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 3, 2023**

Xilio Therapeutics, Inc.

(Exact Name of Registrant as Specified in Charter)

Delaware	**001-40925**	**85-1623397**
(State or Other Jurisdiction of Incorporation)	(Commission File Number)	(IRS Employer Identification No.)

828 Winter Street, Suite 300 **Waltham, Massachusetts**	**02451**
(Address of Principal Executive Offices)	(Zip Code)

Registrant's telephone number, including area code: **(857) 524-2466**

Not applicable
(Former Name or Former Address, if Changed Since Last Report)

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 (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(c) 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, par value $0.0001 per share	**XLO**	**Nasdaq Global Select Market**

Indicate by check mark whether the registrant is an emerging growth company as defined in Rule 405 of the Securities Act of 1933 (§230.405 of this chapter) or Rule 12b-2 of the Securities Exchange Act of 1934 (§240.12b-2 of this chapter).

Emerging growth company ☒

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

Item 8.01 Other Events.

On November 3, 2023, Xilio Therapeutics, Inc. (the "Company") issued a press release announcing preliminary data from its ongoing Phase 1/2 clinical trial evaluating XTX202 in patients with advanced solid tumors and outlining plans for potential key milestones across its clinical-stage pipeline, subject to obtaining sufficient additional capital. The full text of the press release is filed as Exhibit 99.1 to this Current Report on Form 8-K and is incorporated herein by reference. The information contained on, or accessible through, the websites referenced in the press release is not incorporated by reference into this Current Report on Form 8-K and should not be considered to be a part hereof.

Cautionary Note Regarding Forward-Looking Statements

This Current Report on Form 8-K contains forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995, as amended, including, without limitation, statements regarding plans, timing and expectations related to: activating clinical trial sites for the Phase 1 dose escalation portion of the clinical trial evaluating XTX101 in combination with atezolizumab; reporting preliminary Phase 1 safety data for XTX301; additional plans and anticipated milestones for XTX101, XTX202 and XTX301 in 2024 and 2025, subject to obtaining sufficient additional capital; the potential benefits of any of the Company's current or future product candidates in treating patients, including without limitation XTX202; and the Company's strategy, goals and anticipated financial performance, milestones, business plans and focus. The words "aim," "may," "will," "could," "would," "should," "expect," "plan," "anticipate," "intend," "believe," "estimate," "predict," "project," "potential," "continue," "seek," "target" and similar expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words. Any forward-looking statements in this Current Report on Form 8-K are based on management's current expectations and beliefs and are subject to a number of important risks, uncertainties and other factors that may cause actual events or results to differ materially from those expressed or implied by any forward-looking statements contained in this Current Report on Form 8-K, including, without limitation, risks and uncertainties related to: ongoing and planned research and development activities, including initiating, conducting or completing preclinical studies and clinical trials and the timing and results of such preclinical studies or clinical trials; the delay of any current or planned preclinical studies or clinical trials or the development of the Company's current or future product candidates; the Company's ability to obtain and maintain sufficient preclinical and clinical supply of current or future product candidates; the Company's advancement of multiple early-stage programs; interim or preliminary preclinical or clinical data or results, which may not be predictive of future preclinical or clinical data or results; the Company's ability to successfully demonstrate the safety and efficacy of its product candidates and gain approval of its product candidates on a timely basis, if at all; the potential for results from preclinical studies or clinical trials for the Company's product candidates not supporting further development of such product candidates; actions of regulatory agencies, which may affect the initiation, timing and progress of current or future clinical trials; the Company's ability to obtain, maintain and enforce patent and other intellectual property protection for current or future product candidates; the Company's ability to obtain and maintain sufficient cash resources to fund its operations beyond the end of the second quarter of 2024; the impact of international trade policies on the Company's business, including U.S. and China trade policies; and the Company's ability to maintain its clinical trial collaboration with Roche to develop XTX101 in combination with atezolizumab. These and other risks and uncertainties are described in greater detail in the sections entitled "Risk Factor Summary" and "Risk Factors" in the Company's filings with the U.S. Securities and Exchange Commission ("SEC"), including the Company's most recent Quarterly Report on Form 10-Q and any other filings that the Company has made or may make with the SEC in the future. Any forward-looking statements contained in this Current Report on Form 8-K represent the Company's views only as of the date hereof and should not be relied upon as representing its views as of any subsequent date. Except as required by law, the Company explicitly disclaims any obligation to update any forward-looking statements.

