Xilio Therapeutics Announces Encouraging Preliminary Phase 1 Dose-Escalation Data for XTX101, a Tumor-Selective Anti-CTLA-4, and Reports Pipeline and Business Updates and Second Quarter 2022 Financial Results

August 9, 2022

XTX101, tumor-selective anti-CTLA-4, has successfully reached dose levels exceeding the target dose with limited active (unmasked) molecule in the periphery in ongoing Phase 1 clinical trial

XTX202, tumor-selective IL-2, advancing in dose-escalation of Phase 1 clinical trial

Investigational new drug application planned for XTX301, tumor selective IL-12, in fourth quarter of 2022

Uli Bialucha, Ph.D., promoted to Chief Scientific Officer and Chris Frankenfield promoted to Chief Legal and Administrative Officer

Strong financial position with $159.4 million in cash and cash equivalents as of June 30, 2022 expected to provide cash runway into first half of 2024; multiple data milestones anticipated for XTX101 and XTX202 in 2023

WALTHAM, Mass., Aug. 09, 2022 (GLOBE NEWSWIRE) -- Xilio Therapeutics, Inc. (Nasdaq: XLO), a biotechnology company developing tumor-selective immuno-oncology therapies for people living with cancer, today announced pipeline and business updates and reported financial results for the second quarter ended June 30, 2022.

"We are encouraged by the preliminary dose-escalation data reported today for XTX101, a tumor-selective anti-CTLA-4. These data provide initial clinical validation of Xilio's geographically precise solutions (GPS) platform and demonstrate that XTX101 has reached dose levels above the target dose with limited active (unmasked) molecule in peripheral circulation. Based on these data, we plan to explore a Phase 2 clinical trial for XTX101 in microsatellite stable (MSS) colorectal cancer," said René Russo, Pharm.D., chief executive officer of Xilio. "With a strong balance sheet and experienced leadership team, we are well-positioned to continue to advance our pipeline and anticipate multiple clinical data milestones for XTX101 and XTX202 in 2023."

XTX101: Preliminary Dose-Escalation Data from Ongoing Phase 1 Clinical Trial

XTX101, an Fc-enhanced, tumor-selective anti-CTLA-4, is being evaluated in a Phase 1 clinical trial in patients with advanced solid tumors. The target dose level for XTX101 of 60 mg is anticipated to provide anti-tumor activity similar to ipilimumab at 10 mg/kg (approximately 600 mg in a 60 kg patient) based on the 10 times greater potency observed for XTX101 relative to an ipilimumab analogue in preclinical studies.

As of August 5, 2022, 12 patients have been treated with XTX101 in the monotherapy dose-escalation cohort (Part 1A) at four dose levels ranging from 7 mg to 180 mg:

- The 180 mg dose level has surpassed the 60 mg target dose level for XTX101. As a result, Xilio recently expanded enrollment at the 180 mg dose level.
- A maximum tolerated dose (MTD) has not yet been determined, and enrollment in the dose-escalation cohort is ongoing.
- Preliminary pharmacokinetic (PK) analyses demonstrated dose-proportional drug exposure, with limited active (unmasked) XTX101 in peripheral circulation (range of % active in periphery: 6% - 16%) consistent with PK data observed in preclinical studies.

Additional XTX101 Development Updates

- Xilio recently opened Part 1B of the clinical trial for patient enrollment, which is a monotherapy cohort designed to evaluate anti-tumor activity, including intra-tumoral PK and pharmacodynamic (PD) data, in patients with anti-CTLA-4 sensitive tumor types, with the goal of characterizing the anti-tumor activity of XTX101 at one or more dose levels selected in Part 1A of the trial.
- Given the potential for Fc-enhanced anti-CTLA-4 agents like XTX101 to demonstrate activity in tumors that are historically resistant to immuno-oncology treatment, Xilio plans to explore evaluating XTX101 in a Phase 2 clinical trial in patients with microsatellite stable (MSS) colorectal cancer in combination with an anti-PD(L)-1.

XTX202: Phase 1 Clinical Trial Progress

XTX202, a tumor-selective, engineered IL-2, is being evaluated in a Phase 1 clinical trial in patients with advanced solid tumors. As of August 5, 2022, six patients have been treated with XTX202 as outpatients in the monotherapy dose-escalation cohort (Part 1A) at three dose levels ranging from 0.27 mg/kg to 0.53 mg/kg. An MTD has not yet been determined, and enrollment in the dose-escalation cohort is ongoing.

