# Xilio Therapeutics Announces Pipeline and Business Updates and Third Quarter 2022 Financial Results

November 9, 2022

*XTX202, a tumor-activated IL-2, successfully reached target dose range of 1 mg/kg in ongoing Phase 1 clinical trial; preliminary evidence of increased CD8+ effector T cells and NK cells observed with no signs of vascular leak syndrome*

*XTX301, a tumor-activated IL-12, received FDA clearance for IND application; anticipate initiating patient dosing in Phase 1 clinical trial in first quarter of 2023*

*Plan to focus resources on advancing clinical-stage cytokine programs and will seek to partner XTX101, a tumor-activated anti-CTLA-4, to advance beyond ongoing Phase 1 monotherapy cohorts*

*$139.1 million in cash and cash equivalents as of September 30, 2022, with anticipated cash runway into the second quarter of 2024*

WALTHAM, Mass., Nov. 09, 2022 (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, business updates and reported financial results for the third quarter ended September 30, 2022.

“We continued to make meaningful progress advancing our clinical-stage cytokine programs, XTX202 and XTX301, during the quarter,” said René Russo, Pharm.D., chief executive officer of Xilio. “XTX202, our tumor-activated IL-2, has successfully reached the target dose range of 1 mg/kg in an outpatient setting in our ongoing Phase 1 clinical trial with no signs of vascular leak syndrome, and preliminary clinical data indicate evidence of IL-2 specific biology, including intra-tumoral pharmacodynamic effects in one patient for whom a tumor biopsy was available. We expect to report initial anti-tumor activity data for XTX202 in the third quarter of 2023. In addition, with the recent FDA clearance of our IND application for XTX301, our tumor-activated IL-12, we look forward to initiating a Phase 1 clinical trial in the first quarter of 2023 and evaluating the therapeutic potential of XTX301 across ‘cold’ and ‘hot’ tumor types.”

Dr. Russo continued, “While we remain enthusiastic about the potential for XTX101, our tumor-activated anti-CTLA-4, we plan to focus our existing resources on advancing our clinical-stage cytokine programs, and we will seek to partner XTX101 to advance the program beyond the ongoing Phase 1 monotherapy cohorts.”

**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. XTX202 is currently being evaluated in monotherapy dose-escalation of an ongoing Phase 1 clinical trial in patients with advanced solid tumors.

- Xilio recently began dosing patients at the 1 mg/kg dose level, which is in the target clinical dose range for XTX202, making it one of the first engineered IL-2 molecules to achieve a dose that is in line with that of traditional high dose treatment with aldesleukin.
- As of November 7, 2022, 11 patients have been treated with XTX202 as outpatients in monotherapy dose-escalation at four dose levels ranging from 0.27 mg/kg to 1.0 mg/kg.
- Preliminary analyses indicated evidence of IL-2 specific biology in patients consistent with data observed in preclinical studies, including CD8+ effector T cells and NK cells increasing in peripheral circulation steadily over time.
- No signs of vascular leak syndrome (VLS) or decreases in albumin (an early sign of VLS) have been observed in patients to date.
- In addition, Xilio today reported preliminary intra-tumoral pharmacodynamic data for a single patient treated with XTX202 who had an optional on-treatment tumor biopsy and was the first patient for whom a tumor biopsy analysis was available to date. This patient tumor biopsy featured increased numbers of stromal tumor infiltrating lymphocytes (TILs), increased frequency of CD8+ effector T cells among these TILs and decreased frequency of immune suppressive regulatory T cells (TREGs). Importantly, in this patient, at the time of the tumor biopsy, these changes occurred in the absence of peripheral changes to either CD8+ effector T cells or TREGs.
- A maximum tolerated dose has not yet been determined, and enrollment in monotherapy dose-escalation is ongoing.

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

- Initiate patient enrollment in a monotherapy expansion cohort of the Phase 1 clinical trial in the fourth quarter of 2022.
- Initiate patient enrollment in a Phase 2 monotherapy clinical trial in the first half of 2023.
- Report preliminary anti-tumor activity and safety data from the Phase 1/2 clinical trial in the third quarter of 2023.

