Association for Cancer Research (the world's largest cancer research organization), a Fellow of the American College of Physicians, and a member and past board member of the American Society of Clinical Oncology. He is a founder of ILEX™ Oncology, Inc. (acquired by Genzyme in 2004 after Ilex had two agents, alemtuzumab and clofarabine, approved by the FDA for patients with leukemia). Dr. Von Hoff is founder and the Editor Emeritus of Investigational New Drugs – The Journal of New Anticancer Agents; and, Editor-in-Chief of Molecular Cancer Therapeutics. He is a co-founder of the AACR/ASCO Methods in Clinical Cancer Research Workshop.

Family Relationships

Eric Forman, our Chief Administrative Officer, is the son of board member Dr. Stephen Forman and son-in-law of board member Gil Schwartzberg. Julie Forman, the wife of Eric Forman and the daughter of Gil Schwartzberg, is Vice President of Morgan Stanley Wealth Management, where the Company's cash is deposited and the Company maintains a continuing banking relationship.

Director Independence

Our Board of Directors undertook a review of the independence of our directors and considered whether any director has a relationship with us that could compromise that director's ability to exercise independent judgment in carrying out that director's responsibilities. Our Board of Directors has affirmatively determined that Philip Palmedo, Stephen Forman, Yun Yen, Gil Schwartzberg and Regina Brown are each an "independent director," as defined under Nasdaq rules.

Committees of Our Board of Directors

Our Board of Directors directs the management of our business and affairs, as provided by Delaware law, and conducts its business through meetings of the Board of Directors and its standing committees. We have a standing audit committee and compensation committee. The Board of Directors serves in place of a nominating and corporate governance committee. In addition, from time to time, special committees may be established under the direction of the Board of Directors when necessary to address specific issues.

Audit Committee

Our audit committee is responsible for, among other things:

- Approving and retaining the independent auditors to conduct the annual audit of our financial statements;
- reviewing the proposed scope and results of the audit;

- reviewing and pre-approving audit and non-audit fees and services;
- reviewing accounting and financial controls with the independent auditors and our financial and accounting staff;
- reviewing and approving transactions between us and our directors, officers and affiliates;
- establishing procedures for complaints received by us regarding accounting matters;
- overseeing internal audit functions, if any; and
- preparing the report of the audit committee that the rules of the SEC require to be included in our annual meeting proxy statement.

Our audit committee consists of Regina Brown, Dr. Yun Yen, and Dr. Philip Palmedo, with Ms. Brown serving as chair. Our Board of Directors has affirmatively determined that each of the committee members meet the definition of "independent director" under the Nasdaq rules, and that they meet the independence standards under Rule 10A-3. Each member of our audit committee meets the financial literacy requirements of the Nasdaq rules. In addition, our Board of Directors has determined that Ms. Brown qualifies as an "audit committee financial expert," as such term is defined in Item 407(d)(5) of Regulation S-K. Our Board of Directors has adopted a written charter for the audit committee, which is available on our principal corporate website at *www.lixte.com.*

Compensation Committee

Our compensation committee is responsible for, among other things:

- reviewing and recommending the compensation arrangements for executive management;
- establishing and reviewing general compensation policies with the objective to attract and retain superior talent, to reward individual performance and to achieve our financial goals;
- administering our stock incentive plans; and
- preparing the report of the compensation committee that the rules of the SEC require to be included in our annual meeting proxy statement.

Our compensation committee consists of Dr. Yun Yen, Dr. Stephen Forman and Dr. Philip Palmedo, with Dr. Yen serving as chair. Our Board of Directors has determined that all three committee members are independent directors under Nasdaq rules. Our Board of Directors has adopted a written charter for the compensation committee, which is available on our principal corporate website at *www.lixte.com.*

Nominating and Corporate Governance

Although our Board of Directors serves in place of a nominating and corporate governance committee, our independent directors on the board are responsible for, among other things:

- nominating members of the Board of Directors;
- developing a set of corporate governance principles applicable to our company; and
- overseeing the evaluation of our Board of Directors.

Our Board of Directors may adopt resolutions addressing, among other things, the nomination process, as may be necessary in the future.

Code of Ethics

Our Board of Directors has adopted a code of ethics covering all of our executive officers and key employees. A copy of our code of ethics will be furnished without charge to any person upon written request. Requests should be sent to: Secretary, Lixte Biotechnology Holdings, Inc., 680 East Colorado Boulevard, Suite 180, Pasadena, California 91101.

Limitations on Liability and Indemnification Matters

Our Certificate of Incorporation contains provisions that limit the liability of our current and former directors for monetary damages to the fullest extent permitted by Delaware law. Delaware law provides that directors of a corporation will not be personally liable for monetary damages for any breach of fiduciary duties as directors, except liability for:

- any breach of the director's duty of loyalty to the corporation or its stockholders;
- any act or omission not in good faith or that involves intentional misconduct or a knowing violation of law;
- unlawful payments of dividends or unlawful stock repurchases or redemptions as provided in Section 174 of the Delaware General Corporation Law; or
- any transaction from which the director derived an improper personal benefit.

This limitation of liability does not apply to liabilities arising under federal securities laws and does not affect the availability of equitable remedies such as injunctive relief or rescission.

Our Certificate of Incorporation provides that we are authorized to indemnify our directors and officers to the fullest extent permitted by Delaware law. Our Amended and Restated Bylaws provide that we are required to indemnify our directors and executive officers to the fullest extent permitted by Delaware law. Our Amended and Restated Bylaws also provide that, upon satisfaction of certain conditions, we are required to advance expenses incurred by a director or executive officer in advance of the final disposition of any action or proceeding, and permit us to secure insurance on behalf of any officer, director, employee or other agent for any liability arising out of his or her actions in that capacity regardless of whether we would otherwise be permitted to indemnify him or her under the provisions of Delaware law. Our Amended and Restated

Bylaws also provide our Board of Directors with discretion to indemnify our other officers and employees when determined appropriate by our Board of Directors. We have entered into agreements to indemnify our directors, executive officers and other employees as determined by the Board of Directors. With certain exceptions, these agreements provide for indemnification for related expenses, including, among other things, attorneys' fees, judgments, fines and settlement amounts incurred by any of these individuals in any action or proceeding. We believe that these provisions and agreements are necessary to attract and retain qualified persons as directors and officers. We have obtained customary directors' and officers' liability insurance.

The limitation of liability and indemnification provisions in our Certificate of Incorporation and Amended and Restated Bylaws may discourage stockholders from bringing a lawsuit against our directors for breach of their fiduciary duty. They may also reduce the likelihood of derivative litigation against our directors and officers, even though an action, if successful, might benefit us and other stockholders. Furthermore, a stockholder's investment may be adversely affected to the extent that we pay the costs of settlement and damage awards against directors and officers as required by these indemnification provisions. At present, there is no pending litigation or proceeding involving any of our directors, officers or employees for which indemnification is sought, and we are not aware of any threatened litigation that may result in claims for indemnification.

Compliance with Section 16(a) of the Securities Exchange Act of 1934, as Amended

Section 16(a) of the Securities Exchange Act of 1934, as amended, requires the Company's directors and executive officers and persons who own more than 10% of a registered class of the Company's equity securities to file various reports with the Securities and Exchange Commission concerning their holdings of, and transactions in, securities of the Company. Copies of these filings must be furnished to the Company.

To the Company's knowledge, based solely on its review of the copies of the Section 16(a) reports furnished to the Company and any written representations to the Company, that no other reports were required, the Company believes that all individual filing requirements applicable to a director, officer, or beneficial owner of more than 10% of the Company's common stock were complied with under Section 16(a) of the Exchange Act during the year ended December 31, 2021, except as follows: Eric Forman was late in filing one Form 4 and Glenn Krinsky was late in filing one Form 3, each document relating to the change of the trustee from Mr. Forman to Mr. Krinsky with respect to the John and Barbara Kovach 2015 Trust.

ITEM 11. EXECUTIVE COMPENSATION

EXECUTIVE AND DIRECTOR COMPENSATION

Summary Compensation Table

The table set forth below presents the compensation awarded to, earned by or paid to our named executive officers for the years ended December 31, 2021, 2020 and 2019.

OFFICER COMPENSATION TABLE

Executive	Year	Salary ($)	Bonus ($)	Stock Awards ($)	Option Awards ($)(1)	Non-Equity Incentive Plan Compensation ($)	Non-Qualified Deferred Compensation Earnings ($)	All Other Compensation ($)	Total ($)
John S. Kovach (2)	2021	250,000	-	-	-	-	-	-	250,000
	2020	107,500	-	-	-	-	-	-	107,500
	2019	60,000	-	-	-	-	-	-	60,000
James S. Miser (3)	2021	166,667	-	-	-	-	-	-	166,667
	2020	62,500	-	-	572,650	-	-	-	635,150
	2019	-	-	-	-	-	-	-	-
Robert N. Weingarten (4)	2021	156,667	-	-	-	-	-	-	156,667
	2020	46,451	-	-	400,855	-	-	-	447,306
	2019	-	-	-	-	-	-	-	-
Eric J. Forman (5)	2021	156,667	-	-	-	-	-	-	156,667
	2020	30,000	-	-	400,855	-	-	-	430,855
	2019	-	-	-	-	-	-	-	-

(1) Consists of grant date fair value of option award calculated pursuant to the Black-Scholes option-pricing model.

(2) John S. Kovach has been the Company's President and Chief Executive Officer since inception and entered into an employment agreement with the Company effective July 15, 2020.

(3) James S. Miser has been the Company's Chief Medical Officer since August 1, 2020. In connection with his employment agreement, Dr. Miser was awarded an option grant for 83,333 shares of the Company's common stock valued at $6.8718 per share.

(4) Robert N. Weingarten has been the Company's Vice President and Chief Financial Officer since August 12, 2020. In connection with his employment agreement, Mr. Weingarten was awarded an option grant for 58,333 shares of the Company's common stock valued at $6.8718 per share.

(5) Eric J. Forman has been the Company's Chief Administrative Officer since July 15, 2020. In connection with his employment agreement, Mr. Forman was awarded an option grant for 58,333 shares of the Company's common stock valued at $6.8718 per share.

There were no option exercises during the years ended December 31, 2019, 2020 or 2021.

Outstanding Equity Awards at December 31, 2021

The table set forth below presents information regarding outstanding stock options held by our named executive officers as of December 31, 2021. There were no stock options issued and outstanding to our executive officers at December 31, 2019.

NAME	GRANT DATE	VESTING COMMENCEMENT DATE	NUMBER OF SECURITIES UNDERLYING UNEXERCISED OPTIONS EXERCISABLE (#)	NUMBER OF SECURITIES UNDERLYING UNEXERCISED OPTIONS UNEXERCISABLE (#)	OPTION EXERCISE PRICE ($)	OPTION EXPIRATION DATE
Dr. John S. Kovach	N/A	N/A	N/A	N/A	N/A	N/A
Dr. James S. Miser	August 1, 2020	August 1, 2020	41,667	41,667	$ 7.14	August 1, 2025
Robert N. Weingarten	August 12, 2020	August 12, 2020	29,167	29,166	$ 7.14	August 12, 2025
Eric J. Forman	June 7, 2016	June 7, 2016	16,667	-	$ 0.90	June 7, 2021
	October 16, 2017	October 16, 2017	16,667	-	$ 0.90	October 16, 2022
	May 22, 2019	May 22, 2019	16,667	-	$ 6.60	May 22, 2024
	August 12, 2020	August 12, 2020	29,167	29,166	$ 7.14	August 12, 2025

The intrinsic value of exercisable but unexercised in-the-money stock options held by our named executive officers at December 31, 2021 was approximately $9,667, based on a fair market value of $1.19 per share on December 31, 2021.

Employment Agreements; Compensation

During July and August 2020, the Company entered into one-year employment agreements with its executive officers, consisting of Dr. John S. Kovach, Eric J. Forman, Dr. James S. Miser, and Robert N. Weingarten, payable monthly, as described below. The employment agreements are automatically renewable for additional one-year periods unless terminated by either party upon 60 days written notice prior to the end of the applicable one-year period, or by death, or by termination for cause. These employment agreements were automatically renewed for an additional one-year period in July and August 2021.

Dr. John Kovach. On July 15, 2020, the Company entered into an employment agreement with Dr. John Kovach to continue to act as the Company's President, Chief Executive Officer and Chief Scientific Officer, with an annual salary of $250,000, payable monthly. His responsibilities include the oversight of the Company's entire operations and strategic planning, and he will act as the primary contact between the Company's executive team and the Board of Directors, to whom he shall report. Dr. Kovach shall supervise all scientific endeavors, providing guidance to the Chief Medical Officer. He shall be the principal spokesperson for the Company. The effective date of the agreement was October 1, 2020 and shall remain in effect until the earlier of (i) one year from the effective date, automatically renewable for additional one-year periods unless terminated by either party upon 60 days written notice prior to the end of the applicable one-year period, (ii) his death, or (iii) termination for cause.

Eric Forman. On July 15, 2020, as amended on August 12, 2020, the Company entered into an employment agreement with Eric Forman, to act as the Company's Chief Administrative Officer reporting directly to the Company's Chief Executive Officer, with an annual salary of $120,000, payable monthly. Effective May 1, 2021, Mr. Forman's annual salary was increased to $175,000. Mr. Forman's primary function is to oversee the Company's internal operations, including IT, licensing, legal, personnel, marketing, and corporate governance. Mr. Forman was also granted stock options to acquire 350,000 shares of the Company's common stock. The effective date of the agreement was October 1, 2020 and shall remain in effect until the earlier of (i) one year from the effective date, automatically renewable for additional one-year periods unless terminated by either party upon 60 days written notice prior to the end of the applicable one-year period, (ii) his death, or (iii) termination for cause.

Dr. James Miser. On August 1, 2020, the Company entered into an employment agreement with Dr. James Miser, M.D., pursuant to which Dr. Miser was appointed as the Company's Chief Medical Officer, with an annual salary of $150,000. Effective May 1, 2021, Dr. Miser's annual salary was increased to $175,000. Under the employment agreement, Dr. Miser will play a leadership role in planning, implementation and oversight of clinical trials. Dr. Miser will be responsible for assisting and developing strategic clinical goals and the implementation and safety monitoring of investigational studies. Dr. Miser will be the primary medical monitor for all clinical investigational studies and for the oversight of third party CRO monitors. Dr. Miser will work closely with the Company's Chief Executive Officer on the development of specific goals needed to ensure the timely implementation of appropriate clinical studies needed for successful registration of therapeutic products and new drug development. Dr. Miser will be required to devote at least 50% of his business time to the Company's activities. Dr. Miser was also granted stock options to acquire 500,000 shares of the Company's common stock. The effective date of the agreement was August 1, 2020. The agreement shall remain in effect until the earlier of (i) one year from the effective date, automatically renewable for additional one-year periods unless terminated by either party upon 60 days written notice prior to the end of the applicable one-year period, (ii) his death, or (iii) termination for cause.

Robert N. Weingarten. On August 12, 2020, the Company entered into an employment agreement with Robert N. Weingarten pursuant to which Mr. Weingarten was appointed as the Company's Vice-President and Chief Financial Officer, with an annual salary of $120,000. Effective May 1, 2021, Mr. Weingarten's annual salary was increased to $175,000. Mr. Weingarten was also granted stock options to acquire 350,000 shares of the Company's common stock. The effective date of the agreement was August 12, 2020. The agreement shall remain in effect until the earlier of (i) one year from the effective date, automatically renewable for additional one-year periods unless terminated by either party upon 60 days written notice prior to the end of the applicable one-year period, (ii) his death, or (iii) termination for cause.

Consulting Agreements

On September 12, 2007, the Company entered into a consulting agreement with Gil N Schwartzberg for Mr. Schwartzberg to provide financial advisory and consulting services to the Company with respect to financing matters, capital structure and strategic development, and to assist management in communications with investors and stockholders. Mr. Schwartzberg is currently a significant stockholder and director of the Company. Consideration under this consulting agreement, including amendments thereto, has been paid exclusively in the form of stock options. On August 2, 2018, the Company entered into a third amendment to the consulting agreement to extend it to January 28, 2024, as well as to extend the exercise date of previously issued, fully-vested stock options for 666,667 shares of common stock, exercisable at $3.00 per share, from January 28, 2019 to January 28, 2024.

Board of Director Compensation

Effective May 22, 2019, in recognition of their service as directors over the past year, we granted to Dr. Winson Sze Chun Ho, Dr. Yun Yen, Dr. Stephen Forman, and Dr. Philip Palmedo, fully-vested stock options to purchase an aggregate of 33,333 shares (8,333 shares each) of our common stock, exercisable for a period of five years from the vesting date at $6.60 per share, which was the approximate fair market value of our common stock on such date. The fair value of these stock options, as calculated pursuant to the Black-Scholes option-pricing model, was determined to be $189,060 ($5.6718 per share) and was charged to general and administrative costs in the consolidated statement of operations on the grant date.

Effective January 6, 2021, in recognition of their service as directors of the Company over the past year, the Company granted fully-vested stock options to purchase 50,000 shares of common stock to each of Dr. Winson Sze Chun Ho, Dr. Yun Yen, Dr. Stephen Forman, and Dr. Philip Palmedo (an aggregate of 200,000 shares), exercisable for a period of five years from the grant date at $3.21 per share, which was the approximate fair market value of the Company's common stock on such date. The fair value of these stock options, as calculated pursuant to the Black-Scholes option-pricing model, was determined to be $571,312 ($2.8566 per share) and was charged to general and administrative costs in the consolidated statement of operations on the grant date.

