Xilio Therapeutics Announces Initial Phase 2 Data for Vilastobart (XTX101), a Tumor-Activated Anti-CTLA-4, in Combination with Atezolizumab in Patients with Metastatic Microsatellite Stable Colorectal Cancer

January 21, 2025

27% preliminary response rate observed in heavily pre-treated microsatellite stable colorectal cancer (MSS CRC) patients without liver metastases

Responses were accompanied by decreases in levels of carcinoembryonic antigen (CEA) and circulating tumor DNA (ctDNA) and improvement in clinical symptoms

Data continue to demonstrate differentiated safety and tolerability profile for the combination with low incidence of immune-related adverse events

Xilio Therapeutics to host investor conference call and webcast on Wednesday, January 22, 2025, at 8:30 am ET

WALTHAM, Mass., Jan. 21, 2025 (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 initial data from its ongoing Phase 2 clinical trial evaluating vilastobart (XTX101), a tumor-activated, Fc-enhanced, high affinity binding anti-CTLA-4, in combination with atezolizumab (Tecentriq®) in patients with metastatic microsatellite stable colorectal cancer (MSS CRC). The data will be presented in a poster session (abstract #206) at the American Society of Clinical Oncology 2025 Gastrointestinal Cancer Symposium (ASCO GI) being held January 23-25, 2025, in San Francisco.

"We are very encouraged by the initial Phase 2 proof-of-concept data for the combination of vilastobart and atezolizumab in heavily pre-treated patients with MSS colorectal cancer, including partial responses accompanied by marked decreases in tumor biomarkers and improvement in clinical symptoms," said Katarina Luptakova, M.D., chief medical officer of Xilio. "We believe these data highlight the important contribution of vilastobart in this combination, as PD-(L)1 inhibitors alone have demonstrated no meaningful efficacy in patients with MSS CRC to date. The preliminary evidence of anti-tumor activity, together with continued evidence of a well-tolerated safety profile, support the potential for the combination in MSS colorectal cancer, as well as in other tumors that have traditionally been resistant to treatment with immunotherapy. We look forward to sharing additional Phase 2 data, including further follow-up, in patients with metastatic MSS CRC in the middle of this year."

"These preliminary Phase 2 data for the combination of vilastobart and atezolizumab show clear responses for patients with MSS colorectal cancer, an area of very high and increasing unmet medical need," said J. Randolph Hecht, M.D., Professor of Clinical Medicine at the David Geffen School of Medicine at UCLA, Director of the UCLA Gastrointestinal Oncology Program and the lead author for the presentation at ASCO GI. "I am excited to see these initial data highlighting the potential for vilastobart, a tumor-activated anti-CTLA-4, in combination with PD-(L)1 inhibitors to have clinically meaningful benefit in a classically immunotherapy-resistant major malignancy."

Data from Phase 2 Trial for Vilastobart (XTX101), a Tumor-Activated Anti-CTLA-4, in Combination with Atezolizumab in Patients with Metastatic MSS CRC

As of a data cutoff date of January 13, 2025, 40 patients with metastatic MSS CRC had been treated with the combination of vilastobart at a dose of 100 mg once every six weeks (Q6W) and atezolizumab at 1200 mg once every three weeks (Q3W). The median age was 55 years (ranging from 25 to 82 years), and patients were heavily pre-treated, with 70% of patients having previously received three or more prior lines of anti-cancer therapy.

Preliminary Anti-Tumor Activity Data

In patients without liver metastases, the preliminary objective response rate (ORR) was 27% with three partial responses (PRs), including two confirmed PRs. Responses were accompanied by decreases in levels of carcinoembryonic antigen (CEA) and circulating tumor DNA (ctDNA) as well as improvement in clinical symptoms.

As of the data cutoff date, 18 patients had at least one imaging scan reported and were evaluable for response assessment (per RECIST version 1.1 criteria), including 11 patients without liver metastases and seven patients with liver metastases.

In response-evaluable MSS CRC patients without liver metastases, investigators reported three PRs (two confirmed, one pending confirmation), with each patient ongoing on treatment as of the data cutoff date:

- PR (confirmed) with a 47% decrease in the sum of diameters of target lesions at 13 weeks accompanied by a decrease in levels of the serum tumor marker CEA, a multi-log fold decrease in levels of ctDNA and improvement of clinical symptoms, such as cough. CEA is a serum biomarker that is often elevated in many malignancies, including colorectal cancer, and ctDNA is a biomarker found in the bloodstream of patients with cancer.

- PR (confirmed) that continued to deepen over time with a 57% reduction in the sum of diameters of target lesions at 18

weeks accompanied by a multi-log fold decrease in ctDNA to undetectable levels and significant decrease in levels of the serum tumor marker CEA to normal values.

- PR (pending confirmation) with a 35% decrease in the sum of diameters of target lesions at nine weeks accompanied by a decrease in levels of the tumor marker CEA to normal values, a substantial decrease in levels of ctDNA and improvement of clinical symptoms, such as cough. For this patient, the initial response on CT imaging was assessed by the investigator and the radiology assessment is pending.

In addition, an MSS CRC patient without liver metastases but with a peritoneal metastasis had a 24% decrease in the sum of diameters of target lesions assessed by CT imaging at their initial nine-week scan accompanied by a decrease in levels of the serum tumor marker CEA to normal values. This patient was ongoing on treatment as of the data cutoff date.

