Xilio Therapeutics Announces Pipeline and Business Updates for the Fourth Quarter and Full Year 2022 Financial Results

March 2, 2023

Initial clinical data from XTX101, XTX202 and XTX301 clinical trials anticipated in 2023

XTX202, a tumor-activated IL-2, demonstrated preliminary clinical pharmacodynamic evidence of tumor-selective activation, providing initial clinical platform validation

Anticipate initiating Phase 2 monotherapy clinical trial for XTX202 in melanoma and renal cell carcinoma in April 2023

Ended 2022 with $120.4 million in cash and cash equivalents; continue to anticipate cash runway into the second quarter of 2024

WALTHAM, Mass., March 02, 2023 (GLOBE NEWSWIRE) -- Xilio Therapeutics, Inc. (Nasdaq: XLO), a biotechnology company developing tumor-activated immuno-oncology therapies for people living with cancer, today announced pipeline progress and business updates and reported financial results for the fourth quarter and full year ended December 31, 2022.

“In 2022, we made significant progress against our goals, advancing the clinical development of all three of our novel tumor-activated immuno-oncology programs. Importantly, we observed promising early clinical evidence of our platform in the first two on-treatment tumor samples from patients treated with XTX202, where both the pharmacodynamics in the tumor and in the patients’ peripheral blood were consistent with our expectations for how our tumor-activated molecules are designed to perform,” said René Russo, Pharm.D., chief executive officer of Xilio. “In addition, we look forward to several anticipated milestones in 2023, including reporting clinical data from our trials for XTX101, XTX202 and XTX301.”

Pipeline and Business Updates

XTX202: tumor-activated, engineered IL-2

XTX202 is an investigational tumor-activated beta-gamma biased (non-alpha), 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). XTX202 is currently being evaluated in an ongoing Phase 1 clinical trial in patients with advanced solid tumors.

- Xilio recently completed dosing patients at the 1 mg/kg dose level (dose level four) and is currently dosing patients at the 1.4 mg/kg dose level (dose level five) in monotherapy dose-escalation (Part 1A) for the Phase 1 clinical trial.
- As of March 1, 2023, a total of 16 patients have been treated with XTX202 in the outpatient setting at five dose levels ranging from 0.27 mg/kg to 1.4 mg/kg once every three weeks (Q3W) in Part 1A for the Phase 1 clinical trial, and monotherapy dose expansion (Part 1B) is open for enrollment.
- No signs of vascular leak syndrome (VLS), including hypotension or decreases in albumin (an early sign of VLS) or hemodynamic compromise, have been observed in patients to date.
- Xilio recently reported preliminary intra-tumoral pharmacokinetics (PK) and pharmacodynamic (PD) data for two patients treated with XTX202, each of whom had an optional on-treatment tumor biopsy and are the only two patients from whom a tumor sample analysis is available to date. For each patient, the tumor sample featured increased numbers of stromal tumor infiltrating lymphocytes (TILs) and increased frequency of CD8+ effector T cells among these TILs. At the time of the tumor sample, these changes occurred in each patient in the absence of peripheral changes to CD8+ effector T cells demonstrating preliminary evidence of tumor-selective activation.
- A maximum tolerated dose has not yet been determined, and enrollment in Part 1A and Part 1B of the clinical trial is ongoing.

Xilio anticipates multiple milestones for XTX202 through the end of 2023:

- Initiate patient enrollment in a Phase 2 clinical trial evaluating XTX202 as a monotherapy in patients with unresectable or metastatic melanoma and metastatic renal cell carcinoma in April 2023.
- Report preliminary anti-tumor activity, safety, PK and PD data from the Phase 1/2 clinical trial in the third quarter of 2023. Xilio anticipates the reported data will include approximately 15-20 patients across a range of solid tumors treated at the 1 mg/kg dose or higher across all cohorts in the Phase 1/2 clinical trial.