On April 9, 2021, Winson Sze Chun Ho resigned from the Company's Board of Directors to focus on clinical and pre-clinical cancer research in academic medicine. Concurrent with his resignation, the Board of Directors appointed Gil Schwartzberg to fill the vacancy created by Dr. Ho's resignation. In connection with his appointment to the Board of Directors, and in accordance with the Company's cash and equity compensation package for the members of the Board of Directors, Mr. Schwartzberg was granted options exercisable for a period of five years to purchase 250,000 shares of the Company's common stock at an exercise price of $3.20 per share (the closing market price on the grant date), vesting 50% on the grant date and the remainder vesting 12.5% on the last day of each subsequent calendar quarter-end until fully vested. The fair value of these stock options, as calculated pursuant to the Black-Scholes option-pricing model, was determined to be $753,611 ($3.0144 per share), of which $376,800 was attributable to the stock options fully-vested on April 9, 2021 and was therefore charged to operations on that date. The remaining unvested portion of the fair value of the stock options is being charged to operations ratably from April 9, 2021 through June 30, 2023. During the year ended December 31, 2021, the Company recorded charges to general and administrative costs in the consolidated statement of operations of $500,235 with respect to these stock options.

On May 11, 2021, the Board of Directors appointed Regina Brown to the Board of Directors. In connection with her appointment to the Board of Directors, and in accordance with the Company's cash and equity compensation package for the members of the Board of Directors, Ms. Brown was granted options exercisable for a period of five years to purchase 250,000 shares of the Company's common stock at an exercise price of $2.80 per share (the closing market price on the grant date), vesting 50% on the grant date and the remainder vesting 12.5% on the last day of each subsequent calendar quarter-end until fully vested. The fair value of these stock options, as calculated pursuant to the Black-Scholes option-pricing model, was determined to be $658,363 ($2.6335 per share), of which $329,188 was attributable to the stock options fully-vested on May 11, 2021 and was therefore charged to operations on that date. The remaining unvested portion of the fair value of the stock options is being charged to operations ratably from May 11, 2021 through June 30, 2023. During the year ended December 31, 2021, the Company recorded charges to general and administrative costs in the consolidated statement of operations of $427,944 with respect to these stock options.

On June 30, 2021, the Board of Directors, in accordance with the Company's cash and equity compensation package for the independent members of the Board of Directors, granted to each of the five non-officer directors of the Company stock options exercisable for a period of five years to purchase 100,000 shares (a total of 500,000 shares) of the Company's common stock at an exercise price of $3.03 per share (the closing market price on the grant date), vesting 12.5% on the last day of each subsequent calendar quarter-end until fully vested. The total fair value of the 500,000 stock options, as calculated pursuant to the Black-Scholes option-pricing model, was determined to be $1,421,095 ($2.84225 per share), which is being charged to operations ratably from July 1, 2021 through June 30, 2023. During the year ended December 31, 2021, the Company recorded charges to general and administrative costs in the consolidated statement of operations of $358,200 with respect to these stock options.

Summary Compensation Table

The table set forth below presents the compensation awarded to, earned by or paid to our named directors for the years ended December 31, 2021, 2020 and 2019.

DIRECTOR COMPENSATION TABLE

Name and Principal Position	Year	Salary ($)	Bonus ($)	Stock Awards ($)	Option Awards ($)(1)	Non-Equity Incentive Plan Compensation ($)	Non-Qualified Deferred Compensation Earnings ($)	All Other Compensation ($)	Total ($)
John S. Kovach	2021	-	-	-	-	-	-	-	-
Director (2)	2020	-	-	-	-	-	-	-	-
	2019	-	-	-	-	-	-	-	-
Philip F. Palmedo	2021	-	-	-	427,047	-	-	20,458	447,505
Director	2020	-	-	-	-	-	-	-	-
	2019	-	-	-	47,265	-	-	-	47,265
Stephen J. Forman	2021	-	-	-	427,047	-	-	16,819	443,866
Director	2020	-	-	-	-	-	-	-	-
	2019	-	-	-	47,265	-	-	-	47,265
Winson Sze Chun Ho	2021	-	-	-	142,828	-	-	-	142,828
Director(3)	2020	-	-	-	-	-	-	-	-
	2019	-	-	-	47,265	-	-	-	47,265
Yun Yen	2021	-	-	-	427,047	-	-	21,833	448,880
Director	2020	-	-	-	-	-	-	-	-
	2019	-	-	-	47,265	-	-	-	47,265
Gil Schwartzberg	2021	-	-	-	1,037,830	-	-	14,556	1,052,386
Director(4)	2020	-	-	-	-	-	-	-	-
	2019	-	-	-	-	-	-	-	-
Regina Brown	2021	-	-	-	942,582	-	-	19,167	961,749
Director(5)	2020	-	-	-	-	-	-	-	-
	2019	-	-	-	-	-	-	-	-

(1) Consists of grant date fair value of option award calculated pursuant to the Black-Scholes option-pricing model.

(2) Dr. Kovach is also the Company's President, Chief Executive Officer and Chief Scientific Officer.

(3) Resigned as a director of the Company effective April 9, 2021.

(4) Appointed as a director of the Company effective April 9, 2021.

(5) Appointed as a director of the Company effective May 11, 2021.

Scientific Advisory Committee Compensation

On December 24, 2013, wr entered into an agreement with NDA Consulting Corp. for consultation and advice in the field of oncology research and drug development. As part of the agreement, NDA also agreed to cause its president, Dr. Daniel D. Von Hoff, M.D., to become a member of our Scientific Advisory Committee. The term of the agreement was for one year and provided for a quarterly cash fee of $4,000. The agreement has been automatically renewed for additional one-year terms on its anniversary date since 2014. Consulting and advisory fees charged to operations pursuant to this agreement were $16,000 and $16,000 for the years ended December 31, 2021 and 2020, respectively, which were included in research and development costs in the consolidated statements of operations.

2020 Stock Incentive Plan

Summary

On July 14, 2020, our Board of Directors adopted the 2020 Stock Incentive Plan (the "2020 Plan"), which provides for the granting of equity-based awards, consisting of stock options, restricted stock, restricted stock units, stock appreciation rights, and other stock-based awards to employees, officers, directors and consultants for up to 2,333,333 shares of common stock, under terms and conditions as determined by our Board of Directors. Stockholders holding a majority of the voting power of our common stock approved the 2020 Plan pursuant to an action by written consent dated July 31, 2020. Stockholders were notified of such action by written consent pursuant to an Information Statement dated August 31, 2020 and mailed to stockholders on or about September 3, 2020. As of December 31, 2021, unexpired stock options for 1,400,000 shares were issued and outstanding under the 2020 Plan.

Having an adequate number of shares available for future equity compensation grants is necessary to promote our long-term success and the creation of stockholder value by:

- Enabling us to continue to attract and retain the services of key service providers who would be eligible to receive grants;
- Aligning participants' interests with stockholders' interests through incentives that are based upon the performance of our common stock;
- Motivating participants, through equity incentive awards, to achieve long-term growth in our business, in addition to short-term financial performance; and
- Providing a long-term equity incentive program that is competitive as compared to other companies with whom we compete for talent.

The 2020 Plan permits the discretionary award of incentive stock options ("ISOs"), non-statutory stock options ("NQSOs"), restricted stock, restricted stock units ("RSUs"), stock appreciation rights ("SARs"), other equity awards and/or cash awards to selected participants. The 2020 Plan will remain in effect until July 14, 2030.

The 2020 Plan provides for the reservation of 2,333,333 shares of common stock for issuance thereunder (the "Share Limit"), and provides that the maximum number of shares that may be issued pursuant to the exercise of ISOs is 2,333,333 (the "ISO Limit").

Key Features of the 2020 Plan

Certain key features of the 2020 Plan are summarized as follows:

- If not terminated earlier by our Board of Directors, the 2020 Plan will terminate on July 14, 2030.
- Up to a maximum aggregate of 2,333,333 shares of common stock may be issued under the 2020 Plan. The maximum number of shares that may be issued pursuant to the exercise of ISOs is also 2,333,333.
- The 2020 Plan is administered by the Compensation Committee, which is comprised solely of independent members of our Board of Directors. The Board of Directors may designate a separate committee to make awards to employees who are not officers subject to the reporting requirements of Section 16 of the Exchange Act.

- Employees, consultants and board members are eligible to receive awards, provided that the Compensation Committee has the discretion to determine (i) who shall receive any awards, and (ii) the terms and conditions of such awards.
- Awards may consist of ISOs, NQSOs, restricted stock, RSUs, SARs, other equity awards and/or cash awards.
- Stock options and SARs may not be granted at a per share exercise price below the fair market value of a share of our common stock on the date of grant.
- Stock options and SARs may not be repriced or exchanged without stockholder approval.
- The maximum exercisable term of stock options and SARs may not exceed ten years.
- Awards are subject to recoupment of compensation policies adopted by us.

Eligibility to Receive Awards. Employees, consultants and members of our Board of Directors are eligible to receive awards under the 2020 Plan. The Compensation Committee determines, in its discretion, the selected participants who will be granted awards under the 2020 Plan.

Shares Subject to the 2020 Plan. The maximum number of shares of common stock that can be issued under the 2020 Plan is 2,333,333 shares.

The shares underlying forfeited or terminated awards (without payment of consideration), or unexercised awards become available again for issuance under the 2020 Plan. No fractional shares may be issued under the 2020 Plan. No shares will be issued with respect to a participant's award unless applicable tax withholding obligations have been satisfied by the participant.

Administration of the 2020 Plan. The 2020 Plan is administered by the Compensation Committee of the Board of Directors, which consists of independent board members. With respect to certain awards issued under the 2020 Plan, the members of the Compensation Committee also must be "Non-Employee Directors" under Rule 16b-3 of the Exchange Act. Subject to the terms of the 2020 Plan, the Compensation Committee has the sole discretion, among other things, to:

- Select the individuals who will receive awards;
- Determine the terms and conditions of awards (for example, performance conditions, if any, and vesting schedule);
- Correct any defect, supply any omission, or reconcile any inconsistency in the 2020 Plan or any award agreement;

- Accelerate the vesting, extend the post-termination exercise term or waive restrictions of any awards at any time and under such terms and conditions as it deems appropriate, subject to the limitations set forth in the 2020 Plan;

- Permit a participant to defer compensation to be provided by an award; and

- Interpret the provisions of the 2020 Plan and outstanding awards.

The Compensation Committee may suspend vesting, settlement, or exercise of awards pending a determination of whether a selected participant's service should be terminated for cause (in which case outstanding awards would be forfeited). Awards may be subject to any policy that the Board of Directors may implement on the recoupment of compensation (referred to as a "clawback" policy). The members of the Board of Directors, the Compensation Committee and their delegates shall be indemnified by us to the maximum extent permitted by applicable law for actions taken or not taken regarding the 2020 Plan.

Types of Awards.

Stock Options. A stock option is the right to acquire shares at a fixed exercise price over a fixed period of time. The Compensation Committee determines, among other terms and conditions, the number of shares covered by each stock option and the exercise price of the shares subject to each stock option, but such per share exercise price cannot be less than the fair market value of a share of our common stock on the date of grant of the stock option. The exercise price of each stock option granted under the 2020 Plan must be paid in full at the time of exercise, either with cash, or through a broker-assisted "cashless" exercise and sale program, or net exercise, or through another method approved by the Compensation Committee. Stock options granted under the 2020 Plan may be either ISOs or NQSOs. In order to comply with Treasury Regulation Section 1.422-2(b), the 2020 Plan provides that no more than 2,333,333 shares may be issued pursuant to the exercise of ISOs.

SARs. A SAR is the right to receive, upon exercise, an amount equal to the difference between the fair market value of the shares on the date of the SAR's exercise and the aggregate exercise price of the shares covered by the exercised portion of the SAR. The Compensation Committee determines the terms of SARs, including the exercise price (provided that such per share exercise price cannot be less than the fair market value of a share of our common stock on the date of grant), the vesting and the term of the SAR. Settlement of a SAR may be in shares of common stock or in cash, or any combination thereof, as the Compensation Committee may determine. SARs may not be repriced or exchanged without stockholder approval.

Restricted Stock. A restricted stock award is the grant of shares of our common stock to a selected participant and such shares may be subject to a substantial risk of forfeiture until specific conditions or goals are met. The restricted shares may be issued with or without cash consideration being paid by the selected participant as determined by the Compensation Committee. The Compensation Committee also will determine any other terms and conditions of an award of restricted stock.

RSUs. RSUs are the right to receive an amount equal to the fair market value of the shares covered by the RSU at some future date after the grant. The Compensation Committee will determine all of the terms and conditions of an award of RSUs. Payment for vested RSUs may be in shares of common stock or in cash, or any combination thereof, as the Compensation Committee may determine. RSUs represent an unfunded and unsecured obligation for us, and a holder of a stock unit has no rights other than those of a general creditor.

Other Awards. The 2020 Plan also provides that other equity awards, which derive their value from the value of our shares or from increases in the value of our shares, may be granted. In addition, cash awards may also be issued. Substitute awards may be issued under the 2020 Plan in assumption of or substitution for or exchange for awards previously granted by an entity which we may acquire.

Limited Transferability of Awards. Awards granted under the 2020 Plan generally are not transferrable other than by will or by the laws of descent and distribution. However, the Compensation Committee may in its discretion permit the transfer of awards other than ISOs.

Change in Control. In the event that we are a party to a merger or other reorganization or similar transaction, outstanding 2020 Plan awards will be subject to the agreement pertaining to such merger or reorganization. Such agreement may provide for (i) the continuation of the outstanding awards by us if we are a surviving corporation, (ii) the assumption or substitution of the outstanding awards by the surviving entity or its parent, (iii) full exercisability and/or full vesting of outstanding awards, or (iv) cancellation of outstanding awards either with or without consideration, in all cases with or without consent of the selected participant. The Compensation Committee will decide the effect of a change in control of us on outstanding awards.

Amendment and Termination of the 2020 Plan. The Board of Directors generally may amend or terminate the 2020 Plan at any time and for any reason, except that it must obtain stockholder approval of material amendments to the extent required by applicable laws, regulations or rules.

ITEM 12. SECURITY OWNERSHIP OF CERTAIN BENEFICIAL OWNERS AND MANAGEMENT AND RELATED STOCKHOLDER MATTERS

The table set forth below presents certain information regarding beneficial ownership of our common stock (the only class of our voting equity securities issued and outstanding) as of March 11, 2022 by (i) each person or entity who is known by us to own beneficially more than 5% of our outstanding shares of common stock, (ii) each of our directors, and (iii) all of our directors and executive officers as a group. As of March 11, 2022, there were 13,746,593 shares of our common stock issued and outstanding. In computing the number and percentage of shares beneficially owned by a person, shares of common stock that a person has a right to acquire within sixty (60) days of March 11, 2022 pursuant to stock options, warrants, convertible preferred stock or other rights are counted as outstanding, while these shares are not counted as outstanding for computing the percentage ownership of any other person. This table is based upon information supplied by our directors, officers and principal stockholders and reports filed with the Securities and Exchange Commission.

Name and Address of Beneficial Owner	Amount and Nature of Beneficial Ownership	Percent of Class
Officers and Directors		
Dr. John S. Kovach 608 East Colorado Boulevard, Suite 180 Pasadena, California 91101	1,561,284(1)	11.3%
Dr. Philip F. Palmedo 608 East Colorado Boulevard, Suite 180		

Pasadena, California 91101	432,275(2)	3.1%
Dr. Stephen J. Forman 608 East Colorado Boulevard, Suite 180 Pasadena, California 91101	216,690(3)	1.6%
Dr. Yun Yen 608 East Colorado Boulevard, Suite 180 Pasadena, California 91101	234,430(13)	1.7%
Gil Schwartzberg 608 East Colorado Boulevard, Suite 180 Pasadena, California 91101	2,324,360(6)	15.6%
Regina Brown 608 East Colorado Boulevard, Suite 180 Pasadena, California 91101	209,375(12)	1.5%
Robert Weingarten 608 East Colorado Boulevard, Suite 180 Pasadena, California 91101	29,166(14)	0.2%
Eric J. Forman 608 East Colorado Boulevard, Suite 180 Pasadena, California 91101	104,430(5)	0.8%
Dr. James S. Miser 608 East Colorado Boulevard, Suite 180 Pasadena, California 91101	41,667(15)	0.3%
All officers and directors as a group (nine persons)	6,153,677	32.8%
Other Stockholders Owning More Than 5%		
John and Barbara Kovach 2015 Trust Glenn L. Krinsky, Trustee 608 East Colorado Boulevard, Suite 180 Pasadena, California 91101	1,333,333(4)	9.7%
Dr. Debbie Schwartzberg 5500 Military Trail, Suite 22, Box 356 Jupiter, Florida 33458	1,645,807(7)	11.4%
Dr. Arthur and Jane Riggs 4852 Saint Andres Avenue La Verne, California 91750	1,957,500(8)	13.3%
Robert and Susan Greenberg 228 Manhattan Beach Boulevard Manhattan Beach, California 90266	1,380,264(9)	9.8%
Lalit R. Bahl and Kavit K. Kinra 3 Pheasant Run Setauket, New York 11733	1,000,000(16)	7.2%
Lawrence J. Goldstein 1865 Palmer Avenue Larchmont, New York 10538	666,668(10)	4.7%
Hung Tak Ho Mayfair by the Sea II Tower T8, 1/F, Unit A 21 Fo Chun Road Pak ShekKok Taipo NT, Hong Kong SAR	1,084,210(11)	7.9%
Glenn L. Krinsky 608 East Colorado Boulevard, Suite 180 Pasadena, California 91101	1,474,988(17)	10.7%

(1) Includes 1,540,184 shares of common stock and stock warrants to purchase 21,100 shares of common stock owned as of record by the John S. Kovach Trust. Dr. Kovach is a co-trustee of the Trust and has the exclusive right to control the investment of the assets of the Trust.

(2) Includes 183,333 shares of common stock and stock warrants to purchase 16,667 shares of common stock owned by the Philip Palmedo Partnership, and 107,056 shares of common stock, stock warrants to purchase 21,053 shares of common stock and stock options to purchase 104,166 shares of common stock owned by Dr. Philip Palmedo. Dr. Palmedo, as the general partner of the Philip Palmedo Partnership, has voting, dispositive and investment control with respect to the common stock and common stock warrants owned by the partnership. All stock options and common stock warrants are immediately exercisable or within 60 days.

