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

FORM 8-K

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

Date of Report (Date of earliest event reported): November 29, 2024

LIXTE BIOTECHNOLOGY HOLDINGS, INC.

DELAWARE	001-39717	20-2903526
(State or other jurisdiction of incorporation)	(Commission File Number)	(IRS Employer Identification No.)

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

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

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

☐ Written communications pursuant to Rule 425 under the Securities Act of 1933 (17 CFR 230.425)

☐ Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)

☐ Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))

☐ Pre-commencement communications pursuant to Rule 13e-4(e) under the Exchange Act (17 CFR 240.13e-4(c))

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

Title of Each Class	Trading Symbol(s)	Name of each exchange on which registered
Common Stock	LIXT	The Nasdaq Stock Market LLC
Warrant to Purchase Common Stock	LIXTW	The Nasdaq Stock Market LLC

Item 1.01 Entry into a Material Definitive Agreement.

Amendment to Development Collaboration Agreement

On October 8, 2021, Lixte Biotechnology Holdings, Inc. (the "Company") entered into a Development Collaboration Agreement (the "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.

On November 29, 2024, the parties signed an amendment ("Amendment 3") to the Collaboration Agreement. This Amendment provides for a pause in the ongoing study activities and any payments thereunder until the initiation of a Phase 1b clinical trial combining LB-100 with a WEE1 inhibitor in metastatic colorectal cancer patients. The collaboration will resume upon dosing of the first patient in this clinical trial (the "Effective Date"), with the termination date revised to be one (1) year from the dosing date of the first patient.

Under Amendment 3, the parties will seek to study translational data derived from patient samples in clinical trials at NKI. Amendment 3 provides for a reduced annual budget of €100,000, invoiced quarterly, for one year from the Effective Date as compered to the initial budget of €250,000. The foregoing description of Amendment 3 does not purport to be complete and is subject to and qualified in its entirety by the full text of Amendment 3, a copy of which is filed hereto as Exhibit 10.1.

Item 9.01 Financial Statements and Exhibits.

(d) Exhibits

Filed as part of this Current Report on Form 8-K are the exhibits listed on the accompanying Index to Exhibits, which information is incorporated herein by reference.

SIGNATURES

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

Date: December 2, 2024

LIXTE BIOTECHNOLOGY HOLDINGS, INC.

By: */s/ BASTIAAN VAN DER BAAN*
Bastiaan van der Baan,
President and Chief Executive Officer

INDEX TO EXHIBITS

Exhibit No.	Description
10.1	Amendment 3 to Development Collaboration Agreement
104	Cover Page Interactive Data File (embedded within the Inline XBRL Document)

Exhibit 10.1

AMENDMENT 3 TO DEVELOPMENT COLLABORATION AGREEMENT

THIS AMENDMENT IS MADE ON 4 OCTOBER 2024 AND ENTERED INTO BY AND BETWEEN:

1. **LIXTE BIOTECHNOLOGY HOLDINGS, INC. and its wholly owned subsidiary LIXTE BIOTECHNOLOGY, INC. (collectively "Lixte"), with its office and place of business at 680 E Colorado Blvd., Suite 180, Pasadena, CA 91101 and**
2. **STICHTING HET NEDERLANDS KANKER INSTITUUT – ANTONI VAN LEEUWENHOEK ZIEKENHUIS, a foundation incorporated under the laws of The Netherlands, with its registered office at Plesmanlaan 121, 1066 CX Amsterdam ("NKI-AVL" or "Institution") and**
3. **STICHTING ONCODE INSTITUTE, a foundation incorporated under the laws of The Netherlands, with its registered office at Jaarbeursplein 6, 3521AL, Utrecht, and registered with the chamber of commerce with number 69303010 ("Oncode").**

Each of Lixte, NKI-AVL and Oncode are referred to as a "Party" and together as, the "Parties." each a **"Party"** and together the **"Parties"**.

WHEREAS

1. Parties have entered into a Development Collaboration Agreement with effective date of 8 October 2021 (the "**Agreement**");
2. Parties wish to suspend the Agreement by adding language to cover a pause of the Study, as set forth in this amendment (the "**Amendment**");

NOW, THEREFORE, IT IS AGREED AS FOLLOWS:

1 In Section 9, the ''fifth anniversary" as termination date shall be replaced by a Suspension Date (the "Suspension Date") of 30 September 2024. The new Effective Date (the "Effective Date") shall be the date that the first patient is dosed in the Phase 1b study with the combination of LB−100 (PP2A inhibitor) and a WEE1 inhibitor in patients with metastatic colorectal cancer (the "COLLEE Trial"). The new termination date shall be one (1) year from the date of the dosing of the first patient in the COLLEE Trial.