***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 tumor microenvironment (TME) of poorly immunogenic "cold" tumors towards an inflamed, or "hot," state. IL-12 plays a key role in bridging innate and adaptive cellular immunity, making it a compelling target for immunotherapy. However, life-threatening toxicity observed with systemically active IL-12, including severe liver toxicity, have limited the therapeutic potential of IL-12 agents. Preclinical studies using a murine surrogate molecule for XTX301 demonstrated *in vivo* anti-tumor activity at doses as low as 0.04 mg/kg, and XTX301 demonstrated favorable tolerability in non-human primates at doses up to 2 mg/kg given weekly over four cycles.

- Xilio today announced that the U.S. Food and Drug Administration has cleared the company's investigational new drug (IND) application for the evaluation of XTX301 as a potential treatment for patients with advanced solid tumors.

Xilio anticipates multiple milestones for XTX301 through the end of 2023:

- Initiate patient enrollment in monotherapy dose-escalation in a Phase 1 clinical trial in the first quarter of 2023 evaluating the safety and tolerability of XTX301 in patients with advanced solid tumors.
- Report preliminary safety data from the Phase 1 clinical trial in the fourth quarter of 2023.

***XTX101: tumor-activated anti-CTLA-4***

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

- Xilio is currently dosing patients at 150 mg once every six weeks (Q6W) in the monotherapy dose-escalation cohort, which the company anticipates completing by the end of 2022. Enrollment in a monotherapy dose expansion cohort is currently ongoing.
- Preliminary pharmacokinetic (PK) analyses continue to demonstrate dose-proportional drug exposure, with limited active (unmasked) XTX101 in peripheral circulation consistent with PK data observed in preclinical studies.
- Xilio anticipates reporting preliminary data from the Phase 1 clinical trial in the second quarter of 2023.
- Xilio plans to continue to explore opportunities for strategic collaborations to advance XTX101 and does not plan to initiate an anti-PD-1 combination cohort in the Phase 1 clinical trial or initiate a Phase 2 clinical trial for XTX101 without a partner.

**Corporate Highlights**

- In September 2022, Xilio announced the appointment of Tomas J. Heyman as a member of the board of directors and John Maraganore, Ph.D. joined as a strategic advisor to the company.
- In August 2022, Xilio announced the promotion of Uli Bialucha, Ph.D. to Chief Scientific Officer and Chris Frankenfield to Chief Legal and Administrative Officer.

**Upcoming Presentations**

Xilio will present a poster outlining preclinical data demonstrating anti-tumor activity and sustained memory T-cell response in mice for XTX202 in combination with immune checkpoint blockade at the Society for Immunotherapy in Cancer 37$^{th}$ Annual Meeting.

- **Presentation title:** XTX202, a tumor-activated protein-engineered IL-2, exhibited enhanced anti-tumor activity in combination with checkpoint inhibition in mice
- **Session date and time:** Thursday, November 11, 2022, at 11:40 am to 1:10 pm and 7:30 pm to 9:00 pm ET
- **Abstract number:** 841

Uli Bialucha, Ph.D., Xilio's chief scientific officer, will present at the 14 $^{th}$ Annual Protein & Antibody Engineering Summit (PEGS) Europe meeting and will highlight preclinical data for XTX301, a tumor-activated IL-12, and Xilio's emerging research portfolio developing tumor-activated multifunctional biologics.

- **Presentation title:** Engineering Tumor-Selective Biologics for Immune-Oncology
- **Session date and time:** Monday, November 14, 2022, at 3:20 pm CET (10:20 am ET)

**Third Quarter 2022 Financial Results**

- **Cash Position:** Cash and cash equivalents were $139.1 million as of September 30, 2022, compared to $198.1 million as of December 31, 2021.
- **Research & Development (R&D) Expenses:** R&D expenses were $13.0 million for the third quarter of 2022, compared to $10.5 million for the third quarter of 2021. The increase was primarily driven by higher personnel-related costs mainly due to increased headcount and a $0.2 million increase in non-cash equity-based compensation expense, as well as increased

costs associated with XTX301 preclinical, clinical and manufacturing development activities.