(3) Includes 58,137 shares of common stock, stock warrants to purchase 21,053 shares of common stock and stock options to purchase 104,166 shares of common stock which are immediately exercisable or within 60 days, owned by Dr. Stephen Forman. Also includes 16,667 shares of common stock and stock warrants to purchase 16,667 shares of common stock owned by the Stephen Forman Living Trust dated 12/16/98. Stephen Forman is trustee of the trust and holds voting and dispositive power over the common

stock and common stock warrants owned by the trust.

(4) Includes 1,333,333 shares of common stock transferred by John Kovach and his wife, Barbara C.H. Kovach, as grantors, to the John and Barbara Kovach 2015 Trust, an irrevocable trust dated July 6, 2015. The primary beneficiaries of the trust are the two adult daughters of John and Barbara Kovach. Eric J. Forman is the trustee of the John and Barbara Kovach 2015 Trust.

(5) Includes 38,598 shares of common stock, stock warrants to purchase 3,333 shares of common stock and stock options to purchase 62,500 shares of common stock owned by Eric J. Forman. Eric Forman is the husband of Julie (Schwartzberg) Forman, and the son-in-law of Gil and Debbie Schwartzberg. All stock options and common stock warrants are immediately exercisable or within 60 days.

Excludes the following:

- 186,667 shares of common stock, stock options to purchase 291,666 shares of common stock and common stock warrants to purchase 83,333 of common stock owned by the Julie Schwartzberg Trust, as to which Julie (Schwartzberg) Forman is the beneficiary, and as to which Eric Forman disclaims beneficial ownership or control.
- 33,333 shares of common stock owned by the Julie Forman 2015 Trust, the beneficiary of which is Cole Forman, the son of Eric and Julie Forman, as to which David Sterling, as trustee, has voting, dispositive and investment control.
- 16,667 shares of common stock owned by each of the Savannah Sterling Trust, Amanda Sterling Trust, Daniel Sterling Trust and Charles Sterling Trust, as to which Julie Forman is the trustee.

(6) Includes 343,926 shares of common stock owned by the Gil & Debbie Schwartzberg Family Trust dated November 19, 2003, Gil Schwartzberg Separate Property, as to which Gil Schwartzberg, as trustee, has voting, dispositive and investment control, stock warrants to purchase 105,264 shares of common stock and stock options to purchase 292,709 shares of common stock owned by Gil Schwartzberg. All stock options and common stock warrants are immediately exercisable or within 60 days.

Also includes the following:

- 247,775 shares of common stock owned by the Gil Schwartzberg IRA;
- 106,353 shares of common stock owned by Continuum Capital Partners, LP, as to which Gil Schwartzberg has sole voting, dispositive and investment control;
- 186,667 shares of common stock, stock options to purchase 291,666 shares of common stock and common stock warrants to purchase 83,333 shares of common stock owned by the Julie Schwartzberg Trust, as to which Gil Schwartzberg is the co-trustee;
- 191,667 shares of common stock, stock options to purchase 291,666 shares of common stock and common stock warrants to purchase 83,333 shares of common stock owned by the David N. Sterling Trust, as to which Gil Schwartzberg is the co-trustee;
- 16,667 shares of common stock owned by each of the Savannah Sterling Trust, Amanda Sterling Trust, Daniel Sterling Trust and Charles Sterling Trust, as to which Julie Forman is the trustee;
- 33,333 shares of common stock owned by the Julie Forman 2015 Trust, David Sterling trustee.

Excludes the following:

- 417,474 shares of common stock owned by the Gil & Debbie Schwartzberg Family Trust dated November 19, 2003, Debbie Schwartzberg Separate Property, the wife of Gil Schwartzberg, as to which Gil Schwartzberg disclaims beneficial ownership or control.

(7) Includes 417,474 shares of common stock owned by the Gil & Debbie Schwartzberg Family Trust dated November 19, 2003, Debbie Schwartzberg Separate Property, as to which Debbie Schwartzberg, as trustee, has voting, dispositive and investment control. All stock options and common stock warrants are immediately exercisable or within 60 days.

Also includes the following:

- 186,667 shares of common stock, stock options to purchase 291,666 shares of common stock and common stock warrants to purchase 83,333 shares of common stock owned by the Julie Schwartzberg Trust, as to which Debbie Schwartzberg is the co-trustee;
- 191,667 shares of common stock, stock options to purchase 291,666 shares of common stock and common stock warrants to purchase 83,333 shares of common stock owned by the David N. Sterling Trust, as to which Debbie Schwartzberg is the co-trustee;
- 16,667 shares of common stock owned by each of the Savannah Sterling Trust, Amanda Sterling Trust, Daniel Sterling Trust and Charles Sterling Trust, as to which Julie Forman is the trustee;
- 33,333 shares of common stock owned by the Julie Forman 2015 Trust, David Sterling trustee.

Excludes the following:

- 375,926 shares of common stock and stock options to purchase 292,709 shares of common stock owned by the Gil & Debbie Schwartzberg Family Trust dated November 19, 2003, Gil Schwartzberg Separate Property, as to which Debbie Schwartzberg, the wife of Gil Schwartzberg, disclaims beneficial ownership or control;
- 215,775 shares of common stock owned by the Gil Schwartzberg IRA;
- 106,353 shares of common stock owned by Continuum Capital Partners, LP, as to which Gil Schwartzberg has sole voting, dispositive and investment control.

(8) Includes 1,018,333 shares of common stock, 729,167 shares of common stock issuable upon conversion of 350,000 shares of Series A Convertible Preferred Stock, and common stock warrants to purchase 210,000 shares of common stock owned by the Arthur and Jane Riggs 1990 Revocable Trust. Arthur Riggs and his wife, Jane Riggs, are co-trustees of the trust and share voting and dispositive power over the shares of preferred stock. The shares of Series A Convertible Preferred Stock were acquired on March 17, 2015 and January 15, 2016, are non-voting, and are immediately convertible into common stock.

(9) Consists of 994,299 shares of common stock and common stock warrants to purchase 385,965 shares of common stock owned by the Greenberg Family Trust dated May 3, 1988. The trust is a revocable trust, and Arthur Greenberg and his wife, Susan Greenberg, are co-trustees of the trust and share voting and dispositive power over the shares of common stock.

(10) Includes 166,667 shares of common stock and stock warrants to purchase 166,667 shares of common stock owned by Lawrence J. Goldstein. Also includes 166,667 shares of common stock and stock warrants to purchase 166,667 shares of common stock owned by the Santa Monica Partners, L.P. Lawrence J. Goldstein is the sole managing member of the general partner, SMP Asset Management LLC.

(11) Includes 1,042,105 shares of common stock and stock warrants to purchase 42,105 shares of common stock. Excludes stock options to purchase shares of common stock owned by Dr. Winson Sze Chun Ho, a former director of of the Company, and the son of Hung Tak Ho, as to which Hung Tak Ho disclaims beneficial ownership or control.

(12) Includes stock options to purchase 209,375 shares of common stock.

(13) Includes 52,632 shares of common stock, stock warrants to purchase 52,632 shares of common stock and stock options to purchase 129,163 shares of common stock which are immediately exercisable or within 60 days.

(14) Consists of stock options to purchase 26,166 shares of common stock which are immediately exercisable or within 60 days.

(15) Consists of stock options to purchase 41,667 shares of common stock which are immediately exercisable or within 60 days.

(16) Includes 833,333 shares of common stock and stock warrants to purchase 166,667 shares of common stock.

(17) Includes 141,655 shares of common stock owned by Glenn L. Krinsky. Also includes 1,333,333 shares of common stock owned by the John and Barbara Kovach 2015 Trust, as to which Glenn L. Krinsky, as trustee, has voting, dispositive and investment control.

ITEM 13. CERTAIN RELATIONSHIPS AND RELATED PARTY TRANSACTIONS, AND DIRECTOR INDEPENDENCE

(a) Related Party Transactions

During the years ended December 31, 2019, 2020 and 2021, there have been no transactions, whether directly or indirectly, between the Company and any of its officers, directors or affiliates, including their family members, except as described herein or elsewhere in this document.

(b) Director Independence

The Company considers Dr. Philip Palmedo, Dr. Stephen Forman, Dr. Yun Yen, Gil Schwartzberg and Regina Brown to each be an "independent director," as defined under Nasdaq rules and by Rule 10-A-3 of the Exchange Act.

ITEM 14. PRINCIPAL ACCOUNTING FEES AND SERVICES

Weinberg & Company, P.C. acted as our independent registered public accounting firm for the fiscal years ended December 31, 2020 and 2021 and for the interim periods in such fiscal years. The following table shows the fees that were incurred by us for audit and other services provided by Weinberg & Company, P.C for the years ended December 31, 2020 and 2021.

	Years Ended December 31,	
	2020	2021
Audit Fees[1]	$ 78,567	$ 93,681
Audit-Related Fees[2]	—	—
Tax Fees[3]	14,134	28,140
Other Fees[4]	71,537	25,200
Total	$ 164,238	$ 147,021

(1) Audit fees represent fees for professional services provided in connection with the audit of our annual financial statements included in our Annual Reports on Form 10-K and the review of our interim financial statements included in our Quarterly Reports on Form 10-Q and services that are normally provided in connection with statutory or regulatory filings, excluding those fees included in Other Fees.

(2) Audit-related fees represent fees for assurance and related services that are reasonably related to the performance of the audit or review of our financial statements and not reported above under "Audit Fees."

(3) Tax fees represent fees for professional services related to tax compliance, tax advice and tax planning.

(4) Other fees represent fees incurred with respect to our Registration Statements on Forms S-1, S-3 and S-8 declared effective by the SEC during the years ended December 31, 2020 and 2021.

All audit and audit-related services, tax services and other services rendered by Weinberg & Company, P.C. during the fiscal years ended December 31, 2020 and 2021 were pre-approved by either our Audit Committee or by our Board of Directors. The Board of Directors has adopted a pre-approval policy that provides for the pre-approval of all services performed for us by our independent registered public accounting firm.

PART IV

ITEM 15. EXHIBITS AND FINANCIAL STATEMENT SCHEDULES

(a) List of documents filed as part of this report:

(1) Financial Statements

Reference is made to the Index to Consolidated Financial Statements on page F-1, where these documents are listed.

(2) Financial Statement Schedules

The financial statement schedules have been omitted because the required information is not applicable, or not present in amounts sufficient to require submission of the schedules, or because the information is included in the financial statements or notes thereto.

(3) Exhibits

See (b) below.

(b) Exhibits:

A list of exhibits required to be filed as part of this Annual Report on Form 10-K is set forth in the Index to Exhibits, which is presented elsewhere in this document, and is incorporated herein by reference.

ITEM 16. FORM 10-K SUMMARY

None

INDEX TO EXHIBITS

Exhibit Number	Description of Document
1.1	Form of Underwriter Agreement[22]
2.1	Share Exchange Agreement dated as of June 8, 2006 among the Company, John S. Kovach and Lixte Biotechnology, Inc.[1]
3.1	Certificate of Incorporation, as filed with the Delaware Secretary of State on May 24, 2005[2]
3.2	Certificate of Amendment of Certificate of Incorporation[3]
3.3	Certificate of Designations for the Company's Series A Convertible Preferred Stock[6]
3.4	Certificate of Amendment of Certificate of Designations of the Series A Convertible Preferred Stock[8]
3.6	Amended and Restated Bylaws[15]
3.7	Certificate of Amendment of Certificate of Incorporation[23]
4.1	Form of Warrant included in Unit[22]
4.2	Form of Warrant Agent Agreement[22]
4.3	Description of Registrant's Securities Registered Pursuant to Section 12 of the Securities Exchange Act of 1934, as amended[21]
10.1	Master Agreement between Lixte Biotechnology Holdings, Inc. and Theradex Systems, Inc. dated January 12, 2010[4]
10.2	Materials Cooperative Research and Development Agreement between Lixte Biotechnology Holdings, Inc. and the National Institute of Neurological Disorders and Stroke dated October 18, 2013[5]
10.3	Scientific Advisory Board Agreement between Lixte Biotechnology Holdings, Inc. and NDA Consulting Corp. dated December 24, 2013[5]
10.4	Collaboration Agreement between Lixte Biotechnology Holdings, Inc. and BioPharmaWorks LLC effective September 14, 2015[7]
10.5	Form of First Warrant to purchase common stock issued to BioPharmaWorks LLC dated September 14, 2015[7]
10.6	Form of Second Warrant to purchase common stock issued to BioPharmaWorks LLC dated September 14, 2015[7]
10.7	Clinical Trial Research Agreement between H. Lee Moffitt Cancer Center and Research Institute Hospital, Inc. and Lixte Biotechnology Holdings, Inc. dated and effective as of August 20, 2018[9]
10.8	Exclusive License Agreement between H. Lee Moffitt Cancer Center and Research Institute Hospital, Inc. and Lixte Biotechnology Holdings, Inc. dated and effective as of August 20, 2018 (certain portions of this exhibit have been omitted based on a request for confidential treatment filed by the Company with the Securities and Exchange Commission that was granted on September 17, 2018)[9]
10.9	Form of Warrant to Purchase Common Stock of Llxte Biotechnology Holdings, Inc. (issued in connection with common stock unit rights offering that closed on November 30, 2018)[10]
10.10	Collaboration Agreement for an Investigator-Initiated Clinical Trial between Lixte Biotechnology Holdings, Inc. and the Spanish Sarcoma Group as of July 31, 2019 (certain portions of this exhibit have been omitted based on a request for confidential treatment filed by the Company with the Securities and Exchange Commission that was granted on September 19, 2019)[11]
10.11	Employment Agreement Between the Company and Dr. James Miser[13+]
10.12	Employment Agreement Between the Company and Robert N. Weingarten[17+]
10.13	Employment Agreement Between the Company and Dr. John Kovach[14+]
10.14	Employment Agreement Between the Company and Eric Forman[15+]
10.15	2020 Stock Incentive Plan[16+]
10.16	Master Services Agreement between Foundation for Angelman Syndrome Therapeutics ("FAST") and Lixte Biotechnology Holdings, Inc. dated as of August 12, 2020[17]
10.17	Clinical Trial Research Agreement between the Company and the City of Hope National Medical Center[18]
10.18	Amendment to Employment Agreement between the Company and Eric Forman[22+]
10.19	Development Collaboration Agreement by and between Lixte Biotechnology Holdings, Inc. and the Netherlands Cancer Institute, Amsterdam, and Oncode Institute, Utrecht, entered into on October 8, 2021 (certain portions of this Exhibit have been omitted based on a pending request for confidential treatment being filed with the Securities and Exchange Commission).[23]
21.1	Subsidiaries of the Registrant*
23.1	Consent of Weinberg & Company, P.A., Independent Registered Public Accounting Firm*
31.1	Officer's Certification Pursuant to Section 302 of the Sarbanes-Oxley Act of 2002*
31.2	Officer's Certification Pursuant to Section 302 of the Sarbanes-Oxley Act of 2002*
32.1	Officer's Certification Pursuant to Section 906 of the Sarbanes-Oxley Act of 2002*
32.2	Officer's Certification Pursuant to Section 906 of the Sarbanes-Oxley Act of 2002*
101.INS	Inline XBRL Instance Document (does not appear in the Interactive Data File because its XBRL tags are embedded within the Inline XBRL document)
101.SCH	Inline XBRL Taxonomy Extension Scheme Document
101.CAL	Inline XBRL Taxonomy Extension Calculation Linkbase Document
101.LAB	Inline XBRL Taxonomy Extension Label Linkbase Document
101.PRE	Inline XBRL Taxonomy Extension Presentation Linkbase Document
101.DEF	Inline XBRL Taxonomy Extension Definition Linkbase Document
104	Cover Page Interactive Data File (formatted as Inline XBRL document and included in Exhibit 101.INS)

1 Filed as an Exhibit to the Company's Current Report on Form 8-K, as filed with the Securities and Exchange Commission on July 7, 2006 and incorporated herein by reference.

2 Filed as an Exhibit to the Company's Registration Statement on Form 10-SB, as filed with the Securities and Exchange Commission on August 3, 2005 and incorporated herein by reference.

3 Filed as Appendix A to the Company's Information Statement, as filed with the Securities and Exchange Commission on September 20, 2006 and incorporated herein by reference.

4 Filed as an Exhibit to the Company's Annual Report on Form 10-K, as filed with the Securities and Exchange Commission on March 15, 2013 and incorporated herein by reference.

5 Filed as an Exhibit to the Company's Annual Report on Form 10-K, as filed with the Securities and Exchange Commission on March 21, 2014 and incorporated herein by reference.

6 Filed as an Exhibit to the Company's Current Report on Form 8-K, as filed with the Securities and Exchange Commission on March 18, 2015 and incorporated herein by reference.

7 Filed as an Exhibit to the Company's Current Report on Form 8-K, as filed with the Securities and Exchange Commission on September 18, 2015 and incorporated herein by reference.

8 Filed as an Exhibit to the Company's Annual Report on Form 10-K, as filed with the Securities and Exchange Commission on March 28, 2016 and incorporated herein by reference.

9 Filed as an Exhibit to the Company's Current Report on Form 8-K, as filed with the Securities and Exchange Commission on August 23, 2018 and incorporated herein by reference.

10 Filed as an Exhibit to the Company's Current Report on Form 8-K, as filed with the Securities and Exchange Commission on December 5, 2018 and incorporated herein by reference.

11 Filed as an Exhibit to the Company's Current Report on Form 8-K, as filed with the Securities and Exchange Commission on August 6, 2019 and incorporated herein by reference.

12 Filed as an Exhibit to the Company's Current Report on Form 8-K, as filed with the Securities and Exchange Commission on July 17, 2020 and incorporated herein by reference.

13 Filed as an Exhibit to the Company's Current Report on Form 8-K, as filed with the Securities and Exchange Commission on July 17, 2020 and incorporated herein by reference.