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 recently opened clinical trial sites and is actively screening patients for enrollment at a starting dose of 5.0 ug/kg (0.005 mg/kg) in monotherapy dose-escalation for its Phase 1 clinical trial evaluating the safety and tolerability of XTX301 in patients with advanced solid tumors.
- In addition, Xilio anticipates reporting preliminary safety data from the Phase 1 clinical trial into at least the third dose level in the fourth quarter of 2023.

XTX101: tumor-activated anti-CTLA-4

XTX101, an investigational Fc-enhanced, tumor-activated anti-CTLA-4, is currently being evaluated in an ongoing Phase 1 clinical trial in patients with advanced solid tumors.

- As of March 1, 2023, 24 patients have been treated with XTX101 in the Phase 1 clinical trial. Enrollment in monotherapy dose-escalation (Part 1A) has been completed, and enrollment in monotherapy dose-expansion (Part 1B) is ongoing.
- Xilio has determined a recommended Phase 2 dose (RP2D) of 150 mg once every six weeks (Q6W).
- Xilio anticipates reporting preliminary safety, PK, PD and anti-tumor activity data from the Phase 1 clinical trial in the second quarter of 2023.
- In addition, as previously announced, Xilio plans to continue to explore strategic opportunities to advance XTX101 with a partner beyond the current Phase 1 trial.

Upcoming Presentations

Xilio today announced the acceptance of the following two abstracts for presentation at the American Association for Cancer Research (AACR) Annual Meeting 2023 in Orlando, Florida.

Xilio will present a poster highlighting preclinical data demonstrating anti-tumor activity of XTX301 in preclinical mouse models with improved tolerability compared to a systemically active IL-12 molecule.

- **Presentation title:** A half-life extended, tumor-activated IL-12 increased the infiltration of effector immune cells into the tumor microenvironment and demonstrated anti-tumor activity in syngeneic mouse models.
- **Session date and time:** Sunday, April 16, 2023, at 1:30 pm to 5:00 pm E.T.
- **Abstract number:** 587
- **Poster Board Number:** 21

Xilio will present a poster highlighting preclinical data for a discovery-stage, tumor-activated multi-functional molecule.

- **Presentation title:** Tumor-activated PD1-directed IL-2 increased antigen specific T cells in tumors and demonstrated anti-tumor activity in mice.
- **Session date and time:** Sunday, April 16, 2023, at 1:30 pm to 5:00 pm E.T.
- **Abstract number:** 572
- **Poster Board Number:** 6

Year-End and Fourth Quarter 2022 Financial Results

- **Cash Position:** Cash and cash equivalents were $120.4 million as of December 31, 2022, compared to $198.1 million as of December 31, 2021.
- **Research & Development (R&D) Expenses:** R&D expenses were $15.0 million for the quarter ended December 31, 2022, compared to $11.4 million for the quarter ended December 31, 2021. R&D expenses were $59.2 million for the year ended December 31, 2022, compared to $51.2 million for the year ended December 31, 2021. The year-over-year increase was primarily driven by increased manufacturing, preclinical and clinical development activities for XTX301, increased clinical development activities for XTX202, increased personnel-related costs and increased costs related to the company’s earlier-stage programs. These increases were partially offset by a decrease in manufacturing and preclinical expenses for XTX202 as the program advanced further into clinical development in 2022.
- **General & Administrative (G&A) Expenses:** G&A expenses were $8.2 million for the quarters ended December 31, 2022 and December 31, 2021, respectively. G&A expenses were $29.9 million for the year ended December 31, 2022, compared to $23.9 million for the year ended December 31, 2021. The year-over-year increase was primarily driven by increased personnel-related costs and an increase in expenses associated with operating as a public company.
- **Net Loss:** Net loss was $22.5 million for the quarter ended December 31, 2022, compared to $19.7 million for the quarter ended December 31, 2021. Net loss was $88.2 million for the year ended December 31, 2022, compared to $75.8 million for the year ended December 31, 2021.