Upcoming Anticipated Milestones

Xilio anticipates multiple milestones through the end of 2023:

XTX101

- Report data from Part 1A of the trial (monotherapy dose-escalation cohort) supporting the recommended Phase 2 dose (RP2D) in the first half of 2023. Xilio anticipates the data for Part 1A will include available safety and anti-tumor activity, as well as peripheral PK and PD data.
- Report preliminary data from Part 1B of the trial (monotherapy expansion cohort) in the middle of 2023. Xilio anticipates the data for Part 1B will include available safety and anti-tumor activity, as well as intra-tumoral PK and PD data.
- Initiate patient enrollment in Part 1C of the trial (pembrolizumab combination cohort) in the fourth quarter of 2022.
- Report preliminary data from Part 1C of the trial in the first half of 2023. Xilio anticipates the data will include available safety and anti-tumor activity, as well as peripheral PK and PD data for XTX101 in combination with pembrolizumab.

XTX202

- Report data from Part 1A of the trial (monotherapy dose-escalation cohort) supporting the RP2D in the first half of 2023. Xilio anticipates the data will include available safety and anti-tumor activity, as well as peripheral PK and PD data.
- Initiate patient enrollment in Part 1B (monotherapy expansion cohort) in the fourth quarter of 2022. Part 1B is a monotherapy cohort designed to evaluate anti-tumor activity of XTX202 in a basket of indications potentially sensitive to IL-2.
- Report preliminary data from Part 1B of the trial (monotherapy expansion cohort) in the second half of 2023. Xilio anticipates the data will include available safety and anti-tumor activity data.
- Following the determination of a RP2D, Xilio anticipates initiating a Phase 2 monotherapy trial in the first half of 2023 designed to evaluate the safety and efficacy of XTX202 in patients with melanoma and renal cell carcinoma (RCC). Xilio anticipates enrolling a total of approximately 35 patients across both cohorts in the Phase 2 clinical trial.

XTX301

- Submit an investigational new drug application (IND) to the U.S. Food and Drug Administration (FDA) for XTX301 in the fourth quarter of 2022.
- Subject to FDA clearance of the IND, Xilio plans to initiate a Phase 1 clinical trial in the first half of 2023 evaluating the safety and tolerability of XTX301 as a monotherapy in patients with advanced solid tumors. The Phase 1 clinical trial will consist of a monotherapy dose-escalation cohort with the goal of determining a RP2D for XTX301 and monotherapy expansion cohorts at the RP2D.

Corporate Highlights

- Today, Xilio announced the promotions of Uli Bialucha, Ph.D., to chief scientific officer and Chris Frankenfield to chief legal and administrative officer, each effective as of August 8, 2022. Dr. Bialucha previously served as the company's senior vice president of research since April 2021, and Mr. Frankenfield previously served as the company's general counsel since March 2021.
- In June 2022, Xilio announced the promotion of Martin Huber, M.D., to president, the election of Paul Clancy as chair of the board of directors, and the appointment of Robert Ross, M.D., as a member of the board of directors.
- In May 2022, Xilio announced the appointment of Stacey Davis as chief business officer.

Second Quarter 2022 Financial Results

- **Cash Position:** Cash and cash equivalents were $159.4 million as of June 30, 2022, compared to $198.1 million as of December 31, 2021.
- **Research & Development (R&D) Expenses:** R&D expenses were $16.2 million for the second quarter of 2022, compared to $17.7 million for the second quarter of 2021. The decrease was primarily driven by decreased costs associated with XTX202 manufacturing and preclinical activities, partially offset by increased costs associated with XTX301, as well as higher personnel-related costs mainly due to increased headcount, including a $0.3 million increase in non-cash equity-based compensation expense.
- **General & Administrative (G&A) Expenses:** G&A expenses were $8.3 million for the second quarter of 2022, compared to $5.3 million for the second quarter of 2021. The increase was primarily driven by higher personnel-related costs, primarily due to increased headcount and a $1.4 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 $24.6 million for the second quarter of 2022, compared to $23.2 million for the second quarter of 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 first half of 2024.

About the Phase 1 Clinical Trial for XTX101

XTX101 is an investigational Fc-enhanced, tumor-selective anti-CTLA-4 monoclonal antibody designed to deplete regulatory T cells when activated selectively (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 as a monotherapy, as well as a combination therapy with pembrolizumab, for the treatment of adult patients with advanced solid tumors. The Phase 1 portion of the trial consists of three cohorts. The first cohort (Part 1A) is an accelerated and standard 3+3 dose-escalation monotherapy cohort designed to assess the tolerability of XTX101 in patients with advanced solid tumors who have progressed after receiving the standard-of-care treatment for their tumor. The second cohort (Part 1B) is a monotherapy cohort designed to evaluate evidence of anti-CTLA-4 pharmacodynamic activity in patients who have progressed on anti-PD-1 or anti-PD-L1 treatment but have not received prior treatment with an anti-CTLA-4 therapy. The third cohort (Part 1C) is a combination therapy cohort designed to evaluate XTX101 in combination with pembrolizumab in patients who have not previously been treated with an anti-PD-1 or anti-PD-L1 treatment. The Phase 1 clinical trial is designed to enroll a total of up to approximately 104 patients across all cohorts at multiple sites in the United States. Please refer to NCT04896697 on www.clinicaltrials.gov for additional details.