2 The Exhibit A shall be amended with the following research activities and budget and shall read as follows:

EXHIBIT A

THE STUDY

It is proposed to focus the research collaboration on 1 topic, as described below.

1. Translational studies on patient material derived from upcoming clinical trials at NKI testing combinations of LB-100 with PDL1 or ZN-C3.

Our pre-clinical studies have identified several new aspects of LB-100 biology, including misregulation of mRNA splicing, generation of neo-antigens and a form of acquired drug resistance associated with reduced levels of tumor aneuploidy. Moreover, our data indicate that PEBP1 can be a potential biomarker of response to LB-100 (combination) therapies.

The potential performance of two clinical trials at NKI, combining LB-100 with either PDL1 or ZN-C3 provides an opportunity to ask if these aspects of LB-100 biology are also seen in patient tumor samples during LB-100

therapy. To address this, we will use biopsies from patients in NKI trials before and during LB-100 therapy for several translational studies.

1. We will perform RNAseq on RNA isolated from tumor biopsies before therapy and on treatment to ask if mRNA missplicing is also induced in patients.
2. If we see evidence for missplicing, we will perform immunopeptidomic analyses to ask if neo-antigens are presented by the MHC class I antigens on the tumor cells during LB-100 treatment.
3. We will perform low coverage Next Generation Sequencing to assess changes in aneuploidy during LB-100 treatment.
4. We will measure protein levels of PEBP1 using immunohistochemistry to ask if tumors with low PEBP1 are less responsive to LB-100 based therapies.

Budget:

Duration of the extension of the Study is one (1) year and starts upon the dosing of the first patient in the COLLEE Trial.

Annual project cost of €100.000, which includes salary cost, consumable costs, infrastructure support and overhead. This amount shall be invoiced quarterly at the end of each quarter of the extended Study.

The Study:

The research collaboration shall focus on the topics referenced in Exhibit A of this Amendment No. 3.

3 The Parties agree that the terms of this Amendment are intended to be supplemental to the terms of the Agreement. Except as specifically set forth in this Amendment, all provisions of the Agreement shall remain in full force and effect and shall apply to this Amendment as well. Capitalized terms used but not defined in this Amendment shall have the respective meaning defined in the Agreement.

4 This Amendment shall enter into force on the date of the last signature to this Amendment.

-signature page follows-

IN WITNESS WHEREOF the Parties have caused this Amendment to be executed by their duly authorised representatives.

LIXTE BIOTECHNOLOGY HOLDINGS, INC. /

LIXTE BIOTECHNOLOGY, INC.

Name(s): Bas van der Baan

Title(s): Chief Executive Officer

Date(s): 11/29/24

Signature(s):

Stichting Oncode Institute

Name: Chris de Jonghe

Title: Valorization Director

Date: 28/11/24

Signature:

STICHTING HET NEDERLANDS KANKER INSTITUUT – ANTONI VAN LEEUWENHOEK ZIEKENHUIS

Name: Henri van Luenen

Title: Director of Operations

Date: 18 November 2024

Signature:

DocuSigned by:
Henri van Luenen
9326534DE89D408...

docusign

Certificaat betreffende voltooiing

Envelop-id: 35DC7762-2524-4984-AB2B-A0D38799EE36
Onderwerp: 12943 redline_v2_Amendment 3 Lixte-NKI-Oncode project_sg2 2024.11.14 - Si...
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Certificaatpagina's: 2
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Stempel met envelop-id plaatsen: Ingeschakeld
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Opdrachtgever van envelop:
Frank Hoorn
f.hoorn@nki.nl
IP-adres: 194.171.7.38

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18-11-2024 16:37:43

Houder: Frank Hoorn
f.hoorn@nki.nl

Locatie: DocuSign

Ondertekenaargebeurtenissen	Handtekening	Tijdstempel
Henri van Luenen h.v.luenen@nki.nl Director of Operations Beveiligingsniveau: E-mailadres, Accountverificatie (geen)	DocuSigned by: Henri van Luenen 9326534DE89D408...	Verzonden: 18-11-2024 16:41:48 Bekeken: 18-11-2024 16:58:56 Ondertekend: 18-11-2024 17:00:00
	Aanneming van de handtekening Vooraf geselecteerde stijl IP-adres gebruiken: 194.171.7.39	

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Gebeurtenissen voor persoonlijke ondertekenaar	Handtekening	Tijdstempel

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Verzendingsgebeurtenissen voor vertegenwoordiger	Status	Tijdstempel

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Gecertificeerde verzendingsgebeurtenissen	Status	Tijdstempel

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Getuige evenementen	Handtekening	Tijdstempel

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