14 Filed as an Exhibit to the Company's Current Report on Form 8-K, as filed with the Securities and Exchange Commission on July 17, 2020 and incorporated herein by reference.

15 Filed as an Exhibit to the Company's Current Report on Form 8-K, as filed with the Securities and Exchange Commission on July 17, 2020 and incorporated herein by reference.

16 Filed as an Exhibit to the Company's Current Report on Form 8-K, as filed with the Securities and Exchange Commission on July 17, 2020 and incorporated herein by reference.

17 Filed as an Exhibit to the Company's Current Report on Form 8-K, as filed with the Securities and Exchange Commission on August 18, 2020 and incorporated herein by reference.

18 Filed as an Exhibit to the Company's Current Report on Form 8-K, as filed with the Securities and Exchange Commission on January 22, 2021 and incorporated herein by reference.

19 Filed as an Exhibit to the Company's Registration Statement on Form S-1/A, as filed with the Securities and Exchange Commission on November 16, 2020.

20 Filed as an Exhibit to the Company's Current Report on Form 8-K, as filed with the Securities and Exchange Commission on November 27, 2020 and incorporated herein by reference.

21 Filed as an Exhibit to the Company's Annual Report on Form 10-K, as filed with the Securities and Exchange Commission on March 25, 2020 and incorporated herein by reference.

22 Filed as an Exhibit to the Company's Annual Report on Form 10-K, as filed with the Securities and Exchange Commission on March 26, 2021 and incorporated herein by reference.

23 Filed as an Exhibit to the Company's Quarterly Report on Form 10-Q, as filed with the Securities and Exchange Commission on November 10, 2021 and incorporated herein by reference.

* Filed herewith.

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

SIGNATURES

In accordance with Section 13 and 15(d) of the Securities Exchange Act of 1934, the Registrant caused this report to be signed on its behalf by the undersigned thereunto duly authorized.

Date: March 21, 2022

LIXTE BIOTECHNOLOGY HOLDINGS, INC.
(Registrant)

By: */s/ JOHN S. KOVACH*

Name: John S. Kovach
Title: President and Chief Executive Officer

In accordance with the Securities Exchange Act of 1934, this Report has been signed below by the following persons on behalf of the Registrant in the capacity and on the dates indicated.

Signature	Title	Date
/s/ JOHN S. KOVACH John S. Kovach	President and Chief Executive Officer	March 21, 2022
/s/ ROBERT N. WEINGARTEN Robert N. Weingarten	Vice President and Chief Financial Officer	March 21, 2022
/s/ PHILIP F. PALMEDO Philip F. Palmedo	Director	March 21, 2022
/s/ STEPHEN J. FORMAN Stephen J. Forman	Director	March 21, 2022
/s/ GIL N SCHWARTZBERG Gil N Schwartzberg	Director	March 21, 2022
/s/ YUN YEN Yun Yen	Director	March 21, 2022
/s/ REGINA BROWN Regina Brown	Director	March 21, 2022

LIXTE BIOTECHNOLOGY HOLDINGS, INC.
AND SUBSIDIARY

INDEX TO CONSOLIDATED FINANCIAL STATEMENTS
(INCLUDING REPORT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM)

Years Ended December 31, 2021 and 2020

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REPORT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

To the Board of Directors and Stockholders
Lixte Biotechnology Holdings, Inc.
Pasadena, California

Opinion on the Consolidated Financial Statements

We have audited the accompanying consolidated balance sheets of Lixte Biotechnology Holdings, Inc. and subsidiary (the "Company") as of December 31, 2021 and 2020, and the related consolidated statements of operations, stockholders' equity and cash flows for the years then ended, and the related notes (collectively referred to as the "consolidated financial statements"). In our opinion, the consolidated financial statements present fairly, in all material respects, the consolidated financial position of the Company as of December 31, 2021 and 2020, and the results of its consolidated operations and its consolidated cash flows for the years then ended, in conformity with accounting principles generally accepted in the United States of America.

Going Concern

The accompanying consolidated financial statements have been prepared assuming that the Company will continue as a going concern. As discussed in Note 1 to the consolidated financial statements, the Company has no recurring source of revenue and has experienced negative operating cash flows since inception. The Company has financed its working capital requirements primarily through the recurring sale of its equity securities. These matters raise substantial doubt about the Company's ability to continue as a going concern. Management's plans in regard to these matters are also described in Note 1 to the consolidated financial statements. These consolidated financial statements do not include any adjustments that might result from the outcome of this uncertainty.

Basis for Opinion

These consolidated financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on the Company's consolidated financial statements based on our audits. We are a public accounting firm registered with the Public Company Accounting Oversight Board (United States) (the "PCAOB") and are required to be independent with respect to the Company in accordance with the U.S. federal securities laws and the applicable rules and regulations of the Securities and Exchange Commission (the "SEC") and the PCAOB.

We conducted our audits in accordance with the standards of the PCAOB. Those standards require that we plan and perform the audits to obtain reasonable assurance about whether the financial statements are free of material misstatement, whether due to error or fraud. The Company is not required to have, nor were we engaged to perform, an audit of its internal control over financial reporting. As part of our audits, we are required to obtain an understanding of internal control over financial reporting, but not for the purpose of expressing an opinion on the effectiveness of the Company's internal control over financial reporting. Accordingly, we express no such opinion.

Our audits included performing procedures to assess the risks of material misstatement of the financial statements, whether due to error or fraud, and performing procedures that respond to those risks. Such procedures included examining, on a test basis, evidence regarding the amounts and disclosures in the financial statements. Our audits also included evaluating the accounting principles used and significant estimates made by management, as well as evaluating the overall presentation of the financial statements. We believe that our audits provide a reasonable basis for our opinion.

Critical Audit Matter Description

The critical audit matter communicated below is a matter arising from the current period audit of the financial statements that was communicated or required to be communicated to the audit committee and that (1) relates to accounts or disclosures that are material to the financial statements and (2) involved especially challenging, subjective, or complex judgments. The communication of critical audit matters does not alter in any way our opinion on the consolidated financial statements, taken as a whole, and we are not, by communicating the critical audit matters below, providing separate opinions on the critical audit matters or on the accounts or disclosures to which they relate.

As discussed in Note 5 to the consolidated financial statements, the Company issues equity awards to certain officers, employees and consultants as compensation (the "Equity Awards"). The fair values of these Equity Awards were determined as of the grant date using a Black-Scholes option-pricing model (the "Black-Scholes Model"). The selection of the valuation methodology and assumptions utilized in the Black-Scholes Model are based, in part, upon assumptions for which management is required to use judgment, particularly the risk-free interest rate, volatility, and dividend yield.

We identified the valuation of the Equity Awards as a critical audit matter because of the significant judgments made by management to determine the grant date fair values. This required a high degree of auditor judgment and an increased expenditure of effort when performing audit procedures to evaluate the reasonableness of management's valuation methodology and related assumptions, including the risk-free interest rate, volatility, and dividend yield.

Our audit procedures related to the determination of the fair values of the Equity Awards, including the valuation methodology and related assumptions such as the risk-free interest rate, volatility, and dividend yield, consisted of the following, among others:

- We obtained an understanding of management's process over the valuation of the Equity Awards, including those over the determination of the valuation methodology and related assumptions, including the risk-free interest rate, volatility, and dividend yield.
- We obtained and read the Equity Award agreements and management's valuation analyses, including supporting schedules and related narrative information.
- We evaluated management's valuation methodology, including the selection of the model to determine the fair values of the Equity Awards.
- We evaluated the reasonableness of management's valuation assumptions and the underlying source information of significant valuation assumptions, including the risk-free interest rate, volatility, and dividend yield.
- We assessed whether management's calculations of the fair values were applied in accordance with the selected methodology, including testing the mathematical accuracy of the valuation analyses.
- We developed independent estimates for the fair values of the Equity Awards based on assumptions utilized by the Company in its calculations.

We have served as the Company's auditor since 2008.

/s/ Weinberg & Company, P.A.

Los Angeles, California
March 21, 2022

LIXTE BIOTECHNOLOGY HOLDINGS, INC.
AND SUBSIDIARY

CONSOLIDATED BALANCE SHEETS

	December 31,	
	2021	**2020**
ASSETS		
Current assets:		
Cash	$ 4,823,745	$ 5,069,266
Advances on research and development contract services	150,241	76,898
Prepaid insurance	109,029	67,311
Other prepaid expenses and current assets	10,249	15,000
Total current assets	5,093,264	5,228,475
Total assets	$ 5,093,264	$ 5,228,475
LIABILITIES AND STOCKHOLDERS' EQUITY		
Current liabilities:		
Accounts payable and accrued expenses, including $32,500 and $0 to related parties at December 31, 2021 and 2020, respectively	$ 225,965	$ 190,292
Accrued offering costs	—	10,467
Research and development contract liabilities	76,961	15,765
Total current liabilities	302,926	216,524

Commitments and contingencies		
Stockholders' equity:		
Preferred Stock, $0.0001 par value; authorized – 10,000,000 shares; issued and outstanding – 350,000 shares of Series A Convertible Preferred Stock, $10.00 per share stated value, liquidation preference based on assumed conversion into common shares – 729,167 shares	3,500,000	3,500,000
Common stock, $0.0001 par value; authorized – 100,000,000 shares; issued and outstanding – 13,746,593 shares and 12,402,157 shares at December 31, 2021 and 2020, respectively	1,374	1,240
Additional paid-in capital	38,371,128	31,864,479
Accumulated deficit	(37,082,164)	(30,353,768)
Total stockholders' equity	4,790,338	5,011,951
Total liabilities and stockholders' equity	$ 5,093,264	$ 5,228,475

See accompanying notes to consolidated financial statements.

LIXTE BIOTECHNOLOGY HOLDINGS, INC.
AND SUBSIDIARY

CONSOLIDATED STATEMENTS OF OPERATIONS

	Years Ended December 31,	
	2021	**2020**
Revenues	$ —	$ —
Costs and expenses:		
General and administrative costs:		
Compensation to related parties, including stock-based compensation of $2,201,280 and $480,634 for the years ended December 31, 2021 and 2020, respectively	2,931,280	765,085
Patent and licensing legal and filing fees and costs	729,171	553,173
Other	1,323,218	724,506
Research and development costs, including $397,642 and $670,715 of stock-based compensation costs to a consultant for the years ended December 31, 2021 and 2020, respectively	1,736,776	1,223,676
Total costs and expenses	6,720,445	3,266,440
Loss from operations	(6,720,445)	(3,266,440)
Interest income	626	4,342
Interest expense	(7,414)	(3,674)
Foreign currency gain (loss)	(1,163)	890
Net loss	$ (6,728,396)	$ (3,264,882)
Net loss per common share – basic and diluted	$ (0.50)	$ (0.29)
Weighted average common shares outstanding – basic and diluted	13,473,839	11,277,126

See accompanying notes to consolidated financial statements.

LIXTE BIOTECHNOLOGY HOLDINGS, INC.
AND SUBSIDIARY

CONSOLIDATED STATEMENTS OF STOCKHOLDERS' EQUITY

Years Ended December 31, 2021 and 2020

	Series A Convertible Preferred Stock		Common Stock		Additional Paid-in	Accumulated	Total Stockholders'
	Shares	**Amount**	**Shares**	**Par Value**	**Capital**	**Deficit**	**Equity**
Balance, December 31, 2019	350,000	$ 3,500,000	11,174,737	$ 1,117	$ 26,021,904	$ (27,088,886)	$ 2,434,135
Proceeds from sale of common stock units in public offering, net of offering costs	—	—	1,200,000	120	4,591,229	—	4,591,349
Stock-based compensation expense, including $670,715 for extension of stock options	—	—	—	—	1,151,349	—	1,151,349
Common stock issued for services	—	—	27,420	3	99,997	—	100,000
Net loss	—	—	—	—	—	(3,264,882)	(3,264,882)
Balance, December 31, 2020	350,000	3,500,000	12,402,157	1,240	31,864,479	(30,353,768)	5,011,951
Proceeds from sale of common stock in direct equity offering, net of offering costs	—	—	1,133,102	113	3,689,648	—	3,689,761
Exercise of warrants			3,000	1	17,099	—	17,100
Exercise of options	—	—	208,334	20	200,980	—	201,000
Stock-based compensation expense	—	—	—	—	2,598,922	—	2,598,922
Net loss	—	—	—	—	—	(6,728,396)	(6,728,396)
Balance, December 31, 2021	350,000	$ 3,500,000	13,746,593	$ 1,374	$ 38,371,128	$ (37,082,164)	$ 4,790,338

See accompanying notes to consolidated financial statements.

LIXTE BIOTECHNOLOGY HOLDINGS, INC.
AND SUBSIDIARY

CONSOLIDATED STATEMENTS OF CASH FLOWS

	Years Ended December 31,	
	2021	**2020**
Cash flows from operating activities:		
Net loss	$ (6,728,396)	$ (3,264,882)
Adjustments to reconcile net loss to net cash used in operating activities:		
Stock-based compensation expense included in -		
General and administrative costs	2,201,280	580,634
Research and development costs	397,642	670,715
Changes in operating assets and liabilities:		
(Increase) decrease in -		
Advances on research and development contract services	(73,343)	(76,898)
Accrued interest receivable	—	14,367
Prepaid insurance	(41,718)	(32,803)
Other prepaid expenses and current assets	4,751	9,294
Increase (decrease) in -		
Accounts payable and accrued expenses	35,673	46,743
Research and development contract liabilities	61,196	(78,584)
Net cash used in operating activities	(4,142,915)	(2,131,414)
Cash flows from financing activities:		
Proceeds from sale of common stock units in public offering, net of offering costs	—	4,601,816
Proceeds from sale of common stock in direct equity offering, net of offering costs	3,689,761	—
Exercise of common stock warrants	17,100	—
Exercise of common stock options	201,000	—
Payment of costs incurred in connection with sale of common stock units	(10,467)	—
Net cash provided by financing activities	3,897,394	4,601,816
Cash:		
Net increase (decrease)	(245,521)	2,470,402
Balance at beginning of period	5,069,266	2,598,864
Balance at end of period	$ 4,823,745	$ 5,069,266
Supplemental disclosures of cash flow information:		
Cash paid for -		
Interest	$ 7,414	$ 3,674
Income taxes	$ —	$ —
Non-cash investing and financing activities:		
Accrued offering costs (paid subsequent to December 31, 2020)	$ —	$ 10,467

See accompanying notes to consolidated financial statements.

LIXTE BIOTECHNOLOGY HOLDINGS, INC.
AND SUBSIDIARY

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS

Years Ended December 31, 2021 and 2020

1. Organization and Basis of Presentation

Lixte Biotechnology Holdings, Inc., a Delaware corporation ("Holdings"), including its wholly-owned Delaware subsidiary, Lixte Biotechnology, Inc. ("Lixte") (collectively, 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 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 the Company believes have broad therapeutic potential not only for cancer but also for other debilitating and life-threatening diseases. The Company has developed two classes of drugs for the treatment of cancer, consisting of protein phosphatase inhibitors (PTase-i), designated by us as the LB-100 series of compounds, and histone deacetylase inhibitors (HDACi), designated by us as the LB-200 series of compounds.

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.

The Company's common stock and the warrants issued in the public offering (see Note 3) are traded on The Nasdaq Capital Market under the symbols "LIXT" and. "LIXTW", respectively.

Going Concern

At December 31, 2021, the Company had cash of $4,823,745 available to fund its operations. Because the Company is currently engaged in Phase 2 clinical trials, it is

expected that it will take a significant amount of time and resources to develop any product or intellectual property capable of generating sustainable revenues. Accordingly, the Company's business is unlikely to generate any sustainable operating revenues in the next several years and may never do so. Even if the Company is able to generate revenues through licensing its technologies or through product sales, there can be no assurance that the Company will be able to achieve positive earnings and operating cash flows.

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. The Company has financed its working capital requirements primarily through the recurring sale of its equity securities.

As a result, management has concluded that there is substantial doubt about the Company's ability to continue as a going concern. The Company's independent registered public accounting firm, in its report on the Company's consolidated financial statements for the year ended December 31, 2021, has also expressed substantial doubt about the Company's ability to continue as a going concern. The Company's consolidated financial statements do not include any adjustments that might result from the outcome of this uncertainty.

The Company's ability to continue as a going concern is dependent upon its ability to raise additional equity capital to fund its research and development activities and to ultimately achieve sustainable operating revenues and profitability. The amount and timing of future cash requirements depends on the pace and design of the Company's clinical trial program, which, in turn, depends on the availability of operating capital to fund such activities.

Based on current operating plans, the Company estimates that it will need to raise additional capital to fund its operations, including its various clinical trial commitments, during the quarter ending September 30, 2022. In addition, the Company's operating plans may change as a result of many factors which are currently unknown to the Company, including possible additional clinical trials, and the Company may need additional funds sooner than currently planned.

As market conditions present uncertainty as to the Company's ability to secure additional funds, there can be no assurances that the Company will be able to secure additional financing on acceptable terms, as and when necessary, to continue to conduct operations. There is also significant uncertainty as to the effect that the coronavirus pandemic may have on the Company's clinical trial schedule and the amount and type of financing available to the Company in the future.

If cash resources are insufficient to satisfy the Company's ongoing cash requirements, the Company would be required to scale back or discontinue its clinical trial program, as well as its licensing and patent prosecution efforts and its technology and product development efforts, or obtain funds, if available, through strategic alliances or joint ventures that could require the Company to relinquish rights to and/or control of LB-100, or to discontinue operations entirely.

Reverse Stock Split

On November 18, 2020, the Company effected a 1-for-6 reverse split of its outstanding shares of common stock. No fractional shares were issued in connection with the reverse split, with any fractional shares resulting from the reverse split being rounded up to the nearest whole share.

All share and per share amounts and information presented herein has been retroactively adjusted to reflect the reverse stock split for all periods presented.