Investigators reported stable disease in three patients without liver metastases and one patient with liver metastases, representing a preliminary disease control rate of 55% and 14%, respectively, and highlighting additional evidence of anti-tumor activity for the combination.

As of the data cutoff date, 23 patients were ongoing on treatment, including 13 patients who had not yet had a first response assessment.

Preliminary Safety Data

Safety data continue to support the potential for vilastobart to be a differentiated next-generation anti-CTLA-4 in combination with PD-(L)1 inhibitors. Consistent with the tumor-selective design for vilastobart, the combination was generally well-tolerated, with patients experiencing a low incidence of immune-related adverse events (irAEs) and only 5% of patients reporting colitis.

As of the data cutoff date, 40 patients were evaluable for safety. Across all patients treated:

- Investigators reported only six patients with Grade 3 or 4 treatment-related adverse events (AEs), including only two Grade 4 treatment-related AEs (laboratory abnormalities of thrombocytopenia and neutropenia, one patient each), and no Grade 5 treatment-related AEs.
- No patients experienced a dose reduction for vilastobart due to an AE, and only three patients discontinued treatment for the combination of vilastobart and atezolizumab due to a treatment-related AE.
- Investigators reported minimal endocrine irAEs (5%) and limited skin irAEs (13%), and the incidence of endocrine and skin irAEs was consistent with the incidence reported for atezolizumab alone.
- The most common treatment-related AEs (≥10% incidence) of any grade reported by investigators were the following: fatigue (30%); diarrhea (20%); infusion-related reactions (13%, with 8% deemed related to vilastobart and 5% deemed related to atezolizumab); pyrexia (10%); aspartate aminotransferase (AST) increase (10%); and alanine aminotransferase (ALT) increase (10%).
- The only Grade 3 treatment-related AE with ≥5% incidence reported by investigators was colitis (5%). Non-laboratory Grade 3 treatment-related AEs (<5% incidence) consisted of the following: maculopapular rash and febrile neutropenia in one patient; lower gastrointestinal hemorrhage in one patient with thrombocytopenia; and one patient with Triple M overlap syndrome (myocarditis, myositis and myasthenia gravis).

Clinical Development Plans for Vilastobart

The Phase 2 clinical trial evaluating vilastobart in combination with atezolizumab in patients with MSS CRC is currently ongoing, and Xilio expects to report updated data from the Phase 2 trial in the middle of 2025, including additional response assessments and follow-up.

These initial Phase 2 proof-of-concept data demonstrate the potential for vilastobart as a combination therapy in patients with MSS CRC and a range of other tumor types, including “cold” tumors historically resistant to immunotherapy. Based on these data, Xilio plans to seek opportunities for partnering to prioritize and expand further development beyond the initial Phase 2 proof-of-concept trial in MSS CRC.

In addition, Xilio continues to enroll patients in Phase 1C dose escalation and evaluate the combination of vilastobart at the 150 mg Q6W dose level and atezolizumab at 1200 mg Q3W.

Investor Conference Call Information

Xilio will host a conference call and webcast tomorrow (Wednesday, January 22, 2025) at 8:30 am ET to discuss the initial Phase 2 data for the combination of vilastobart and atezolizumab. Viewers can access the webcast by using this link. Listeners who require dial-in access should register here to receive a unique PIN and information to join the call. Listeners are encouraged to join at least 15 minutes prior to the scheduled start time. The webcast will also be accessible under “Events & Presentations” in the Investors & Media section of the Xilio Therapeutics website at https://ir.xiliotx.com. A replay of the webcast will be archived on the website for 30 days following the presentation.

About Vilastobart (XTX101) and the Phase 1/2 Combination Clinical Trial

Vilastobart 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 in the tumor microenvironment (TME). In 2023, Xilio entered into a co-funded clinical trial collaboration with Roche to evaluate vilastobart in combination with atezolizumab (Tecentriq®) in a multi-center, open-label Phase 1/2 clinical trial. Xilio is currently evaluating the safety of the combination in Phase 1C dose escalation in patients with advanced solid tumors and the safety and efficacy of the combination in Phase 2 in patients with metastatic microsatellite stable colorectal cancer with and without liver metastases. 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 advance a pipeline of novel, tumor-activated clinical and preclinical I-O molecules that are designed to optimize the therapeutic index by localizing anti-tumor activity within the tumor microenvironment, including tumor-activated cytokines, antibodies, bispecifics and immune cell engagers. 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, expectations and anticipated milestones for vilastobart (XTX101), including plans and timing for reporting Phase 2 clinical data for vilastobart in combination with atezolizumab in patients with MSS CRC; the potential benefits of vilastobart (as a monotherapy or combination therapy with a PD-(L)1 or other agent) or any of Xilio's other current or future product candidates in treating patients as a monotherapy or combination therapy in any indication; the ultimate safety profile of vilastobart; 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, general market conditions; 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 immune cell engager programs, including tumor-activated immune cell engagers and tumor-activated effector-enhanced immune cell engagers; initial, preliminary or interim preclinical or clinical data or results (including without limitation, the Phase 2 data for vilastobart and the preliminary investigator-reported PR awaiting radiology confirmation), which may not be replicated in or 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; the impact of international trade policies on Xilio's business, including U.S. and China trade policies; Xilio's ability to maintain its clinical trial collaboration with Roche to develop vilastobart in combination with atezolizumab; and Xilio's ability to maintain its license agreement with Gilead to develop and commercialize XTX301. 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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