In May 2021, Xilio entered into a clinical trial collaboration and supply agreement with Merck & Co., Inc. (known as MSD outside the US and Canada) to explore the therapeutic potential of XTX101 in combination with pembrolizumab in patients with advanced solid tumors.

About the Phase 1 Clinical Trial for XTX202

XTX202 is an investigational tumor-selective beta-gamma biased (non-alpha), engineered IL-2 molecule designed to potently stimulate CD8 and natural killer (NK) cells without concomitant stimulation of regulatory T cells when activated selectively (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 XTX202 as a monotherapy in patients with advanced solid tumors. The Phase 1 clinical trial is designed to enroll a total of up to approximately 48 patients across all cohorts at multiple sites in the United States. Please refer to NCT05052268 on www.clinicaltrials.gov for additional details.

About XTX301

XTX301 is an investigational tumor-selective, engineered IL-12 designed to potently stimulate anti-tumor immunity and reprogram the 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, dose-limiting toxicities observed with systemically active IL-12, including life-threatening liver toxicity, have limited the therapeutic potential of IL-12 agents to date. 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 favorable tolerability. Xilio has completed GLP toxicology studies for XTX301.

About Xilio Therapeutics

Xilio Therapeutics is a clinical-stage biotechnology company focused on harnessing the immune system to achieve deep and durable clinical responses to improve the lives of patients with cancer. The company is using its proprietary geographically precise solutions (GPS) platform to rapidly engineer novel molecules, including cytokines and other biologics, that are designed to optimize their therapeutic index. These molecules are designed to localize activity within the tumor microenvironment without systemic effects, resulting in the potential to achieve enhanced anti-tumor activity. Xilio is building a pipeline of wholly owned, tumor-selective, GPS-enabled cytokine and checkpoint inhibitor product candidates, including its clinical-stage programs, XTX101, a tumor-selective anti-CTLA-4 monoclonal antibody, and XTX202, a tumor-selective IL-2, as well as its earlier pipeline, including XTX301, a tumor-selective IL-12. For more information, please visit 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 plans, timing and expectations for reporting data from Part 1A, Part 1B and Part 1C of the Phase 1 clinical trial for XTX101; plans to explore a Phase 2 clinical trial for XTX101 in MSS colorectal cancer in combination with an anti-PD(L)-1; plans, timing and expectations for reporting data from Part 1A and Part 1B of the Phase 1 clinical trial for XTX202; plans to initiate a Phase 2 clinical trial for XTX202 in patients with melanoma and RCC, including plans, timing and expectations for reporting preliminary objective response rates for both indications; plans to submit an IND to the FDA for XTX301; plans to initiate a Phase 1 clinical trial for XTX301; 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; 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 the impact of the COVID-19 pandemic on Xilio’s business, operations, strategy, goals and anticipated milestones. 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)

	June 30, 2022	December 31, 2021
Assets		
Cash and cash equivalents	$ 159,410	$ 198,053
Other assets	18,717	20,007
Total assets	$ 178,127	$ 218,060
Liabilities and Stockholders' Equity		
Liabilities	$ 33,910	$ 32,631
Stockholders' equity	144,217	185,429
Total liabilities and stockholders' equity	$ 178,127	$ 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 June 30,		Six Months Ended June 30,	
	2022	2021	2022	2021
Operating expenses [1]				
Research and development	$ 16,246	$ 17,745	$ 31,166	$ 29,366
General and administrative	8,306	5,262	14,610	10,161
Total operating expenses	24,552	23,007	45,776	39,527
Loss from operations	(24,552)	(23,007)	(45,776)	(39,527)
Other expense, net				
Other expense, net	(61)	(174)	(190)	(321)
Total other expense, net	(61)	(174)	(190)	(321)
Net loss and comprehensive loss	$ (24,613)	$ (23,181)	$ (45,966)	$ (39,848)
Net loss per share, basic and diluted	$ (0.90)	$ (31.48)	$ (1.68)	$ (55.16)
Weighted average common shares outstanding, basic and diluted	27,384,614	736,473	27,376,043	722,424

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

	Three Months Ended June 30,		Six Months Ended June 30,	
	2022	2021	2022	2021
Research and development expense	$ 637	$ 351	$ 1,233	$ 486
General and administrative expense	2,072	651	3,505	1,310

Total equity-based compensation expense	$ 2,709	$ 1,002	$ 4,738	$ 1,796