Xilio Therapeutics Announces Pipeline and Business Updates and Third Quarter 2023 Financial Results

November 9, 2023

Demonstrated initial clinical validation of tumor-selective activation technology for both XTX101, a tumor-activated, Fc-enhanced anti-CTLA-4, and XTX202, a tumor-activated, beta-gamma IL-2

On track to activate trial sites for XTX101 dose escalation in combination with atezolizumab under clinical collaboration with Roche in the fourth quarter of 2023

Reported initial Phase 1/2 data for XTX202, including a 50% disease control rate at higher doses (≥2.8 mg/kg), and plans to evaluate XTX202 as monotherapy at 4.0 mg/kg in ongoing Phase 2 trial in patients with melanoma and renal cell carcinoma

Anticipate reporting preliminary Phase 1 safety data for XTX301, a tumor-activated, engineered IL-12, in the fourth quarter of 2023

WALTHAM, Mass., Nov. 09, 2023 (GLOBE NEWSWIRE) -- 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 pipeline progress and business updates and reported financial results for the third quarter ended September 30, 2023.

“Colorectal cancer is the third largest solid tumor cancer in terms of number of patients diagnosed annually and the second leading cause of cancer-related deaths globally,” said René Russo, Pharm.D., president and chief executive officer of Xilio. “Rates of MSS colorectal cancer are rising in younger people, particularly in men under 50 years old, and patients often present with advanced Stage 4 disease along with liver metastases. Despite these alarming trends, there are few treatment options and no approved immunotherapies for these patients today. We believe the unique tumor-selective mechanism of XTX101 combined with atezolizumab has the potential to treat MSS colorectal cancer, and we are focused on initiating the co-funded collaboration with Roche to study this combination in patients. We are also encouraged by the recent Phase 1/2 data reported at SITC for XTX202 demonstrating a 50% disease control rate at higher doses (≥2.8 mg/kg), including patients with cold tumors, and a generally well-tolerated safety profile across all dose levels. We look forward to evaluating the 4 mg/kg dose for XTX202 in Phase 2 for patients with melanoma and renal cell carcinoma.”

Pipeline and Business Updates

XTX101: tumor-activated, Fc-enhanced anti-CTLA-4

XTX101 is an investigational tumor-activated, Fc-enhanced, high affinity binding anti-CTLA-4 designed to block CTLA-4 and deplete regulatory T cells when activated (unmasked) in the tumor microenvironment (TME). XTX101 is currently being evaluated at the recommended Phase 2 dose and schedule of 150 mg once every six weeks in monotherapy dose expansion of an ongoing Phase 1 clinical trial in patients with advanced solid tumors.

- In the third quarter of 2023, Xilio reported updated data from the Phase 1 trial for XTX101, including an ongoing durable confirmed partial response through 36 weeks as of an August 3, 2023 data cutoff date in a patient with Stage 4 non-small cell lung cancer treated with XTX101 monotherapy, including resolution of liver metastases.

- Additionally, Xilio recently reported pharmacokinetic (PK) data showing activation of XTX101 in two on-treatment biopsies from patients in the Phase 1 trial, which included a primary melanoma tumor and a metastatic lesion in the liver from a patient with microsatellite stable colorectal cancer (MSS CRC). For both patients, XTX101 was more than 70% activated in the tumor while maintaining a peripheral activation level of 13%, consistent with the tumor-selective design for XTX101.

- In the third quarter of 2023, Xilio entered into a clinical trial collaboration with Roche to evaluate XTX101 in combination with atezolizumab in Phase 1 combination dose escalation in patients with advanced solid tumors and a planned Phase 2 trial in patients with MSS CRC. Xilio anticipates activating clinical trial sites for the Phase 1 combination dose escalation in the fourth quarter of 2023.

In addition, subject to obtaining sufficient additional capital, Xilio 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.

XTX202: tumor-activated, engineered, beta-gamma biased IL-2

XTX202 is an investigational tumor-activated, engineered, beta-gamma biased 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 TME. XTX202 is currently being evaluated in an ongoing Phase 1/2 clinical trial in patients with advanced solid tumors.