2. Summary of Significant Accounting Policies

Principles of Consolidation

The accompanying consolidated financial statements of the Company have been prepared in accordance with United States generally accepted accounting principles ("GAAP") and include the financial statements of Holdings and its wholly owned subsidiary, Lixte. Intercompany balances and transactions have been eliminated in consolidation.

Use of Estimates

The preparation of financial statements in conformity with GAAP requires management to make estimates and assumptions that affect the reported amounts of assets and liabilities at the date of the financial statements and the reported amounts of expenses during the reporting period. Some of those judgments can be subjective and complex, and therefore, actual results could differ materially from those estimates under different assumptions or conditions. Management bases its estimates on historical experience and on various assumptions that are believed to be reasonable in relation to the financial statements taken as a whole under the circumstances, the results of which form the basis for making judgments about the carrying values of assets and liabilities that are not readily apparent from other sources. Management regularly evaluates the key factors and assumptions used to develop the estimates utilizing currently available information, changes in facts and circumstances, historical experience and reasonable assumptions. After such evaluations, if deemed appropriate, those estimates are adjusted accordingly. Actual results could differ from those estimates. Significant estimates include those related to assumptions used in accruals for potential liabilities, valuing equity instruments issued for services, and the realization of deferred tax assets.

Cash

Cash is primarily held in a cash bank deposit program maintained by a major financial institution. The Company's policy is to maintain its cash balances with financial institutions with high credit ratings and in accounts insured by the Federal Deposit Insurance Corporation (the "FDIC") and/or by the Securities Investor Protection Corporation (the "SIPC"). The Company may periodically have cash balances in financial institutions in excess of the FDIC and SIPC insurance limits of $250,000 and $500,000, respectively. The financial institution that currently holds the Company's cash balances also maintains supplemental insurance coverage for its customers' cash balances. The Company has not experienced any losses to date resulting from this practice.

Research and Development

Research and development costs consist primarily of fees paid to consultants and contractors, and other expenses relating to the acquisition, design, development and clinical trials with respect to the Company's compounds and product candidates. Research and development costs also include the costs to produce the compounds used in research and clinical trials, which are charged to operations as incurred.

Research and development costs are generally charged to operations ratably over the life of the underlying contracts, unless the achievement of milestones, the completion of contracted work, the termination of an agreement, or other information indicates that a different expensing schedule is more appropriate. However, payments for research and development costs that are contractually defined as non-refundable are charged to operations as incurred.

Obligations incurred with respect to mandatory scheduled payments under research agreements with milestone provisions are recognized as charges to research and development costs in the Company's consolidated statement of operations based on the achievement of such milestones, as specified in the agreement. Obligations incurred with respect to mandatory scheduled payments under research agreements without milestone provisions are accounted for when due, are recognized ratably over the appropriate period, as specified in the agreement, and are recorded as liabilities in the Company's consolidated balance sheet, with a corresponding charge to research and development

costs in the Company's consolidated statement of operations.

Payments made pursuant to research and development contracts are initially recorded as advances on research and development contract services in the Company's consolidated balance sheet and are then charged to research and development costs in the Company's consolidated statement of operations as those contract services are performed. Expenses incurred under research and development contracts in excess of amounts advanced are recorded as research and development contract liabilities in the Company's consolidated balance sheet, with a corresponding charge to research and development costs in the Company's consolidated statement of operations. The Company reviews the status of its research and development contracts on a quarterly basis.

Prepaid Insurance

Prepaid insurance represents the premiums paid for directors and officers insurance coverage and for general liability insurance coverage in excess of the amortization of the total policy premium charged to operations at each balance sheet date. Such amortization is determined by amortizing the total policy premium charged on a straight-line basis over the respective policy periods. As the policy premiums incurred are amortizable in the ensuing twelve-month period, they are recorded as a current asset in the Company's consolidated balance sheet at each reporting date and amortized to the Company's consolidated statement of operations for each reporting period.

Patent and Licensing Legal and Filing Fees and Costs

Due to the significant uncertainty associated with the successful development of one or more commercially viable products based on the Company's research efforts and related patent applications, all patent and licensing legal and filing fees and costs related to the development and protection of its intellectual property are charged to operations as incurred. Patent and licensing legal and filing fees and costs were $729,171 and $553,173 for the years ended December 31, 2021 and 2020, respectively. Patent and licensing legal and filing fees and costs are included in general and administrative costs in the Company's consolidated statements of operations.

Concentration of Risk

The Company periodically contracts with vendors and consultants to provide services related to the Company's operations. Charges incurred for these services can be for a specific time period (typically one year) or for a specific project or task. Costs and expenses incurred that represented 10% or more of general and administrative costs or research and development costs for the years ended December 31, 2021 and 2020 are described as follows.

General and administrative costs for the years ended December 31, 2021 and 2020 include combined charges from two legal firms for general licensing and patent prosecution costs relating to the Company's intellectual properties representing 14.6% and 27.1%, respectively, of total general and administrative costs. General and administrative costs for the years ended December 31, 2021 and 2020 also included charges for the fair value of stock options granted to directors and corporate officers representing 44.2% and 23.5%, respectively, of total general and administrative costs for those periods.

Research and development costs for the year ended December 31, 2021 include charges from three vendors and consultants representing 30.3%, 21.8%, and 14.4%, respectively, of total research and development costs for that period. Research and development costs for the year ended December 31, 2020 include charges from a consultant, and the value associated with extending stock options previously granted to that consultant, representing 65.6% of total research and development costs, and charges from a vendor representing 13.7% of total research and development costs.

Income Taxes

The Company accounts for income taxes under an asset and liability approach for financial accounting and reporting for income taxes. Accordingly, the Company recognizes deferred tax assets and liabilities for the expected impact of differences between the financial statements and the tax basis of assets and liabilities.

The Company records a valuation allowance to reduce its deferred tax assets to the amount that is more likely than not to be realized. In the event the Company was to determine that it would be able to realize its deferred tax assets in the future in excess of its recorded amount, an adjustment to the deferred tax assets would be credited to operations in the period such determination was made. Should the Company determine that it would not be able to realize all or part of its deferred tax assets in the future, an adjustment to the deferred tax assets would be charged to operations in the period such determination was made.

The Company is subject to U.S. federal income taxes and income taxes of various state tax jurisdictions. As the Company's net operating losses have yet to be utilized, all previous tax years remain open to examination by Federal authorities and other jurisdictions in which the Company currently operates or has operated in the past. The Company had no unrecognized tax benefits as of December 31, 2021 or 2020 and does not anticipate any material amount of unrecognized tax benefits within the12 months subsequent to December 31, 2021.

The Company accounts for uncertainties in income tax law under a comprehensive model for the financial statement recognition, measurement, presentation and disclosure of uncertain tax positions taken or expected to be taken in income tax returns as prescribed by GAAP. The tax effects of a position are recognized only if it is "more-likely-than-not" to be sustained by the taxing authority as of the reporting date. If the tax position is not considered "more-likely-than-not" to be sustained, then no benefits of the position are recognized. The Company had not recorded any liability for uncertain tax positions as of December 31, 2021 or 2020. Subsequent to December 31, 2021, any interest and penalties related to uncertain tax positions will be recognized as a component of income tax expense.

Stock-Based Compensation

The Company periodically issues common stock and stock options to officers, directors, employees, Scientific Advisory Committee members, contractors and consultants for services rendered. Options vest and expire according to terms established at the issuance date of each grant. Stock grants, which are generally time vested, are measured at the grant date fair value and charged to operations ratably over the vesting period.

The Company accounts for stock-based payments to officers, directors, employees, Scientific Advisory Committee members contractors and consultants by measuring the cost of services received in exchange for equity awards utilizing the grant date fair value of the awards, with the cost recognized as compensation expense on the straight-line basis in the Company's financial statements over the vesting period of the awards.

The fair value of stock options granted as stock-based compensation is determined utilizing the Black-Scholes option-pricing model, and is affected by several variables, the most significant of which are the expected life of the stock option, the exercise price of the stock option as compared to the fair market value of the common stock on the grant date, and the estimated volatility of the common stock. Unless sufficient historical exercise data is available, the expected life of the stock option is calculated as the mid-point between the vesting period and the contractual term (the "simplified method"). The estimated volatility is based on the historical volatility of the Company's common stock, calculated utilizing a look-back period approximately equal to the contractual life of the stock option being granted. The risk-free interest rate is based on the U.S. Treasury yield curve in effect at the time of grant. The fair market value of the common stock is determined by reference to the quoted market price of the Company's common stock on the grant date. The expected dividend yield is based on the Company's expectation of dividend payouts and is assumed to be zero.

The Company recognizes the fair value of stock-based compensation awards in general and administrative costs and in research and development costs, as appropriate, in the Company's consolidated statements of operations. The Company issues new shares of common stock to satisfy stock option exercises.

Earnings (Loss) Per Share

The Company's computation of earnings (loss) per share ("EPS") includes basic and diluted EPS. Basic EPS is measured as the income (loss) attributable to common stockholders divided by the weighted average common shares outstanding for the period. Diluted EPS is similar to basic EPS but presents the dilutive effect on a per share basis of potential common shares (e.g., preferred shares, warrants and stock options) as if they had been converted at the beginning of the periods presented, or issuance date, if later. Potential common shares that have an anti-dilutive effect (i.e., those that increase income per share or decrease loss per share) are excluded from the calculation of diluted EPS.

Loss per common share is computed by dividing net loss by the weighted average number of shares of common stock outstanding during the respective periods. Basic and diluted loss per common share was the same for all periods presented because all preferred shares, warrants and stock options outstanding were anti-dilutive.

At December 31, 2021 and 2020, the Company excluded the outstanding securities summarized below, which entitle the holders thereof to acquire shares of common stock, from its calculation of earnings per share, as their effect would have been anti-dilutive.

	December 31,	
	2021	2020
Series A Convertible Preferred Stock	729,167	729,167
Common stock warrants	3,110,310	3,000,000
Common stock options, including options issued in the form of warrants	2,666,667	1,475,000
Total	6,506,144	5,204,167

Fair Value of Financial Instruments

The authoritative guidance with respect to fair value established a fair value hierarchy that prioritizes the inputs to valuation techniques used to measure fair value into three levels and requires that assets and liabilities carried at fair value be classified and disclosed in one of three categories, as presented below. Disclosure as to transfers in and out of Levels 1 and 2, and activity in Level 3 fair value measurements, is also required.

Level 1. Observable inputs such as quoted prices in active markets for an identical asset or liability that the Company has the ability to access as of the measurement date. Financial assets and liabilities utilizing Level 1 inputs include active-exchange traded securities and exchange-based derivatives.

Level 2. Inputs, other than quoted prices included within Level 1, which are directly observable for the asset or liability or indirectly observable through corroboration with observable market data. Financial assets and liabilities utilizing Level 2 inputs include fixed income securities, non-exchange-based derivatives, mutual funds, and fair-value hedges.

Level 3. Unobservable inputs in which there is little or no market data for the asset or liability which requires the reporting entity to develop its own assumptions. Financial assets and liabilities utilizing Level 3 inputs include infrequently traded non-exchange-based derivatives and commingled investment funds and are measured using present value pricing models.

The Company determines the level in the fair value hierarchy within which each fair value measurement falls in its entirety, based on the lowest level input that is significant to the fair value measurement in its entirety. In determining the appropriate levels, the Company performs an analysis of the assets and liabilities at each reporting period end.

The carrying value of financial instruments (consisting of accounts payable and accrued expenses) is considered to be representative of their respective fair values due to the short-term nature of those instruments.

Recent Accounting Pronouncements

In December 2019, the Financial Accounting Standards Board (the "FASB") issued Accounting Standards Update ("ASU") 2019-12, Income Taxes (Topic 740): Simplifying the Accounting for Income Taxes ("ASU 2019-12"). ASU 2019-12 simplifies the accounting for income taxes by removing certain exceptions and enhances and simplifies various aspects of the income tax accounting guidance in ASC 740. The Company adopted ASU 2019-12 effective January 1, 2021. The adoption of ASU 2019-12 did not have any impact on the Company's consolidated financial statement presentation or disclosures.

In August 2020, the FASB issued ASU 2020-06, Debt — Debt with Conversion and Other Options (Subtopic 470-20) and Derivatives and Hedging—Contracts in Entity's Own Equity (Subtopic 815-40): Accounting for Convertible Instruments and Contracts in an Entity's Own Equity ("ASU 2020-06"). ASU 2020-06 simplifies the accounting for convertible debt by eliminating the beneficial conversion and cash conversion accounting models. Upon adoption of ASU 2020-06, convertible debt proceeds, unless issued with a substantial premium or an embedded conversion feature that is not clearly and closely related to the host contract, will no longer be allocated between debt and equity components. This modification will reduce the issue discount and result in less non-cash interest expense in financial statements. ASU 2020-06 also updates the earnings per share calculation and requires entities to assume share settlement when the convertible debt can be settled in cash or shares. For contracts in an entity's own equity, the type of contracts primarily affected by ASU 2020-06 are freestanding and embedded features that are accounted for as derivatives under the current guidance due to a failure to meet the settlement assessment by removing the requirements to (i) consider whether the contract would be settled in registered shares, (ii) consider whether collateral is required to be posted, and (iii) assess shareholder rights. ASU 2020-06 is effective for fiscal years beginning after December 15, 2023. Early adoption is permitted, but no earlier than fiscal years beginning after December 15, 2020, and only if adopted as of the beginning of such fiscal year. The Company adopted ASU 2020-06 effective January 1, 2021. The adoption of ASU 2020-06 did not have any impact on the Company's consolidated financial statement presentation or disclosures.

In May 2021, the FASB issued ASU 2021-04, Earnings Per Share (Topic 260), Debt — Modifications and Extinguishments (Subtopic 470-50), Compensation — Stock Compensation (Topic 718), and Derivatives and Hedging — Contracts in Entity's Own Equity (Subtopic 815-40): Issuer's Accounting for Certain Modifications or Exchanges of Freestanding Equity-Classified Written Call Options ("ASU 2021-04"). ASU 2021-04 provides guidance as to how an issuer should account for a modification of the terms or conditions or an exchange of a freestanding equity-classified written call option (i.e., a warrant) that remains classified after modification or exchange as an exchange of the original instrument for a new instrument. An issuer should measure the effect of a modification or exchange as the difference between the fair value of the modified or exchanged warrant and the fair value of that warrant immediately before modification or exchange and then apply a recognition model that comprises four categories of transactions and the corresponding accounting treatment for each category (equity issuance, debt origination, debt modification, and modifications unrelated to equity issuance and debt origination or modification). ASU 2021-04 is effective for all entities for fiscal years beginning after December 15, 2021, including interim periods within those fiscal years. An entity should apply the guidance provided in ASU 2021-04 prospectively to modifications or exchanges occurring on or after the effective date. Early adoption is permitted for all entities, including adoption in an interim period. If an entity elects to early adopt ASU 2021-04 in an interim period, the guidance should be applied as of the beginning of the fiscal year that includes that interim period. The adoption of ASU 2021-04 is not expected to have any impact on the Company's consolidated financial statement presentation or disclosures.

Management does not believe that any other recently issued, but not yet effective, authoritative guidance, if currently adopted, would have a material impact on the

Company's financial statement presentation or disclosures.

3. Stockholders' Equity

Preferred Stock

The Company is authorized to issue a total of 10,000,000 shares of preferred stock, par value $0.0001 per share. On March 17, 2015, the Company filed a Certificate of Designations, Preferences, Rights and Limitations of its Series A Convertible Preferred Stock with the Delaware Secretary of State to amend the Company's certificate of incorporation. The Company has designated a total of 350,000 shares as Series A Convertible Preferred Stock, which are non-voting and are not subject to increase without the written consent of a majority of the holders of the Series A Convertible Preferred Stock or as otherwise set forth in the Preferences, Rights and Limitations. The holders of each tranche of 175,000 shares of the Series A Convertible Preferred Stock are entitled to receive a per share dividend equal to 1% of the annual net revenue of the Company divided by 175,000, until converted or redeemed. As of December 31, 2021 and 2020, 9,650,000 shares of preferred stock were undesignated and may be issued with such rights and powers as the Board of Directors may designate.

Each share of Series A Convertible Preferred Stock may be converted, at the option of the holder, into 2.0833 shares of common stock (subject to customary anti-dilution provisions) and the Series A Convertible Preferred Stock is subject to mandatory conversion at the conversion rate in the event of a merger or sale transaction resulting in gross proceeds to the Company of at least $21,875,000. The Series A Convertible Preferred Stock has a liquidation preference based on its assumed conversion into shares of common stock. The Series A Convertible Preferred Stock does not have a cash liquidation preference.

If fully converted, the 350,000 outstanding shares of Series A Convertible Preferred Stock would convert into 729,167 shares of common stock at December 31, 2021 and 2020. The Company had the 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 $50.00. Accordingly, as of December 31, 2020, the Company had the right to redeem the 175,000 shares of Series A Convertible Preferred Stock that were issued on January 21, 2016; however, that right expired on January 21, 2021. The Series A Convertible Preferred Stock has no right to cash, except with respect to the payment of the aforementioned dividend based on the generation of revenues by the Company. The shares of Series A Convertible Preferred Stock do not have any registration rights.

Based on the attributes of the Series A Convertible Preferred Stock as previously described, the Company has accounted for the Series A Convertible Preferred Stock as a permanent component of stockholders' equity.

Common Stock

The Company is authorized to issue a total of 100,000,000 shares of common stock, par value $0.0001 per share. As of December 31, 2021 and 2020, the Company had 13,746,593 shares and 12,402,157 shares, respectively, of common stock issued, issuable and outstanding.