Item 9.01 Financial Statements and Exhibits.

(d) Exhibits.

Exhibit No.	Description
99.1	Press release issued by Xilio Therapeutics, Inc. on November 3, 2023
104	Cover Page Interactive Data File (embedded within the Inline XBRL document and incorporated as Exhibit 101)

SIGNATURES

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

XILIO THERAPEUTICS, INC.

Date: November 3, 2023

By: /s/ Chris Frankenfield
Chris Frankenfield
Chief Operating Officer

Exhibit 99.1

Xilio Announces Initial Monotherapy Safety and Anti-Tumor Activity Data for XTX202, a Tumor-Activated, Engineered, Beta-Gamma IL-2, in Late Line Patients with Advanced Solid Tumors

Initial evidence of dose-dependent disease control rate with 50% disease control rate at higher doses (≥2.8 mg/kg) and 31% disease control rate across all dose levels in a range of solid tumor types, including cold tumors

Treatment-related adverse events primarily Grade 1-2 at doses up to 4 mg/kg administered once every three weeks in outpatient setting, with no reported signs or symptoms of vascular leak syndrome

Two patients continuing treatment for more than 1 year, demonstrating XTX202 was well-tolerated with repeated, long-term dosing

Plan to evaluate XTX202 as a monotherapy in ongoing Phase 2 proof-of-concept trial at 4.0 mg/kg in patients with advanced melanoma and renal cell carcinoma

Xilio Therapeutics to host investor conference call and webcast on Monday, November 6, 2023 at 8:00 a.m. ET

WALTHAM, Mass., November 3, 2023 – Xilio Therapeutics, Inc. (Nasdaq: XLO), a clinical-stage biotechnology company discovering and developing tumor-activated immuno-oncology therapies for people living with cancer, today announced initial safety, pharmacokinetic (PK), pharmacodynamic (PD) and anti-tumor activity data from its ongoing Phase 1/2 clinical trial evaluating XTX202, an investigational tumor-activated, engineered, beta-gamma IL-2, in late line patients with advanced solid tumors. The data were presented at the Society for Immunotherapy of Cancer (SITC) 38th Annual Meeting in San Diego, CA being held on November 1-5, 2023.

“The newly reported data from our Phase 1/2 clinical trial for XTX202 expands the evidence across our programs supporting clinical validation of our tumor-activated technology. We observed a disease control rate of 50% at higher doses (≥2.8 mg/kg) and 31% across all dose levels in a variety of advanced and IO refractory solid tumors, including cold tumors. Importantly, treatment-related adverse events were primarily Grade 1-2 with no evidence of vascular leak syndrome reported at any dose level, and two patients are continuing on treatment for more than one year, highlighting XTX202’s potential for long-term tolerability at high doses,” said Katarina Luptakova, M.D., chief medical officer of Xilio. “In addition, an analysis of an on-treatment biopsy from a patient receiving 2.8 mg/kg of XTX202 demonstrated evidence of activation in the tumor with minimal active drug in peripheral circulation and also suggests that monotherapy doses at or above 2.8 mg/kg are approaching the optimal range to engage CD8+ T effector cell and NK cell expansion while continuing to avoid stimulation of regulatory T cells. Overall, these encouraging data support continued evaluation of XTX202 at a dose of 4.0 mg/kg in our Phase 2 trial of patients with metastatic renal cell carcinoma and unresectable or metastatic melanoma and the exploration of opportunities for combination therapy.”

Investigator Dr. Howard Kaufman, M.D., FACS of Massachusetts General Hospital commented, “As opposed to the trademark toxicities associated with recombinant IL-2, the preliminary data from the XTX202 Phase 1/2 clinical trial demonstrate a marked difference in tolerability and the potential for long-term treatment at high doses for XTX202 that has not been possible previously with systemically active IL-2 molecules. These data showcase the importance of concentrating potent IO molecules directly in the tumor microenvironment and offer an encouraging signal for continued investigation of XTX202 monotherapy at high doses along with its broad combination potential with other mechanisms of action where the stimulation of CD8+ T cells and NK cells without expansion of regulatory T cells would be synergistic.”

