Xilio Therapeutics Announces Preliminary Clinical Data from Phase 1 Trial of XTX101, a Tumor-Activated, Fc-Enhanced Anti-CTLA-4, in Patients with Advanced Solid Tumors

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Encouraging preliminary anti-tumor activity observed in a patient with PD-L1 negative advanced non-small cell lung cancer

Favorable preliminary safety profile for XTX101 observed at the recommended Phase 2 dose of 150 mg once every six weeks

WALTHAM, Mass., May 25, 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 preliminary data from its Phase 1 clinical trial evaluating XTX101, an investigational tumor-activated, Fc-enhanced anti-CTLA-4, in patients with advanced solid tumors.

"We are encouraged by the preliminary data from the Phase 1 trial for XTX101 showing evidence of tumor-selective activation," said Martin Huber, M.D., president and head of research and development at Xilio. "Following treatment with XTX101 monotherapy at the recommended Phase 2 dose of 150 mg once every six weeks, we observed a partial response in a patient with PD-L1 negative advanced non-small cell lung cancer. Importantly, this anti-tumor activity occurred in the absence of meaningful observed activation of the immune system in the periphery, suggesting tumor-selective activation of XTX101. Based on these Phase 1 data, we plan to explore opportunities to evaluate XTX101 in combination with an anti-PD-(L)1 in historically immunotherapy-resistant tumor types."

Data from the Ongoing Phase 1 Clinical Trial for XTX101

As of a data cutoff date of May 2, 2023, 25 patients had been treated with XTX101, including dose levels ranging from 7 mg to 180 mg administered once every three weeks (Q3W) and one dose level at 150 mg administered once every six weeks (Q6W). Of these patients, 20 patients were dosed in monotherapy dose-escalation (Part 1A) and five patients were dosed in monotherapy dose-expansion (Part 1B).

Patients had a wide range of advanced and treatment-refractory solid tumors, including colorectal cancer (CRC), non-small cell lung cancer (NSCLC) and pancreatic cancer. In addition, 76% of patients had been previously treated with at least three prior lines of anti-cancer therapy, and 44% had been previously treated with at least one immuno-oncology (I-O) agent. As of the data cutoff date, three patients were continuing on treatment with XTX101, and 22 patients had discontinued treatment with XTX101.

Preliminary Safety Data

A recommended Phase 2 dose (RP2D) and schedule of 150 mg Q6W was determined based on the favorable preliminary safety, pharmacokinetic (PK) and pharmacodynamic (PD) data for XTX101. At the RP2D, no dose-limiting toxicities were observed, and there was no reported evidence of immune-related endocrine or skin adverse events (AEs) that are commonly associated with systemically active anti-CTLA-4 agents. In addition, evidence of effective masking of XTX101 was demonstrated by low levels of unmasked drug detected in peripheral circulation, and XTX101 achieved target PK exposure at the RP2D, reaching the targeted area under the curve (AUC) and peak concentration (C_{max}).

As of the data cutoff date:

- Across all dosing levels and dosing intervals, no Grade 4 or Grade 5 treatment-related AEs were reported by investigators.
- Among seven patients who received XTX101 administered at the RP2D of 150 mg on a Q6W dosing schedule, the most common treatment-related AEs (≥10% incidence) of any grade reported by investigators were diarrhea (14%), fatigue (14%) and decreased appetite (14%). In these patients, no treatment-related colitis or infusion related reaction of any grade was observed. Investigators reported only one Grade 3 treatment-related AE of diarrhea, which occurred after two doses and resolved after five days without steroid use. This patient tolerated two additional doses of XTX101 after dose reduction to 75 mg Q6W without any symptom recurrence. At the RP2D of 150 mg Q6W, this was the only patient with a dose reduction due to an AE, and no patients discontinued treatment due to a treatment-related AE.
- Among 18 patients who received XTX101 administered on a Q3W dosing schedule, the most common treatment-related AEs (≥10% incidence) of any grade reported by investigators were diarrhea (28%), colitis (28%), infusion related reaction (28%), nausea (17%), vomiting (17%) and abdominal pain (11%). Of these, investigators reported the following Grade 3 treatment-related AEs: diarrhea (6%), colitis (22%) and infusion related reaction (17%). Infusion related reactions were associated with antidrug antibodies. Across all dose levels administered Q3W, two patients had dose reductions due to AEs, and four patients discontinued treatment due to an infusion related reaction.

Preliminary Anti-Tumor Activity

A partial response was observed at nine weeks in one patient with advanced PD-L1 negative NSCLC with hepatic metastases treated with XTX101 at the 150 mg Q6W dose level and confirmed after the data cutoff date at week 27. The only treatment-related AE reported for this patient was Grade 1 fatigue. In addition, PD markers for anti-CTLA-4 reported for this patient showed minimal immune activation in peripheral circulation, demonstrating evidence of tumor-selective activation of XTX101. The patient is currently continuing on treatment with XTX101.

Clinical Development Plan for XTX101

Enrollment in monotherapy dose-expansion (Part 1B) of the Phase 1 trial is currently ongoing, with the goal of further characterizing the safety, PK and PD of XTX101 at the RP2D of 150 mg Q6W. In addition, mandatory tumor biopsies will be obtained from patients in Part 1B to examine intra-tumoral PK and PD for XTX101.

Xilio plans to continue to explore strategic opportunities to advance XTX101 with a partner beyond the current Phase 1 monotherapy cohorts, including in potential Phase 1 dose escalation evaluating XTX101 in combination with a PD-(L)1 and in a potential Phase 2 trial evaluating XTX101 in combination with a PD-(L)1 in patients with microsatellite stable CRC.

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

XTX101 is an investigational tumor-activated, Fc-enhanced anti-CTLA-4 monoclonal antibody designed to 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 patients with advanced solid tumors. The primary outcome measures were the incidence of dose-limiting toxicities (DLTs) and the incidence of treatment-related adverse events, and changes in clinical laboratory abnormalities. 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 geographically precise solutions (GPS) 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 ongoing Phase 1 monotherapy dose expansion cohort for XTX101; plans to continue to explore strategic opportunities to advance XTX101 with a partner beyond the current Phase 1 monotherapy cohorts; the potential safety and anti-tumor activity of any of Xilio's current or future product candidates in treating patients, including without limitation XTX101; 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 the following: 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 replicate in future preclinical studies or clinical trials positive data results from earlier preclinical studies or clinical trials, such as the preliminary safety and anti-tumor data observed in the Phase 1 clinical trial for XTX101 as of the data cutoff date; 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; the potential for results from preclinical studies or clinical trials for Xilio'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; 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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