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 second quarter of 2024.

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

XTX202 is an investigational tumor-activated beta-gamma biased (non-alpha), 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. Please refer to NCT05052268 on www.clinicaltrials.gov for additional details.

The planned Phase 2 clinical trial for XTX202 is a multi-center, open-label trial designed to evaluate the safety and anti-tumor activity of XTX202 as a monotherapy in patients with unresectable or metastatic melanoma and metastatic renal cell carcinoma at the recommended Phase 2 dose. 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. In November 2022, the U.S. Food and Drug Administration cleared Xilio’s investigational new drug application for the evaluation of XTX301 as a potential treatment for patients with advanced solid tumors.

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 XTX101 (anti-CTLA-4) and the Phase 1 Clinical Trial

XTX101 is an investigational Fc-enhanced, tumor-activated anti-CTLA-4 monoclonal antibody designed to deplete regulatory T cells when activated (unmasked) in the 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. Please refer to NCT04896697 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 platform to build a pipeline of novel, tumor-activated molecules, including 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 Twitter (@xiliotx) and 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, timing and expectations related to the initiation of patient enrollment in a Phase 2 clinical trial for XTX202; reporting preliminary data from the Phase 1/2 clinical trial for XTX202, including the anticipated number of patients treated at the 1 mg/kg dose level or higher; reporting preliminary safety data from the Phase 1 clinical trial for XTX301; reporting preliminary data from the Phase 1 clinical trial for XTX101; potential collaborations to advance XTX101; the potential benefits of any of Xilio’s current or future product candidates in treating patients; Xilio’s ability to fund its operating expenses and capital expenditure requirements with its existing cash and cash equivalents; 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; there can be no assurance that interim or preliminary preclinical or clinical data or results will be predictive of future preclinical or clinical data or results, including, without limitation, the preliminary intra-tumoral pharmacodynamic data reported for two patients treated with XTX202 who each had an optional on-treatment tumor biopsy and were the only two patients for whom a tumor biopsy analysis was available as of the date hereof; 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 current or future operating expenses and capital expenditure requirements; the impact of international trade policies on Xilio’s business, including U.S. and China trade policies; and Xilio’s ability to seek, establish and maintain a collaboration or partnership to develop XTX101 with a collaborator or partner. 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)

	December 31, 2022	December 31, 2021
Assets		
Cash and cash equivalents	$ 120,385	$ 198,053
Other assets	18,780	20,007
Total assets	$ 139,165	$ 218,060
Liabilities and Stockholders' Equity		
Liabilities	$ 33,518	$ 32,631
Stockholders' equity	105,647	185,429
Total liabilities and stockholders' equity	$ 139,165	$ 218,060

XILIO THERAPEUTICS, INC.

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

	Three Months Ended December 31,		Years Ended December 31,	
	2022	2021	2022	2021
Operating expenses[1]				
Research and development	$ 14,997	$ 11,352	$ 59,201	$ 51,188
General and administrative	8,170	8,204	29,948	23,856
Total operating expenses	23,167	19,556	89,149	75,044
Loss from operations	(23,167)	(19,556)	(89,149)	(75,044)
Other income (expense), net				
Other income (expense), net	701	(145)	927	(756)
Total other income (expense), net	701	(145)	927	(756)
Net loss and comprehensive loss	$ (22,466)	$ (19,701)	$ (88,222)	$ (75,800)
Net loss per share, basic and diluted	$ (0.82)	$ (0.98)	$ (3.22)	$ (13.52)
Weighted average common shares outstanding, basic and diluted	27,415,832	20,057,208	27,392,087	5,606,308

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

	Three Months Ended December 31,		Years Ended December 31,	
	2022	2021	2022	2021
Research and development expense	$ 600	$ 426	$ 2,427	$ 1,290
General and administrative expense	1,215	1,645	5,997	3,668
Total equity-based compensation expense	$ 1,815	$ 2,071	$ 8,424	$ 4,958