Data from the Ongoing Phase 1/2 Clinical Trial for XTX202

As of a data cutoff date of October 26, 2023, 62 patients with advanced solid tumors had been administered XTX202 in an outpatient setting. Fifty-four (54) patients were treated in Phase 1 monotherapy dose-escalation and dose-expansion at seven dose levels ranging from 0.27 mg/kg to 4 mg/kg administered once every three weeks (Q3W). Eight (8) patients were treated in Phase 2 monotherapy at a dose level of 1.4 mg/kg Q3W.

Patients enrolled in Phase 1 were heavily pre-treated, with 74% of patients previously treated with three or more lines of anti-cancer therapy and 69% of patients previously treated with an immunotherapy. All patients in Phase 2 had been previously treated with an immunotherapy. As of the data cutoff date, 20 patients were continuing treatment with XTX202 across the Phase 1/2 trial.

Preliminary Safety Data

Across all dose levels administered in the Phase 1/2 trial, 62 patients were evaluable for safety.

- No signs or symptoms of vascular leak syndrome were reported by investigators through the 4.0 mg/kg dose.

- XTX202 was generally well-tolerated. Treatment-related adverse events (TRAE) were primarily Grade 1 or 2, and no patients discontinued treatment due to a TRAE. Higher grade TRAEs were primarily asymptomatic laboratory abnormalities, and no Grade 5 TRAEs were reported by investigators.

- The most common TRAEs (≥10% incidence) of any grade reported by investigators across all dose levels were: fatigue (19%, no grade ≥3); pyrexia (18%, no grade ≥3); chills (16%, 2% grade 3); and lymphocyte count decreased (15%, 8% grade 3-4). Grade 3 TRAEs reported in one patient each (2%) were: diarrhea/colitis; myalgia; hypoxia; lymphopenia; and aspartate transferase (AST)/alanine transaminase (ALT) increased. Investigators reported two Grade 4 TRAEs of lymphocyte count decreased/lymphopenia, which were both transient (<3 days) and resolved without intervention, with both patients able to continue on treatment.

- Across all dose levels, only two patients (3%) had a dose reduction due to a TRAE, and only one dose-limiting toxicity was observed, which was a reversible and transient (<5 days) Grade 3 elevation of AST and ALT at the 1 mg/kg dose.

Preliminary Anti-Tumor Activity

Across all dose levels administered in the Phase 1/2 trial, 42 patients were evaluable for anti-tumor activity. Of these response-evaluable patients, 27 patients were treated at dose levels of 1.4 mg/kg or higher, including six patients treated at the 2.8 mg/kg dose level or higher.

- Data demonstrated evidence of a dose-dependent increase in disease control rate (DCR). Among the 42 response-evaluable patients treated across all dose levels, investigators reported stable disease (SD) of at least 9-weeks duration in 13 patients (31% DCR) across a range of solid tumors, including cold tumors: melanoma (n=3); renal cell carcinoma (RCC) (n=2); non-small cell lung cancer (n=2); colorectal cancer (n=2); and myoepithelial carcinoma, vaginal cancer, testicular cancer and squamous penile cancer (n=1 each). Among the six response-evaluable patients treated at the 2.8 mg/kg dose level or higher, investigators reported SD of at least 9-weeks duration in three patients (50% DCR).

- In addition, two patients were ongoing on treatment for more than one year as of the data cutoff date, including a treatment-refractory microsatellite stable colorectal cancer (MSS CRC) patient and an RCC patient, suggesting XTX202 was well-tolerated with repeated, long-term dosing in these patients.

Preliminary PK and PD Data

Preliminary PK analysis demonstrated limited XTX202 activation in peripheral circulation, including:

- Dose-proportional exposure for XTX202 with minimal levels of unmasked XTX202 detected in peripheral circulation that were consistent across dose levels.

- Approximately 15% activated XTX202 in the tumor based on an analysis of an on-treatment patient biopsy for a patient treated with XTX202 at the 2.8 mg/kg dose level as compared to <1% activated XTX202 in plasma across patients treated with XTX202 at the 2.8 mg/kg dose level for whom PK analysis was available. These data along with non-clinical pharmacology data suggest 2.8 mg/kg or higher monotherapy doses of XTX202 are approaching the optimal range to activate CD8+ effector T cells and natural killer (NK) cells in the tumor.

Consistent with IL-2 beta-gamma biology, preliminary PD analysis of four available on-treatment tumor samples showed an average increase >200% of CD8+ effector T cells in the tumor as compared to pre-treatment biopsies.