Effective November 30, 2020, the Company raised gross proceeds of $5,700,000 through a public offering of 1,200,000 units at a sale price of $4.75 per unit. Each unit consisted of one share of common stock and one warrant to purchase one share of common stock exercisable for five years at an exercise price of $5.70 per share. Additionally, on December 7, 2020, the Company received an additional $1,800 from the sale of 180,000 warrants as part of the overallotment option granted to the underwriters in the public offering. The warrants sold are exercisable for five years and represent the right to purchase one share of common stock at an exercise price of $5.70 per share. The total cash costs of the public offering were $1,110,451, resulting in net cash proceeds of $4,591,349. Pursuant to the underwriting agreement, the Company also granted warrants to the underwriters to purchase up to 120,000 shares of common stock commencing on May 24, 2021 and expiring on November 24, 2025, at an exercise price of $5.70 per share.

Effective December 21, 2020, the Company entered into a one-year services agreement with IRTH Communications, LLC for investor/public relations, financial communications, and strategic consulting services. The services agreement provided for the issuance of restricted shares of common stock, fully vested upon issuance, with a grant date fair value of $100,000, which resulted in the issuance of 27,420 shares of common stock with a per share value of $3.65 per share.

During February and March 2021, the Company issued 3,000 shares of common stock upon the exercise of 3,000 warrants at $5.70 per share and received cash proceeds of $17,100.

Effective March 2, 2021, the Company completed the sale of 1,133,102 shares of common stock at a price of $3.70 per share in a registered direct equity offering, generating gross proceeds of $4,192,478. The total cash costs of this offering were $502,717, resulting in net cash proceeds of $3,689,761. Pursuant to the placement agents' agreement, the Company granted warrants to the placement agents to purchase up to 113,310 shares of common stock commencing on March 2, 2021 and expiring on March 2, 2026, at an exercise price of $3.70 per share.

Effective April 22, 2021, stock options held by an officer and two of the Company's directors for 125,001 shares of common stock were exercised. Such stock options consisted of 75,000 options at $0.72 per share, 16,667 options at $0.90 per share, and 33,334 options at $0.96 per share. The exercise of these stock options generated total cash proceeds of $101,000 and resulted in the issuance of 125,001 shares of common stock.

Effective July 14, 2021, a stock option held by a consultant of the Company for 83,333 shares of common stock were exercised at $1.20 per share. The exercise of this stock option generated total cash proceeds of $100,000 and resulted in the issuance of 83,333 shares of common stock.

Common Stock Warrants

A summary of common stock warrant activity, including warrants to purchase common stock that were issued in conjunction with the Company's public offering, during the years ended December 31, 2021 and 2020 is presented below.

	Number of Shares	Weighted Average Exercise Price	Weighted Average Remaining Contractual Life (in Years)
Warrants outstanding at December 31, 2019	1,500,000	$ 6.000	
Issued	1,500,000	5.700	
Exercised	—	—	
Expired	—	—	
Warrants outstanding at December 31, 2020	3,000,000	$ 5.850	

Issued	113,310	3.700	
Exercised	(3,000)	5.700	
Expired	—	—	
Warrants outstanding at December 31, 2021	3,110,310	$ 5.772	2.48
Warrants exercisable at December 31, 2020	3,000,000	$ 5.850	
Warrants exercisable at December 31, 2021	3,110,310	$ 5.772	2.48

At December 31, 2021, the outstanding warrants are exercisable at the following prices per common share:

Exercise Prices	Warrants Outstanding (Shares)
$ 3.700	113,310
$ 5.700	1,497,000
$ 6.000	1,500,000
	3,110,310

Based on a fair market value of $1.19 per share on December 31, 2021, there was no intrinsic value attributed to exercisable but unexercised common stock warrants at December 31, 2021.

Information with respect to the issuance of common stock in connection with various stock-based compensation arrangements is provided at Note 5.

4. Related Party Transactions

Related party transactions include transactions with the Company's officers, directors and affiliates.

Gil N Schwartzberg

On September 12, 2007, the Company entered into a consulting agreement with Gil N Schwartzberg for Mr. Schwartzberg to provide financial advisory and consulting services to the Company with respect to financing matters, capital structure and strategic development, and to assist management in communications with investors and stockholders. Mr. Schwartzberg is currently a significant stockholder and director of the Company. Consideration under this consulting agreement, including amendments thereto, has been paid exclusively in the form of stock options. On August 2, 2018, the Company entered into a third amendment to the consulting agreement to extend it to January 28, 2024, as well as to extend the exercise date of previously issued, fully-vested stock options for 666,667 shares of common stock, exercisable at $3.00 per share, from January 28, 2019 to January 28, 2024.

Employment Agreements with Officers

During July and August 2020, the Company entered into one-year employment agreements with its executive officers, consisting of Dr. John S. Kovach, Eric J. Forman, Dr. James S. Miser, and Robert N. Weingarten, payable monthly, as described below. The employment agreements are automatically renewable for additional one-year periods unless terminated by either party upon 60 days written notice prior to the end of the applicable one-year period, or by death, or by termination for cause. These employment agreements were automatically renewed for an additional one-year period in July and August 2021.

The Company entered into an employment agreement with Dr. Kovach dated July 15, 2020, effective October 1, 2020, for Dr. Kovach to continue to act as the Company's President, Chief Executive Officer and Chief Scientific Officer with an annual salary of $250,000. During the years ended December 31, 2021 and 2020, the Company paid $250,000 and $62,500, respectively, to Dr. Kovach under this employment agreement. During the year ended December 31, 2020, the Company paid Dr. Kovach a salary of $45,000 for services rendered as President, Chief Executive Officer and Chief Scientific Officer prior to the effectiveness of the employment agreement. These amounts were included in general and administrative costs in the Company's consolidated statements of operations for such periods.

The Company entered into an employment agreement with Dr. James S. Miser, M.D., effective August 1, 2020 to act as the Company's Chief Medical Officer with an annual salary of $150,000. Effective May 1, 2021, Dr. Miser's annual salary was increased to $175,000. Dr. Miser is required to devote at least 50% of his business time to the Company's activities. During the years ended December 31, 2021 and 2020, the Company paid $166,667 and $62,500, respectively, to Dr. Miser under this employment agreement, which were included in general and administrative costs in the Company's consolidated statements of operations for such periods.

The Company entered into an employment agreement with Eric J. Forman effective July 15, 2020, as amended on August 12, 2020, to act as the Company's Chief Administrative Officer with an annual salary of $120,000. Eric Forman is the son-in-law of Gil Schwartzberg, a member of the Company's Board of Directors, and a significant stockholder of and consultant to the Company, and is the son of Dr. Stephen Forman, a member of the Company's Board of Directors. Julie Forman, the wife of Eric Forman and the daughter of Gil Schwartzberg, is Vice President of Morgan Stanley Wealth Management, at which firm the Company's cash is on deposit and the Company maintains a continuing banking relationship. Effective May 1, 2021, Mr. Forman's annual salary was increased to $175,000. During the years ended December 31, 2021 and 2020, the Company paid $156,667 and $30,000, respectively, to Mr. Forman under this employment agreement. During the year ended December 31, 2020, the Company paid legal and consulting fees to the Eric Forman Law Office of $38,000 for services rendered prior to Mr. Forman's appointment as Chief Administrative Officer. These amounts were included in general and administrative costs in the Company's consolidated statements of operations for such periods.

The Company entered into an employment agreement with Robert N. Weingarten effective August 12, 2020 to act as the Company's Vice President and Chief Financial Officer with an annual salary of $120,000. Effective May 1, 2021, Mr. Weingarten's annual salary was increased to $175,000. During the years ended December 31, 2021 and 2020, the Company paid $156,667 and $46,451, respectively, to Mr. Weingarten under this employment agreement. During the year ended December 31, 2020, the Company paid $79,995 to Mr. Weingarten for accounting and financial consulting services rendered prior to Mr. Weingarten's appointment as Vice President and Chief Financial Officer. These amounts were included in general and administrative costs in the Company's consolidated statements of operations for such periods.

Compensatory Arrangements for Board of Directors

Effective April 9, 2021, the Board of Directors approved a comprehensive cash and equity compensation package for the members of the Board of Directors and committee members.

The Board of Directors approved the following cash compensation for non-officer independent directors, payable quarterly:

Base director compensation - $20,000 per year
Chairman of audit committee - additional $10,000 per year
Chairman of any other committees - additional $5,000 per year
Member of audit committee - additional $5,000 per year
Member of any other committees - additional $2,500 per year

Total cash compensation paid to independent directors was $92,833 for the year ended December 31, 2021.

Stock-based compensation arrangements involving members of the Company's Board of Directors. officers and affiliates are described at Note 5.

A summary of related party costs, including compensation under employment and consulting agreements and fees paid to non-officer directors for their services on the Board of Directors, for the years ended December 31, 2021 and 2020 is presented below. This summary includes the above-described payments to Mr. Forman in 2020 prior to his appointment as Chief Administrative Officer and excludes the payments to Mr. Weingarten in 2020 prior to his appointment as Vice President and Chief Financial Officer.

	Years Ended December 31,	
	2021	2020
Related party costs:		
Cash-based	$ 822,834	$ 284,451
Stock-based	2,201,280	480,634
Total	$ 3,024,114	$ 765,085

5. Stock-Based Compensation

The Company issues common stock and stock options as incentive compensation to directors and as compensation for the services of employees, contractors, and consultants of the Company.

On July 14, 2020, the Board of Directors of the Company adopted the 2020 Stock Incentive Plan (the "2020 Plan"), which provides for the granting of equity-based awards, consisting of stock options, restricted stock, restricted stock units, stock appreciation rights, and other stock-based awards to employees, officers, directors and consultants of the Company and its affiliates for up to 2,333,333 shares of the Company's common stock, under terms and conditions as determined by the Company's Board of Directors. Stockholders holding a majority of the voting power of the common stock of the Company approved the 2020 Plan pursuant to an action by written consent dated July 31, 2020. Stockholders of the Company were notified of such action by written consent pursuant to an Information Statement dated August 31, 2020 and mailed to stockholders on or about September 3, 2020. As of December 31, 2021, unexpired stock options for 1,400,000 shares were issued and outstanding under the 2020 Plan and 933,333 shares were available for issuance under the 2020 Plan.

Effective April 9, 2021, the Board of Directors approved a comprehensive cash and equity compensation package for the members of the Board of Directors and committee members. Cash-based features of the compensation package are described at Notes 4 and 7.

Stock-based features of the compensation package consisted of the annual granting of stock options to each non-officer director to purchase100,000 shares of common stock at the closing market price on the earlier of the date of the annual meeting of shareholders or the last business day of the month ending June 30, vesting 12.5% on the last day of each subsequent calendar quarter-end until fully vested, and the granting of stock options to a new director to purchase250,000 shares of common stock, exercisable at the closing market price on the grant date for a period of five years, vesting 50% on the grant date and the remainder vesting 12.5% on the last day of each subsequent calendar quarter-end until fully vested.

The fair value of a stock option award is calculated on the grant date using the Black-Scholes option-pricing model. The risk-free interest rate is based on the U.S. Treasury yield curve in effect as of the grant date. The expected dividend yield assumption is based on the Company's expectation of dividend payouts and is assumed to be zero. The estimated volatility is based on the historical volatility of the Company's common stock, calculated utilizing a look-back period approximately equal to the contractual life of the stock option being granted. Unless sufficient historical exercise data is available, the expected life of the stock option is calculated as the mid-point between the vesting period and the contractual term (the "simplified method"). The fair market value of the common stock is determined by reference to the quoted market price of the common stock on the grant date.

For stock options requiring an assessment of value during the year ended December 31, 2021, the fair value of each stock option award was estimated using the Black-Scholes option-pricing model with the following assumptions:

Risk-free interest rate	0.89% to 1.13%
Expected dividend yield	0%
Expected volatility	187.7% to 198.8%
Expected life	3.5 to 5 years

For stock options requiring an assessment of value during the year ended December 31, 2020, the fair value of each stock option award was estimated using the Black-Scholes option-pricing model with the following assumptions:

Risk-free interest rate	0.23% to 0.31%
Expected dividend yield	0%
Expected volatility	207.7%
Expected life	4 to 5 years

Effective September 14, 2015, in connection with the Collaboration Agreement with BioPharmaWorks LLC ("BioPharmaWorks") as described at Note 7, the Company issued to BioPharmaWorks two stock options, in the form of warrants, to purchase 166,667 shares (83,333.5 shares per warrant) of the Company's common stock. The first warrant vested on September 14, 2016 and was exercisable for a period of five years from the grant date at $6.00 per share. The second warrant vested on September 14, 2017 and was exercisable for a period of five years from the grant date at $12.00 per share. On July 3, 2020, the Company's Board of Directors approved an extension of the term of the outstanding warrants to acquire an aggregate of 166,667 shares of the Company's common stock fromSeptember 14, 2020 to September 14, 2025. The Company's closing stock price on July 2, 2020 was $5.40 per share. The fair value of the extension of these stock options, as calculated pursuant to the Black-Scholes option-pricing model, was measured for accounting purposes as the difference in the fair value of the stock options immediately before and immediately after the extension date and was determined to be $670,715 ($4.0242 per share), which was reflected as a charge to general and administrative costs in the consolidated statement of operations on that date.

On July 15, 2020, as amended on August 12, 2020, in connection with the employment agreement entered into with Eric J. Forman, Mr. Forman was granted options for 58,333 shares of the Company's common stock. The options can be exercised on a cashless basis. The options have a term offive years and an exercise price of $7.14 per share, which was equal to the closing market price of the Company's common stock on the grant date. The options vested as to 25% on August 12, 2020 and August 12, 2021, and will vest 25% on each of the second and third anniversaries of the grant date. The fair value of these stock options, as calculated pursuant to the Black-Scholes option-pricing model, was determined to be $400,855 ($6.8718 per share), of which $100,214 was attributable to the stock options fully-vested on August 12, 2020 and was therefore charged to operations on that date. The remaining unvested portion of the fair value of the stock options is being charged to operations ratably from August 12, 2020 through August 12, 2023. During the years ended December 31, 2021 and 2020, the Company recorded charges to general and administrative costs in the consolidated statement of operations of $100,213 and $138,926, respectively, with respect to these stock options.

On August 1, 2020, in connection with an employment agreement entered into withDr. James S. Miser, M.D., Dr. Miser was granted options for 83,334 shares of the Company's common stock. The options can be exercised on a cashless basis. The options have a term of five years and an exercise price of $7.14 per share, which was equal to the closing market price of the Company's common stock on the effective date of the employment agreement. The options vested as to 25% on August 1, 2020 and August 1, 2021, and will vest 25% on each of the second and third anniversaries of the effective date. The fair value of these stock options, as calculated pursuant to the Black-Scholes option-pricing model, was determined to be $572,650 ($6.8718 per share), of which $143,163 was attributable to the stock options fully-vested on August 1, 2020 and was therefore charged to operations on that date. The remaining unvested portion of the fair value of the stock options is being charged to operations ratably from August 1, 2020 through August 1, 2023. During the years ended December 31, 2021 and 2020, the Company recorded charges to general and administrative costs in the consolidated statement of operations of $143,163 and $202,782, respectively, with respect to these stock options.

On August 12, 2020, in connection with the employment agreement entered into with Robert N. Weingarten, Mr. Weingarten was granted options for58,333 shares of the Company's common stock. The options can be exercised on a cashless basis. The options have a term of five years and an exercise price of $7.14 per share, which was equal to the closing market price of the Company's common stock on the grant date. The options vested as to 25% on August 12, 2020 and August 12, 2021, and will vest 25% on each of the second and third anniversaries of the grant date. The fair value of these stock options, as calculated pursuant to the Black-Scholes option-pricing model, was determined to be $400,855 ($6.8718 per share), of which $100,214 was attributable to the stock options fully-vested on August 12, 2020 and was therefore charged to operations on that date. The remaining unvested portion of the fair value of the stock options is being charged to operations ratably from August 12, 2020 through August 12, 2023. During the years ended December 31, 2021 and 2020, the Company recorded charges to general and administrative costs in the consolidated statement of operations of $100,213 and $138,926, respectively, with respect to these stock options.

Effective January 6, 2021, in recognition of their service as directors of the Company over the past year, the Company granted fully-vested stock options to purchase 50,000 shares of common stock to each of Dr. Winson Sze Chun Ho, Dr. Yun Yen, Dr. Stephen Forman, and Dr. Philip Palmedo (an aggregate of 200,000 shares), exercisable for a period of five years from the grant date at $3.21 per share, which was the approximate fair market value of the Company's common stock on such date. The fair value of these stock options, as calculated pursuant to the Black-Scholes option-pricing model, was determined to be $571,312 ($2.8566 per share) and was charged to general and administrative costs in the consolidated statement of operations on the grant date.

On April 9, 2021, Winson Sze Chun Ho resigned from the Company's Board of Directors to focus on clinical and pre-clinical cancer research in academic medicine. Concurrent with his resignation, the Board of Directors appointed Gil Schwartzberg to fill the vacancy created by Dr. Ho's resignation. In connection with his appointment to the Board of Directors, and in accordance with the Company's cash and equity compensation package for members of the Board of Directors, Mr. Schwartzberg was granted options exercisable for a period of five years to purchase 250,000 shares of the Company's common stock at an exercise price of $3.20 per share (the closing market price on the grant date), vesting 50% on the grant date and the remainder vesting 12.5% on the last day of each subsequent calendar quarter-end until fully vested. The fair value of these stock options, as calculated pursuant to the Black-Scholes option-pricing model, was determined to be $753,611 ($3.0144 per share), of which $376,800 was attributable to the stock options fully-vested on April 9, 2021 and was therefore charged to operations on that date. The remaining unvested portion of the fair value of the stock options is being charged to operations ratably from April 9, 2021 through June 30, 2023. During the year ended December 31, 2021, the Company recorded charges to general and administrative costs in the consolidated statement of operations of $500,235 with respect to these stock options.