- In November 2023, Xilio announced initial Phase 1/2 monotherapy safety, PK, pharmacodynamic (PD) and anti-tumor activity data for XTX202 at the Society for Immunotherapy of Cancer (SITC) 38th Annual Meeting. As of a data cutoff date of October 26, 2023, these data included:
    - Initial evidence of a dose-dependent increase in disease control rate (DCR) for XTX202 across all dose levels in a range of solid tumors, including cold tumors, with a 50% DCR in response-evaluable patients at higher doses (≥2.8 mg/kg) and a 31% DCR in response-evaluable patients across all dose levels, including a patient with Stage 4 MSS CRC with ongoing stable disease at 57 weeks and resolution of three out of four non-target lesions.
    - No signs or symptoms of vascular leak syndrome were reported by investigators through the 4.0 mg/kg dose. In addition, XTX202 was generally well-tolerated with treatment-related adverse events (TRAE) primarily Grade 1 or 2 and no treatment discontinuations due to TRAEs.
    - Preliminary PK analysis demonstrated tumor-selective activation of XTX202, including an approximately 40-fold higher concentration of activated XTX202 in the tumor as compared to peripheral blood based on an analysis of an on-treatment biopsy from a patient at the 2.8 mg/kg dose level, which demonstrated approximately 15% activated XTX202 in the tumor compared to <1% activated XTX202 in plasma across patients at the 2.8 mg/kg dose level.
    - 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.
    - For more information, read the press release here.
- As previously announced, 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.
- Subject to obtaining sufficient additional capital, Xilio plans to report Phase 2 monotherapy data for XTX202 in approximately 20 patients treated at the 4.0 mg/kg dose with metastatic renal cell carcinoma (RCC) or unresectable or metastatic melanoma in the second quarter of 2024.

XTX301: tumor-activated, engineered IL-12

XTX301 is an investigational tumor-activated, engineered IL-12 molecule designed to potently stimulate anti-tumor immunity and reprogram the TME of poorly immunogenic “cold” tumors towards an inflamed or “hot” state.

- Xilio is currently dosing patients in monotherapy dose escalation of an ongoing Phase 1 clinical trial evaluating the safety and tolerability of XTX301 in patients with advanced solid tumors.
- As previously announced, Xilio anticipates reporting preliminary safety data from the Phase 1 clinical trial into the third dose level in the fourth quarter of 2023.
- Subject to obtaining sufficient additional capital, Xilio plans to report Phase 1 safety and PK/PD data for XTX301 in advanced solid tumors in the second half of 2024.

Corporate Highlights

- In September 2023, Xilio announced the promotions of Katarina Luptakova, M.D., to Chief Medical Officer and Scott Coleman, Ph.D., to Chief Development Officer.

Upcoming Presentations

Xilio will present a poster for XTX101 with updated preliminary Phase 1 data and outlining the planned Phase 2 trial design at the European Society for

Medical Oncology (ESMO) Immuno-Oncology Annual Congress on December 6-8, 2023.

Title: Phase 1/2 study of XTX101, a masked, tumor-activated Fc-enhanced anti-CTLA-4 in patients with advanced solid tumors
Presentation Date and Time: Thursday, December 7, 2023, from 12:00 to 1:00 p.m. CET
Abstract number: 490

Third Quarter 2023 Financial Results

- **Cash Position:** Cash and cash equivalents were $59.8 million as of September 30, 2023, compared to $120.4 million as of December 31, 2022.

- **Research & Development (R&D) Expenses:** R&D expenses were $11.1 million for the quarter ended September 30, 2023, compared to $13.0 million for the quarter ended September 30, 2022. The decrease was primarily driven by decreased manufacturing and preclinical activities for XTX301 and a reduction of XTX101 costs due to a cost-sharing payment earned under the clinical trial collaboration with Roche. These decreases were partially offset by increases in clinical activities for XTX202 and XTX301, preclinical activities for other early programs and indirect research and development expenses.

- **General & Administrative (G&A) Expenses:** G&A expenses were $6.3 million for the quarter ended September 30, 2023, compared to $7.2 million for the quarter ended September 30, 2022. The decrease was primarily driven by a decrease in professional and consulting fees.

- **Net Loss:** Net loss was $16.7 million for the quarter ended September 30, 2023, compared to $19.8 million for the quarter ended September 30, 2022.

Financial Guidance

Xilio continues to anticipate that its existing cash and cash equivalents will be sufficient to fund its operating expenses and capital expenditure requirements into the end of the second quarter of 2024.

About XTX101 (anti-CTLA-4) and the Phase 1 Monotherapy and Phase 1/2 Combination Clinical Trials

XTX101 is an investigational tumor-activated, Fc-enhanced, high affinity binding anti-CTLA-4 monoclonal antibody designed to block CTLA-4 and deplete regulatory T cells when activated (unmasked) in the tumor microenvironment (TME). The Phase 1 clinical trial is a first-in-human, multi-center, open-label trial designed to evaluate the safety and tolerability of XTX101 for the treatment of adult patients with advanced solid tumors. Xilio has completed monotherapy dose escalation (Part 1A) and is currently enrolling patients at the recommended Phase 2 dose and schedule of 150 mg once every six weeks in monotherapy dose expansion (Part 1B). Please refer to NCT04896697 on www.clinicaltrials.gov for additional details.