Poster Presentation

A copy of Xilio's data presentation from the SITC Annual Meeting for XTX202 is available in the "Our Approach—Publications and Presentations" section of the company's website at www.xiliotx.com.

Clinical Development Plans for XTX202

XTX202 recently cleared dose level seven (4.0 mg/kg) in Phase 1 monotherapy dose-escalation, and Xilio recently opened enrollment at a second dose level of 4.0 mg/kg in the ongoing Phase 2 monotherapy trial for XTX202. Based on the initial monotherapy data for XTX202, Xilio also plans to explore opportunities for strategic partnerships to evaluate XTX202 as a combination therapy.

Key Upcoming Milestones

As previously reported, Xilio anticipates achieving the following milestones in 2023:

- Activate clinical trial sites for the Phase 1 dose escalation portion of the clinical trial evaluating XTX101, a tumor-activated, Fc-enhanced anti-CTLA-4, in combination with atezolizumab in the fourth quarter of 2023
- Report preliminary Phase 1 safety data for XTX301, a tumor-activated, engineered IL-12, into the third dose level in the fourth quarter of 2023

In addition, subject to obtaining sufficient additional capital, Xilio today announced plans to:

- Complete Phase 1 combination dose escalation and select a recommended Phase 2 dose for XTX101 in combination with atezolizumab in the second quarter of 2024
- Subject to the results of Phase 1 combination dose escalation, initiate a Phase 2 trial for XTX101 in combination with atezolizumab in patients with MSS CRC in the third quarter of 2024
- Report initial Phase 2 data for XTX101 in combination with atezolizumab in approximately 20 patients with MSS CRC in the fourth quarter of 2024 and in approximately 20 additional patients (40 patients total) in the first quarter of 2025
- Report Phase 2 monotherapy data for XTX202 in approximately 20 patients treated at the 4.0 mg/kg dose with metastatic RCC or unresectable or metastatic melanoma in the second quarter of 2024
- Report Phase 1 safety and PK/PD data for XTX301 in advanced solid tumors in the second half of 2024

Conference Call Information

As previously announced, Xilio Therapeutics will host a live conference call and webcast Monday, November 6, 2023 at 8:00 a.m. ET to review progress across its pipeline of tumor-activated molecules, including the Phase 1/2 clinical data presented for XTX202 at the SITC Annual Meeting. The webcast may be accessed by clicking here. The webcast of the conference call will also be available under “Events and Presentations” in the Investors & Media section of the Xilio Therapeutics website at https://ir.xiliotx.com/. The archived webcast will become available on the Xilio Therapeutics website approximately two hours after the conference call and will be available for 30 days following the call.

About XTX202 and the Phase 1/2 Clinical Trials

XTX202 is an investigational tumor-activated beta-gamma biased, engineered IL-2 molecule designed to potently stimulate CD8+ effector T cells and natural killer (NK) cells without concomitant stimulation of regulatory T cells when activated (unmasked) in the tumor microenvironment (TME). The Phase 1 clinical trial for XTX202 is a first-in-human, multi-center, open-label trial designed to evaluate the safety and tolerability of XTX202 as a monotherapy in patients with advanced solid tumors. The Phase 2 clinical trial for XTX202 is a multi-center, open-label trial designed to evaluate the safety and efficacy of XTX202 as a monotherapy in patients with unresectable or metastatic melanoma and metastatic renal cell carcinoma who have progressed on standard-of-care treatment. Please refer to NCT05052268 on www.clinicaltrials.gov for additional details.

About Xilio Therapeutics

Xilio Therapeutics is a clinical-stage biotechnology company discovering and developing tumor-activated immuno-oncology (I-O) therapies with the goal of significantly improving outcomes for people living with cancer without the systemic side effects of current I-O treatments. The company is using its proprietary geographically precise solutions (GPS) platform to build a pipeline of novel, tumor-activated molecules, including antibodies, cytokines and other biologics, which are designed to optimize their therapeutic index and localize anti-tumor activity within the tumor microenvironment. Xilio is currently advancing multiple programs for tumor-activated I-O treatments in clinical development, as well as programs in preclinical development. Learn more by visiting www.xiliotx.com and follow us on LinkedIn (Xilio Therapeutics, Inc.).

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This press release contains hyperlinks to information that is not deemed to be incorporated by reference in this press release.

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