- **General & Administrative (G&A) Expenses:** G&A expenses were $7.2 million for the third quarter of 2022, compared to $5.5 million for the third quarter of 2021. The increase was primarily driven by higher personnel-related costs, primarily due to increased headcount and a $0.6 million increase in non-cash equity-based compensation expense, as well as certain costs related to operating as a publicly traded company.
- **Net Loss:** Net loss was $19.8 million for the third quarter of 2022, compared to $16.3 million for the third quarter of 2021.

**Financial Guidance**

Xilio anticipates 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 the Phase 1/2 Clinical Trial for XTX202 (IL-2)**

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 1 clinical trial is designed to enroll up to approximately 119 patients across all cohorts at multiple sites in the United States, Europe and other international sites. Please refer to NCT05052268 on www.clinicaltrials.gov for additional details.

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 melanoma and renal cell carcinoma at the recommended Phase 2 dose. The Phase 2 clinical trial is designed to enroll up to approximately 70 patients in the United States and Europe. Please refer to NCT05052268 on www.clinicaltrials.gov for additional details.

**About the Planned Phase 1 Clinical Trial for XTX301 (IL-12)**

The planned 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. The Phase 1 clinical trial is designed to enroll up to approximately 94 patients across all cohorts at multiple sites in the United States.

**About the Phase 1 Clinical Trial for XTX101 (anti-CTLA-4)**

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 monotherapy expansion cohort for the Phase 1 clinical trial for XTX202, the initiation of patient enrollment in a Phase 2 clinical trial for XTX202 and reporting data from the Phase 1/2 clinical trial for XTX202; plans, timing and expectations related to the initiation of patient enrollment in the planned Phase 1 clinical trial for XTX301 and reporting data from the Phase 1 clinical trial for XTX301; plans, timing and expectations related to completing monotherapy dose-escalation for the Phase 1 clinical trial for XTX101 and reporting data from the Phase 1 clinical trial for XTX101; plans, timing and expectations related to potential collaborations to advance XTX101; plans, timing and expectations related to progressing its next research-stage program; 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 a single patient treated with XTX202 who had an optional on-treatment tumor biopsy and was the first patient 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)**

| | September 30, 2022 | December 31, 2021 |
|---|---|---|
| **Assets** | | |
| Cash and cash equivalents | $ 139,143 | $ 198,053 |
| Other assets | 18,271 | 20,007 |
| Total assets | $ 157,414 | $ 218,060 |
| **Liabilities and Stockholders’ Equity** | | |
| Liabilities | $ 31,116 | $ 32,631 |
| Stockholders’ equity | 126,298 | 185,429 |
| Total liabilities and stockholders’ equity | $ 157,414 | $ 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 September 30, | | Nine Months Ended September 30, | |
|---|---|---|---|---|
| | 2022 | 2021 | 2022 | 2021 |
| Operating expenses[(1)] | | | | |
| Research and development | $ 13,038 | $ 10,470 | $ 44,204 | $ 39,836 |
| General and administrative | 7,168 | 5,491 | 21,778 | 15,652 |
| Total operating expenses | 20,206 | 15,961 | 65,982 | 55,488 |
| Loss from operations | (20,206) | (15,961) | (65,982) | (55,488) |
| Other income (expense), net | | | | |
| Other income (expense), net | 416 | (290) | 226 | (611) |
| Total other income (expense), net | 416 | (290) | 226 | (611) |
| Net loss and comprehensive loss | $ (19,790) | $ (16,251) | $ (65,756) | $ (56,099) |
| Net loss per share, basic and diluted | $ (0.72) | $ (21.27) | $ (2.40) | $ (76.18) |
| Weighted average common shares outstanding, basic and diluted | 27,399,906 | 763,869 | 27,384,085 | 736,416 |

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

| | Three Months Ended September 30, | | Nine Months Ended September 30, | |
|---|---|---|---|---|
| | 2022 | 2021 | 2022 | 2021 |
| Research and development expense | $ 594 | $ 378 | $ 1,827 | $ 864 |
| General and administrative expense | 1,277 | 713 | 4,782 | 2,023 |
| Total equity-based compensation expense | $ 1,871 | $ 1,091 | $ 6,609 | $ 2,887 |