In addition, Xilio plans to evaluate the safety, tolerability and efficacy of XTX101 in combination with atezolizumab (Tecentriq®) in the Phase 1/2 clinical trial. The Phase 1 portion is designed to assess the safety and tolerability of XTX101 in combination with atezolizumab in dose escalation in patients with advanced solid tumors. The planned Phase 2 portion is designed to evaluate the safety and efficacy of the combination in patients with microsatellite stable colorectal cancer (MSS CRC).

About XTX202 (IL-2) 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 XTX301 (IL-12) and the Phase 1 Clinical Trial

XTX301 is an investigational tumor-activated, engineered IL-12 molecule designed to potently stimulate anti-tumor immunity and reprogram the tumor microenvironment (TME) of poorly immunogenic “cold” tumors towards an inflamed or “hot” state. The Phase 1 clinical trial for XTX301 is a first-in-human, multi-center, open-label trial designed to evaluate the safety and tolerability of XTX301 as a monotherapy in patients with advanced solid tumors. Please refer to NCT05684965 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.).

Cautionary Note Regarding Forward-Looking Statements

This press release contains forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995, as amended, including, without limitation, statements regarding plans to activate clinical trial sites for the Phase 1 dose escalation portion of the clinical trial

evaluating XTX101 in combination with atezolizumab; plans to report preliminary Phase 1 safety data for XTX301; additional plans and anticipated milestones for XTX101, XTX202 and XTX301, subject to obtaining sufficient additional capital; the potential benefits of any of Xilio's current or future product candidates in treating patients as a monotherapy or combination therapy; the period in which Xilio expects to have cash to fund its operations; and Xilio'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 press release 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 press release, 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 Xilio's current or future product candidates; Xilio's ability to obtain and maintain sufficient preclinical and clinical supply of current or future product candidates; Xilio'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; Xilio'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; results from preclinical studies or clinical trials for Xilio's product candidates, which may not support further development of such product candidates; actions of regulatory agencies, which may affect the initiation, timing and progress of current or future clinical trials; Xilio's ability to obtain, maintain and enforce patent and other intellectual property protection for current or future product candidates; Xilio's ability to obtain and maintain sufficient cash resources to fund its operations until and beyond the end of the second quarter of 2024; the impact of international trade policies on Xilio's business, including U.S. and China trade policies; and Xilio'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 Xilio's filings with the U.S. Securities and Exchange Commission (SEC), including Xilio's most recent Quarterly Report on Form 10-Q and any other filings that Xilio has made or may make with the SEC in the future. Any forward-looking statements contained in this press release represent Xilio'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, Xilio explicitly disclaims any obligation to update any forward-looking statements.

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

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XILIO THERAPEUTICS, INC.
Condensed Consolidated Balance Sheets
(In thousands)
(Unaudited)

	September 30, 2023	December 31, 2022
Assets		
Cash and cash equivalents	$ 59,772	$ 120,385
Other assets	18,070	18,780
Total assets	$ 77,842	$ 139,165
Liabilities and Stockholders' Equity		
Liabilities	$ 25,344	$ 33,518
Stockholders' equity	52,498	105,647
Total liabilities and stockholders' equity	$ 77,842	$ 139,165

XILIO THERAPEUTICS, INC.
Condensed Consolidated Statements of Operations and Comprehensive Loss
(In thousands, except share and per share data)
(Unaudited)

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2023	2022	2023	2022
Operating expenses [1]				
Research and development	$ 11,051	$ 13,028	$ 40,400	$ 44,204
General and administrative	6,310	7,168	20,603	21,778
Total operating expenses	17,361	20,206	61,003	65,982
Loss from operations	(17,361)	(20,206)	(61,003)	(65,982)

Other income, net				
Other income, net	613	416	2,254	226
Total other income, net	613	416	2,254	226
Net loss and comprehensive loss	$ (16,748)	$ (19,790)	$ (58,749)	$ (65,756)
Net loss per share, basic and diluted	$ (0.61)	$ (0.72)	$ (2.14)	$ (2.40)
Weighted average common shares outstanding, basic and diluted	27,523,821	27,399,906	27,475,579	27,384,085

(1) Operating expenses include the following amounts of non-cash stock-based compensation expense:

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2023	2022	2023	2022
Research and development expense	$ 548	$ 594	$ 1,670	$ 1,827
General and administrative expense	1,313	1,277	3,782	4,782
Total stock-based compensation expense	$ 1,861	$ 1,871	$ 5,452	$ 6,609