On May 11, 2021, the Board of Directors appointed Regina Brown to the Board of Directors. In connection with her appointment to the Board of Directors, and in accordance with the Company's cash and equity compensation package for members of the Board of Directors, Ms. Brown was granted options exercisable for a period of five years to purchase 250,000 shares of the Company's common stock at an exercise price of $2.80 per share (the closing market price on the grant date), vesting 50% on the grant date and the remainder vesting 12.5% on the last day of each subsequent calendar quarter-end until fully vested. The fair value of these stock options, as calculated pursuant to the Black-Scholes option-pricing model, was determined to be $658,363 ($2.6335 per share), of which $329,188 was attributable to the stock options fully-vested on May 11, 2021 and was therefore charged to operations on that date. The remaining unvested portion of the fair value of the stock options is being charged to operations ratably from May 11, 2021 through June 30, 2023. During the year ended December 31, 2021, the Company recorded charges to general and administrative costs in the consolidated statement of operations of $427,944 with respect to these stock options.

On June 30, 2021, the Board of Directors, in accordance with the recently adopted cash and equity compensation package for the members of the Board of Directors, granted to each of the five non-officer directors of the Company stock options exercisable for a period of five years to purchase 100,000 shares (a total of500,000 shares) of the Company's common stock at an exercise price of $3.03 per share (the closing market price on the grant date), vesting 12.5% on the last day of each subsequent calendar quarter-end until fully vested. The total fair value of the 500,000 stock options, as calculated pursuant to the Black-Scholes option-pricing model, was determined to be $1,421,095 ($2.84225 per share), which is being charged to operations ratably from July 1, 2021 through June 30, 2023. During the year ended December 31, 2021, the Company recorded charges to general and administrative costs in the consolidated statement of operations of $358,200 with respect to these stock options.

On November 8, 2021, the Company issued to BioPharmaWorks a stock option, in the form of a warrant, to purchase200,000 shares of the Company's common stock. The warrant is exercisable for a period of five years from the issue date at $2.06 per share (the closing market price on the issue date). The fair value of the fully-vested stock warrant, as calculated pursuant to the Black-Scholes option-pricing model, was determined to be $397,642 ($1.9882 per share) and was charged to general and administrative costs in the consolidated statement of operations on that date.

A summary of stock-based compensation costs for the years ended December 31, 2021 and 2020 is as follows:

	Years Ended December 31,	
	2021	2020
Related parties	$ 2,201,280	$ 480,634
Non-related parties	397,642	770,715
Total stock-based compensation costs	$ 2,598,922	$ 1,251,349

A summary of stock option activity, including options issued in the form of warrants, during the years ended December 31, 2021 and 2020 is presented below.

	Number of Shares	Weighted Average Exercise Price	Weighted Average Remaining Contractual Life (in Years)
Stock options outstanding at December 31, 2019	1,308,333	$ 3.648	
Granted	200,000	7.140	
Exercised	—	—	
Expired	(33,333)	3.000	
Stock options outstanding at December 31, 2020	1,475,000	4.136	
Granted	1,400,000	2.906	
Exercised	(208,334)	0.965	
Expired	—	—	
Rounding adjustment attributable to reverse stock split	1	—	
Stock options outstanding at December 31, 2021	2,666,667	$ 3.738	3.42
Stock options exercisable at December 31, 2020	1,325,000	$ 3.796	
Stock options exercisable at December 31, 2021	2,004,167	$ 3.770	3.13

Total deferred compensation expense for the outstanding value of unvested stock options was approximately $2,097,000 at December 31, 2021, which will be recognized subsequent to December 31, 2021 over a weighted-average period of approximately 18 months.

The exercise prices of common stock options outstanding and exercisable, including options issued in the form of warrants, at December 31, 2021 are as follows:

Exercise Prices	Options Outstanding (Shares)	Options Exercisable (Shares)
$ 0.900	33,333	33,333
$ 1.680	66,667	66,667
$ 2.060	200,000	200,000
$ 2.800	250,000	156,250
$ 3.000	666,667	666,667
$ 3.030	500,000	125,000
$ 3.200	250,000	156,250
$ 3.210	200,000	200,000
$ 6.000	166,667	166,667
$ 6.600	50,000	50,000
$ 7.140	200,000	100,000
$ 12.000	83,333	83,333
	2,666,667	2,004,167

The intrinsic value of exercisable but unexercised in-the-money stock options at December 31, 2021 was approximately $0,000, based on a fair market value of $1.19 per share on December 31, 2021.

Outstanding stock options to acquire 662,500 shares of the Company's common stock had not vested at December 31, 2021.

The Company expects to satisfy such stock obligations through the issuance of authorized but unissued shares of common stock.

6. Income Taxes

Deferred income taxes reflect the net tax effects of temporary differences between the carrying amounts of assets and liabilities for financial reporting purposes and the amounts used for income tax purposes. Significant components of the Company's deferred tax assets as of December 31, 2021 and 2020 are summarized below.

	December 31, 2021	December 31, 2020
Start-up and organization costs	$ —	$ 5,000
Research credits	451,000	390,000
Stock-based compensation	1,821,000	1,107,000
Net operating loss carryforwards	6,723,000	5,477,000
Total deferred tax assets	8,995,000	6,979,000
Valuation allowance	(8,995,000)	(6,979,000)
Net deferred tax assets	$ —	$ —

In assessing the potential realization of deferred tax assets, management considers whether it is more likely than not that some portion or all of the deferred tax assets will be realized. The ultimate realization of deferred tax assets is dependent upon the Company attaining future taxable income during the periods in which those temporary differences become deductible. As of December 31, 2021 and 2020, management was unable to determine if it is more likely than not that the Company's deferred tax assets will be realized and has therefore recorded an appropriate valuation allowance against deferred tax assets at such dates.

No federal tax provision has been provided for the years ended December 31, 2021 and 2020 due to the losses incurred during such periods. The reconciliation below presents the difference between the income tax rate computed by applying the U.S. federal statutory rate and the effective tax rate for the years ended December 31, 2021 and 2020.

	Years Ended December 31, 2021	Years Ended December 31, 2020
U. S. federal statutory tax rate	(21.0)%	(21.0)%

State income taxes, net of federal tax benefit	(6.0)%	(6.0)%
Expirations related to stock-based compensation	0.6%	0.5%
Adjustment to deferred tax asset	(0.4)%	(0.8)%
Change in valuation allowance	26.8%	27.3%
Effective tax rate	0.0%	0.0%

At December 31, 2021, the Company has available net operating loss carryforwards for federal and state income tax purposes of approximately $23,173,000 and $23,287,000, respectively. Federal net operating losses, if not utilized earlier, expire through 2041. The state net operating loss carryovers include approximately $19,141,000 that was incurred in the State of New York. New York tax law requires New York net operating loss carryovers from years prior to 2015 to be converted, by applying a formula, into a Prior Net Operating Loss Conversion (PNOLC) subtraction pool. The Company may utilize up to 1/10 of the PNOLC subtraction pool, or $928,313, each year. Unutilized PNOLC amounts carry forward to succeeding years until they expire in 2035. In addition, the full New York net operating losses incurred in post-2015 tax years may be utilized in future tax years. Post-2015 New York net operating losses expire through 2040. The state net operating loss carryovers also include approximately $4,146,000 that was incurred in the State of California. As the Company's net operating losses have yet to be utilized, all previous tax years since 2006 remain subject to adjustment by Federal authorities and other jurisdictions in which the Company currently operates or has operated in the past.

7. Commitments and Contingencies

Legal Claims

The Company may be subject to legal claims and actions from time to time as part of its business activities. As of December 31, 2021, the Company was not subject to any pending or threatened legal claims or actions.

Principal Commitments

Clinical Trial Agreements

At December 31, 2021, the Company's contractual commitments pursuant to clinical trial agreements, clinical trial monitoring agreements, and agreements for the production of LB-100 for clinical use, as described below, aggregated $8,646,000, which are currently scheduled to be incurred through December 31, 2025. The Company's ability to conduct and fund these contractual commitments is subject to the timely availability of sufficient capital to fund such expenditures, as well as any changes in the allocation or reallocation of such funds to the Company's current or future clinical trial programs. The Company expects that the full amount of these expenditures will be incurred only if such clinical trial programs are conducted as originally designed and their respective enrollments and duration are not modified or reduced. Clinical trial programs, such as the types that the Company is engaged in, can be highly variable and can frequently involve a series of changes and modifications over time as clinical data is obtained and analyzed, and are frequently modified, suspended or terminated before the clinical trial endpoint. Accordingly, such contractual commitments as discussed herein should be considered as estimates only based on current clinical assumptions and conditions, and are typically subject to significant revisions over time.

Moffitt. Effective August 20, 2018, the Company 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 the Company 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 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 ("IND") 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. An interim analysis will be done after the first 21 patients are entered. If there are 3 or more responders but fewer than 7, an additional 20 patients will be entered. If at any point there are 7 or more responders, this will be sufficient evidence to support continued development of LB-100 for the treatment of low and intermediate-1 risk MDS. Recruitment has been slow and the Covid-19 pandemic has further reduced recruitment of patients into the protocol. At the current rate of accrual, the clinical trial is expected to be completed by June 30, 2025. However, with additional funds, the Company would consider adding two additional MDS centers to the Phase 2 portion of the study to accelerate patient accrual.

During the years ended December 31, 2021 and 2020, the Company incurred costs of $18,443 and $41,142, respectively, pursuant to this agreement, which have been included in research and development costs in the Company's consolidated statements of operations. As of December 31, 2021, total costs of $104,677 have been incurred pursuant to this agreement. The Company's aggregate commitment pursuant to this agreement, less amounts previously paid to date, totaled approximately $601,000 as of December 31, 2021, which is expected to be incurred through December 31, 2025.

GEIS. Effective July 31, 2019, the Company entered into a Collaboration Agreement for an Investigator-Initiated Clinical Trial with the Spanish Sarcoma Group (Grupo Español de Investigación en Sarcomas or "GEIS"), Madrid, Spain, to carry out a study entitled "Randomized phase I/II trial of LB-100 plus doxorubicin vs. doxorubicin alone in first line of advanced soft tissue sarcoma". The purpose of this clinical trial is to obtain information with respect to the efficacy and safety of LB-100 combined with doxorubicin in soft tissue sarcomas. Doxorubicin is the global standard for initial treatment of advanced soft tissue sarcomas ("ASTS"). Doxorubicin alone has been the mainstay of first line treatment of ASTS for over 40 years, with little 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.

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

The Company had previously expected that this clinical trial would commence during the quarter ended June 30, 2020. However, during July 2020, the Spanish regulatory authority advised the Company that although it had approved the scientific and ethical basis of the protocol, it required that the Company manufacture new inventory of LB-100 under current Spanish pharmaceutical manufacturing standards. These standards were adopted subsequent to the production of the Company's existing LB-100 inventory.

A new batch of LB 100 has been prepared and is now undergoing the multitude of analytical studies of the formulated product necessary to gain approval for use in the

European Union. Regulatory reviews by the European Union have been delayed, as a result of which the final review of the clinical product by Spanish regulatory authorities will also be delayed. Accordingly, the clinical trial is now estimated to begin during the quarter ending June 30, 2022 and be completed by June 30, 2025.

The interim analysis of this clinical trial could indicate either inferiority or superiority of LB-100 plus doxorubicin as compared to doxorubicin alone. A positive study would have the potential to change the standard therapy for this disease after four decades of failure to improve the marginal benefit of doxorubicin alone.

The Company's agreement with GEIS provides for various payments based on achieving specific milestones over the term of the agreement. Through December 31, 2021, the Company has paid GEIS an aggregate of $67,582 towards the second milestone payment for current work being done under this agreement.

During the years ended December 31, 2021 and 2020, the Company incurred costs of $24,171 and $43,411, respectively, pursuant to this agreement, which have been included in research and development costs in the Company's consolidated statements of operations. As of December 31, 2021, total costs of $155,053 have been incurred pursuant to this agreement. The Company's aggregate commitment pursuant to this agreement, less amounts previously paid to date, totaled approximately $4,250,000 as of December 31, 2021, which is expected to be incurred through December 31, 2025.

In order to manufacture a new inventory supply of LB-100 for the GEIS clinical trial, the Company has engaged a number of vendors to carry out the multiple tasks needed to make and gain approval of a new clinical product for investigational study in Spain. These tasks include the synthesis under good manufacturing practices (GMP) of the active pharmacologic ingredient (API), with documentation of each of the steps involved by an independent auditor. The API is then transferred to a vendor that prepares the clinical drug product, also under GMP conditions documented by an independent auditor. The clinical drug product is then sent to a vendor to test for purity and sterility, provide appropriate labels, store the drug, and distribute the drug to the clinical centers for use in the clinical trials. A formal application documenting all steps taken to prepare the clinical drug product for clinical use must be submitted to the appropriate regulatory authorities for review and approval before being used in a clinical trial.

On November 2, 2021, the Company entered into a Development Agreement with Famar Health Care Services Madrid SA ("Famar") to prepare a new batch of clinical LB-100 for use in clinical trials to be conducted in the European Union. During the year ended December 31, 2021, the Company incurred costs of $119,860, pursuant to this agreement, which has been included in research and development costs in the Company's consolidated statements of operations. The Company's aggregate commitment pursuant to this agreement, less amounts previously paid to date, totaled approximately $180,000 as of December 31, 2021, which is expected to be incurred through June 30, 2024.

As of December 31, 2021, the Company estimates that this program to provide new inventory of the clinical drug product for the Spanish sarcoma study, and potentially for subsequent multiple trials within the European Union, including the costs incurred and to be incurred with Famar as described above, will cost approximately $1,076,000. The Company's aggregate commitments under this program, less amounts previously paid to date, totaled approximately $318,000 as of December 31, 2021, which are expected to be incurred through December 31, 2024. As the production of the new inventory of the clinical drug product is being conducted in Europe and is paid for in Euros, final costs are subject to foreign currency fluctuations between the United States Dollar and the Euro.

City of Hope. Effective January 18, 2021, the Company executed a Clinical Research Support Agreement with the City of Hope National Medical Center, an NCI-designated comprehensive cancer center, and City of Hope Medical Foundation (collectively, "City of Hope"), to carry out a Phase 1b clinical trial of LB-100, the Company's first-in-class protein phosphatase inhibitor, combined with a standard regimen for treatment of untreated extensive- stage disease small cell lung cancer (ED-SCLC). LB-100 will be given in combination with carboplatin, etoposide and atezolizumab, an FDA-approved but marginally effective regimen, to previously untreated ED-SCLC patients. The dose of LB-100 will be escalated with the standard fixed doses of the 3-drug regimen to reach a recommended Phase 2 dose (RP2D). Patient entry will be expanded so that a total of 12 patients will be evaluable at the RP2D to confirm the safety of the LB-100 combination and to look for potential therapeutic activity as assessed by objective response rate, duration of overall response, progression-free-survival and overall survival.

The clinical trial was initiated on March 9, 2021, with patient accrual expected to take approximately two years to complete. If LB-100 does potentiate the benefit of the standard regimen, some evidence could be noted at 12 months into the clinical trial, but an assessment of potential increased activity is likely to require at least 24 months. The Company is currently seeking to add two additional centers to increase the rate of accrual. The Company expects this clinical trial to be completed by June 30, 2024.

During the year ended December 31, 2021, the Company incurred costs, and total costs, of $378,511, pursuant to this agreement. The Company's aggregate commitment pursuant to this agreement, less amounts previously paid to date, totaled approximately $2,433,000 as of December 31, 2021, which is expected to be incurred through December 31, 2024, based upon a target of 42 enrollees. If a significant number of patients fail during the dose-escalation process, an increase of up to 12 patients would likely be necessary, at an estimated additional cost of approximately $800,000. The Company currently expects that enrollment in this clinical trial will range from approximately 18 to 30 enrollees, with 24 enrollees as the most likely number. Should fewer than 42 enrollees be required, the Company has agreed to compensate City of Hope on a per enrollee basis.

National Cancer Institute Pharmacologic Clinical Trial. In May 2019, the National Cancer Institute (NCI) initiated a glioblastoma (GBM) pharmacologic clinical trial. During the fourth quarter of 2019, the 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 Cooperative Research and Development Agreement, with the Company being required to provide the LB-100 clinical compound.

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

The NCI study is designed to determine the extent to which LB-100 enters recurrent malignant gliomas. Patients having surgery to remove one or more tumors will receive one dose of LB-100 prior to surgery and have blood and tumor tissue analyzed to determine the amount of LB-100 present and to determine whether the cells in the tumors show the biochemical changes expected to be present if LB-100 reaches its molecular target. The goal is to obtain data in up to eight patients. As a result of the innovative design of the NCI study, data from so few patients should be sufficient to provide a sound rationale for conducting a larger clinical trial to determine the effectiveness of adding LB-100 to the standard treatment regimen for GBMs.

The neurosurgical unit at the NCI, which had been closed due to the Covid-19 epidemic, has reopened, and patient accrual has resumed. Patient entry remains at two, with the goal to enter eight patients before analyzing results. There is an urgent need to improve therapy for this type of aggressive brain tumor. If the NCI study shows that LB-100 does penetrate the brain, a clinical study of LB-100 in combination with standard therapy for GBM, the drug temozolomide and radiation, both of which have been well documented in pre-clinical studies to be significantly enhanced by LB-100, would be of significant interest to neuro-oncologists frustrated by decades of limited advances in therapy for this common brain tumor in adults.

Clinical Trial Monitoring Agreements

Moffitt. On September 12, 2018, the Company finalized a work order agreement with Theradex Systems, Inc. ("Theradex"), an international contract research organization ("CRO"), to monitor the Phase 1b/2 clinical trial being managed and conducted by Moffitt. The clinical trial began in April 2019 and the first patient was entered into the clinical trial in July 2019. At the current rate of accrual, the clinical trial is expected to be completed by June 30, 2025.

Costs under this work order agreement are estimated to be approximately $954,000, with such payments expected to be divided approximately 94% to Theradex for services and approximately 6% for payments for pass-through costs. The costs of the Phase 1b/2 clinical trial being paid to or through Theradex are being recorded and charged to operations based on the periodic documentation provided by the CRO. During the years ended December 31, 2021 and 2020, the Company incurred costs of $9,750 and $18,663, respectively, pursuant to this work order. As of December 31, 2021, total costs of $91,885 have been incurred pursuant to this work order agreement. The Company's aggregate commitment pursuant to this clinical trial monitoring agreement, less amounts previously paid to date, totaled approximately $868,000 as of December 31, 2021, which is expected to be incurred through June 30, 2025.

City of Hope. On February 5, 2021, the Company signed a new work order agreement with Theradex to monitor the City of Hope investigator-initiated clinical trial in small cell lung cancer in accordance with FDA requirements for oversight by the sponsoring party. During the year ended December 31, 2021, the Company incurred costs of $24,626, pursuant to this work order. As of December 31, 2021, total costs of $24,626 have been incurred pursuant to this work order agreement. The Company's aggregate commitment pursuant to this clinical trial monitoring agreement, less amounts previously paid to date, totaled approximately $314,000 as of December 31, 2021, which is expected to be incurred through June 30, 2025.

Patent and License Agreements

On March 22, 2018, the Company entered into a Patent Assignment and Exploitation Agreement with INSERM TRANSFERT SA, acting as delegatee of the French National Institute of Health and Medical Research, for the assignment to the Company of INSERM'S interest in United States Patent No. 9,833,450 entitled "Oxabicyloheptanes and Oxabicycloheptenes for the Treatment of Depressive and Stress Disorders", which was filed with the United States Patent and Trademark Office in the name of INSERM and the Company as co-owners on February 19, 2015 and granted on May 12, 2017, and related patent applications and filings. INSERM is a French public institution dedicated to research in the field of health and medicine that had previously entered into a Material Transfer Agreement with the Company to allow INSERM to conduct research on the Company's proprietary compound LB-100 and/or its analogs for the treatment of depressive or stress disorders in humans. Pursuant to the Agreement, the Company has agreed to make certain milestone payments to INSERM aggregating up to $1,750,000 upon achievement of development milestones and up to $6,500,000 upon achievement of commercial milestones. The Company also agreed to pay INSERM certain commercial royalties on net sales of products attributed to the Agreement. The Company's initial plan was to complete the validation process to evaluate LB-100 for the treatment of depressive or stress disorders in humans within three years; however, the exploitation of this patent for the treatment of depressive and stress disorders in humans will require substantial additional capital and/or a joint venture or other type of business arrangement with a pharmaceutical company with substantially greater capital and business resources than those available to the Company. As there can be no assurances that the Company will be able to obtain the capital or business resources necessary to focus on the exploitation of this patent, it is uncertain as to when, if at all, the Company may reach any of the development or commercialization milestones under the Agreement. As of December 31, 2021 and 2020, no amounts were due under this agreement.

Effective August 20, 2018, the Company entered into an Exclusive License Agreement with Moffitt. Pursuant to the License Agreement, Moffitt granted the Company an exclusive license under certain patents owned by Moffitt (the "Licensed Patents") relating to the treatment of MDS and a non-exclusive license under inventions, concepts, processes, information, data, know-how, research results, clinical data, and the like (other than the Licensed Patents) necessary or useful for the practice of any claim under the Licensed Patents or the use, development, manufacture or sale of any product for the treatment of MDS which would otherwise infringe a valid claim under the Licensed Patents. The Company was obligated to pay Moffitt a non-refundable license issue fee of $25,000 after the first patient is entered into a Phase 1b/2 clinical trial to be managed and conducted by Moffitt. The clinical trial began at a single site in April 2019 and the first patient was entered into the clinical trial in July 2019. The Company is also obligated to pay Moffitt an annual license maintenance fee of $25,000 commencing on the first anniversary of the Effective Date and every anniversary thereafter until the Company commences payment of minimum royalty payments. The Company has also agreed to pay non-refundable milestone payments to Moffitt, which cannot be credited against earned royalties payable by the Company, based on reaching various clinical and commercial milestones aggregating $1,897,000, subject to reduction by 40% under certain circumstances relating to the status of Valid Claims, as such term is defined in the License Agreement. During the years ended December 31, 2021 and 2020, the Company recorded charges to operations of $24,999 and $25,001, respectively, in connection with its obligations under the License Agreement. As of December 31, 2021, no milestones had yet been attained.

The Company will be obligated to pay Moffitt earned royalties of 4% on worldwide cumulative net sales of royalty-bearing products, subject to reduction to 2% under certain circumstances, on a quarterly basis, with a minimum royalty payment of $50,000 in the first four years after sales commence, and $100,000 in year five and each year thereafter, subject to reduction by 40% under certain circumstances relating to the status of Valid Claims, as such term is defined in the License Agreement. The Company's obligation to pay earned royalties under the License Agreement commences on the date of the first sale of a royalty-bearing product, and shall automatically expire on a country-by-country basis on the date on which the last valid claim of the Licensed Patents expires, lapses or is declared invalid, and the obligation to pay any earned royalties under the License Agreement shall terminate on the date on which the last valid claim of the Licensed Patents expires, lapses, or is declared to be invalid in all countries.

Employment Agreements with Officers

During July and August 2020, the Company entered into one-year employment agreements with its executive officers, consisting of Dr. John S. Kovach, Eric J. Forman, Dr. James S. Miser, and Robert N. Weingarten, which provided for aggregate annual compensation of $ 640,000, payable monthly (see Note 4). The employment agreements are automatically renewable for additional one-year periods unless terminated by either party upon 60 days written notice prior to the end of the applicable one-year period, or by death, or by termination for cause. These employment agreements were automatically renewed for an additional one-year period in July and August 2021.

On April 9, 2021, the Board of Directors increased the annual compensation of Eric J. Forman, the Company's Chief Administrative Officer, Dr. James S. Miser, the Company's Chief Medical Officer, and Robert N. Weingarten, the Company's Chief Financial Officer, under the employment agreements such that the total aggregate annual compensation of all officers increased to $775,000, effective May 1, 2021.

Other Significant Agreements and Contracts

On December 24, 2013, the Company entered into an agreement with NDA Consulting Corp. for consultation and advice in the field of oncology research and drug development. As part of the agreement, NDA also agreed to cause its president, Dr. Daniel D. Von Hoff, M.D., to become a member of the Company's Scientific Advisory Committee. The term of the agreement was for one year and provided for a quarterly cash fee of $4,000. The agreement has been automatically renewed for additional one-year terms on its anniversary date since 2014. Consulting and advisory fees charged to operations pursuant to this agreement were $16,000 and $16,000 for the years ended December 31, 2021 and 2020, respectively, which were included in research and development costs in the consolidated statements of operations.

Effective September 14, 2015, the Company entered into a Collaboration Agreement with BioPharmaWorks, pursuant to which the Company engaged BioPharmaWorks to perform certain services for the Company. Those services included, among other things: (a) assisting the Company to (i) commercialize its products and strengthen its patent portfolio, (ii) identify large pharmaceutical companies with potential interest in the Company's product pipeline, and (iii) prepare and deliver presentations

concerning the Company's products; (b) at the request of the Board of Directors, serving as backup management for up to three months should the Company's Chief Executive Officer and scientific leader be temporarily unable to carry out his duties; (c) being available for consultation in drug discovery and development; and (d) identifying providers and overseeing tasks relating to clinical use and commercialization of new compounds.

BioPharmaWorks was founded in 2015 by former Pfizer scientists with extensive multi-disciplinary research and development and drug development experience. The Collaboration Agreement was for an initial term of two years and automatically renews for subsequent annual periods unless terminated by a party not less than 60 days prior to the expiration of the applicable period. In connection with the Collaboration Agreement, the Company agreed to pay BioPharmaWorks a monthly fee of $ 10,000, subject to the right of the Company to pay a negotiated hourly rate in lieu of the monthly payment and agreed to issue to BioPharmaWorks certain equity-based compensation. The Company recorded charges to operations pursuant to this Collaboration Agreement of $ 120,000 and $120,000 for the years ended December 31, 2021 and 2020, respectively, which were included in research and development costs in the consolidated statements of operations.

Effective August 12, 2020, the Company entered into a Master Service Agreement with the Foundation for Angelman Syndrome Therapy (FAST) to collaborate in supporting pre-clinical studies of the potential benefit of LB-100 in a mouse model of Angelman Syndrome (AS) as reported in The Proceedings of The National Academy of Science (Wang et al, June 3, 2019). The pre-clinical studies will be conducted at The University of California - Davis under the direction of Dr. David Segal, an internationally recognized leader in AS research. If the pre-clinical studies confirm that LB-100 reduces AS signs in rodent models, the Company has agreed to enter into discussions with FAST with respect to possible collaborations to most efficiently assess the benefit of LB-100 in patients with AS, which is a rare disease affecting an estimated one out of 12,000 to one out of 20,000 persons in the United States. The genetic cause of AS, reduced function of a specific maternal gene called Ube3, has been understood for some time, but the molecular abnormality resulting from the genetic lesion has now been shown to be increased concentrations of protein phosphatase 2A (PP2A), a molecular target of the Company's investigational compound, LB-100. The Company has agreed to provide FAST with a supply of LB-100 to be utilized in the conduct of this study, which is initially expected to be completed within three years. Conditioned on FAST's completion of this study, the Company has agreed to pay FAST five percent (5%) of all proceeds, as defined in the Master Service Agreement, received by the Company, up to a maximum of $250,000 from the exploitation of the study results.

The research team at the University of California, Davis recently completed their pre-clinical study of the potential benefit of LB-100 in a mouse model of AS, and the results are currently under review by FAST. The preliminary analysis indicates that the positive results previously reported by Chinese investigators were not confirmed in the US model. The Company is awaiting input from FAST as to whether it intends to continue to pursue pre-clinical studies of LB 100.

On October 8, 2021, the Company entered into a Development Collaboration Agreement with the Netherlands Cancer Institute, Amsterdam (NKI), one of the world's leading comprehensive cancer centers, and Oncode Institute, Utrecht, a major independent cancer research center, to identify the most promising drugs to be combined with LB-100, and potentially LB-100 analogues, to be used to treat a range of cancers, as well as to identify the specific molecular mechanisms underlying the identified combinations. The Company has agreed to fund the study and provide a sufficient supply of LB-100 to conduct the study. The study is expected to take approximately two years to conduct. During the year ended December 31, 2021, the Company incurred charges in the amount of $55,248, with respect to this agreement, which amount is included in research and development0 costs in the Company's consolidated statements of operations.

Impact of the Novel Coronavirus (Covid-19) on the Company's Business Activities

The global outbreak of the novel coronavirus (Covid-19) has led to disruptions in general economic activities worldwide, as businesses and governments have taken broad actions to mitigate this public health crisis. In light of the uncertain and continually evolving situation relating to the spread of Covid-19, this pandemic could pose a risk to the Company. The extent to which the coronavirus may impact the Company's business activities will depend on future developments, which are highly uncertain and cannot be predicted at this time. The Company intends to continue to monitor the situation and may adjust its current business plans as more information and guidance become available.

The coronavirus pandemic presents a challenge to medical facilities worldwide. As the Company's clinical trials are conducted on an outpatient basis, it is not currently possible to predict the full impact of this developing health crisis on such clinical trials, which could include delays in and increased costs of such clinical trials. Current indications from the clinical research organizations conducting the clinical trials for the Company are that such clinical trials are being delayed or extended for several months or more as a result of the coronavirus pandemic.

Over the near term, there is also significant and continuing uncertainty as to the effect that the coronavirus may have on the capital markets in general and on the amount and type of financing available to the Company in particular.

The Company is continuing to monitor the situation and will adjust its current business and financing plans as more information and guidance become available.

8. Subsequent Events

The Company performed an evaluation of subsequent events through the date of filing of these consolidated financial statements with the SEC. There were no material subsequent events which affected, or could affect, the amounts or disclosures in the consolidated financial statements.

Exhibit 21.1

Lixte Biotechnology Holdings, Inc.
Subsidiaries as of December 31, 2021

Subsidiary Name	Jurisdiction of Incorporation	Percentage Owned
Lixte Biotechnology, Inc.	Delaware.	100%

Exhibit 23.1

Consent of Independent Registered Public Accounting Firm

We hereby consent to the incorporation by reference in the Registration Statements on Form S-8 (No. 333-255407), Form S-3 (No. 333-252430) and Form S-1 (No. 333-248588) of Lixte Biotechnology Holdings, Inc. of our report dated March 21, 2022 relating to the consolidated financial statements for the years ended December 31, 2021 and 2020, which appears in this Annual Report on Form 10-K.

/s/ Weinberg & Company, P.A.

Weinberg & Company, P.A.
Los Angeles, California
March 21, 2022

Exhibit 31.1

CERTIFICATIONS OF THE CHIEF EXECUTIVE OFFICER
UNDER SECTION 302 OF THE SARBANES-OXLEY ACT OF 2002

I, John S. Kovach, Chief Executive Officer of Lixte Biotechnology Holdings, Inc. (the "Registrant"), certify that:

1. I have reviewed this Annual Report on Form 10-K for the fiscal year ended December 31, 2021 of Lixte Biotechnology Holdings, Inc. (the "Annual Report");

2. Based on my knowledge, this Annual Report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this Annual Report;

3. Based on my knowledge, the financial statements, and other financial information included in this Annual Report, fairly present in all material respects the financial condition, results of operations and cash flows of the Registrant as of, and for, the periods presented in this Annual Report;

4. I am responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the Registrant and I have:

(a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under my supervision, to ensure that material information relating to the Registrant, including its consolidated subsidiaries, is made known to me by others within those entities, particularly during the period in which this Annual Report is being prepared;

(b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under my supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;

(c) Evaluated the effectiveness of the Registrant's disclosure controls and procedures and presented in this Annual Report my conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this Annual Report based on such evaluation; and

(d) Disclosed in this report any change in the Registrant's internal control over financial reporting that occurred during the Registrant's most recent fiscal quarter (the Registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the Registrant's internal control over financial reporting; and

5. I have disclosed, based on my most recent evaluation of internal control over financial reporting, to the Registrant's auditors and the audit committee of the Registrant's Board of Directors (or persons performing the equivalent functions):

(a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the Registrant's ability to record, process, summarize and report financial information; and

(b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the Registrant's internal control over financial reporting.

Date: March 21, 2022

By: */s/ JOHN S. KOVACH*
Name: John S. Kovach
Title: President and Chief Executive Officer

Exhibit 31.2

CERTIFICATIONS OF THE CHIEF FINANCIAL OFFICER
UNDER SECTION 302 OF THE SARBANES-OXLEY ACT OF 2002

I, Robert N. Weingarten, Chief Financial Officer of Lixte Biotechnology Holdings, Inc. (the "Registrant"), certify that:

1. I have reviewed this Annual Report on Form 10-K for the fiscal year ended December 31, 2021 of Lixte Biotechnology Holdings, Inc. (the "Annual Report");

2. Based on my knowledge, this Annual Report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this Annual Report;

3. Based on my knowledge, the financial statements, and other financial information included in this Annual Report, fairly present in all material respects the financial condition, results of operations and cash flows of the Registrant as of, and for, the periods presented in this Annual Report;

4. I am responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the Registrant and I have:

(a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under my supervision, to ensure that material information relating to the Registrant, including its consolidated subsidiaries, is made known to me by others within those entities, particularly during the period in which this Annual Report is being prepared;

(b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under my supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;

(c) Evaluated the effectiveness of the Registrant's disclosure controls and procedures and presented in this Annual Report my conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this Annual Report based on such evaluation; and

(d) Disclosed in this report any change in the Registrant's internal control over financial reporting that occurred during the Registrant's most recent fiscal quarter (the Registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the Registrant's internal control over financial reporting; and

5. I have disclosed, based on my most recent evaluation of internal control over financial reporting, to the Registrant's auditors and the audit committee of the Registrant's Board of Directors (or persons performing the equivalent functions):

(a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the Registrant's ability to record, process, summarize and report financial information; and

(b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the Registrant's internal control over financial reporting.

Date: March 21, 2022

By: */s/ ROBERT N. WEINGATEN*
Name: Robert N. Weingarten
Title: Vice President and Chief Financial Officer

Exhibit 32.1

CERTIFICATIONS OF THE CHIEF EXECUTIVE OFFICER
UNDER SECTION 906 OF THE SARBANES-OXLEY ACT OF 2002

In connection with the filing by Lixte Biotechnology Holdings, Inc. (the "Registrant") of its Annual Report on Form 10-K for the fiscal year ended December 31, 2021 (the "Annual Report") with the Securities and Exchange Commission, I, John S. Kovach, certify, pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002, that:

(i) The Annual Report fully complies with the requirements of Section 13(a) or Section 15(d), as applicable, of the Securities Exchange Act of 1934, as amended; and

(ii) The information contained in the Annual Report fairly presents, in all material respects, the financial condition and results of operations of the Registrant.

A signed original of this written statement required by Section 906 has been provided to the Registrant and will be retained by the Registrant and furnished to the Securities and Exchange Commission or its staff upon request.

Date: March 21, 2022

By: */s/ JOHN S. KOVACH*
Name: John S. Kovach
Title: President and Chief Executive Officer

Exhibit 32.2

CERTIFICATIONS OF THE CHIEF FINANCIAL OFFICER
UNDER SECTION 906 OF THE SARBANES-OXLEY ACT OF 2002

In connection with the filing by Lixte Biotechnology Holdings, Inc. (the "Registrant") of its Annual Report on Form 10-K for the fiscal year ended December 31, 2021 (the "Annual Report") with the Securities and Exchange Commission, I, Robert N. Weingarten, certify, pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002, that:

(i) The Annual Report fully complies with the requirements of Section 13(a) or Section 15(d), as applicable, of the Securities Exchange Act of 1934, as amended; and

(ii) The information contained in the Annual Report fairly presents, in all material respects, the financial condition and results of operations of the Registrant.

A signed original of this written statement required by Section 906 has been provided to the Registrant and will be retained by the Registrant and furnished to the Securities and Exchange Commission or its staff upon request.

Date: March 21, 2022

By: */s/ ROBERT N. WEINGARTEN*
Name: Robert N. Weingarten
Title: Vice President and Chief Financial Officer