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

May 31, 2025

26% preliminary objective response rate observed in heavily pre-treated patients with metastatic microsatellite stable colorectal cancer (MSS CRC) without liver metastases

Deep and durable responses ongoing for up to 37 weeks through the data cutoff, accompanied by substantial decreases in tumor biomarkers and improvements in clinical symptoms

MSS CRC patient with liver metastasis and previously reported confirmed partial response from Phase 1C (combination dose escalation) remains on treatment after more than 14 months

Combination continued to demonstrate differentiated safety and tolerability profile with low incidence of colitis and other immune-related adverse events

Data are being presented in a poster presentation today at the 2025 ASCO Annual Meeting

WALTHAM, Mass., May 31, 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 updated data from its ongoing Phase 2 clinical trial evaluating vilastobart, a tumor-activated, Fc-enhanced, high affinity binding anti-CTLA-4, in combination with atezolizumab (Tecentriq®) in patients with metastatic MSS CRC. The data will be presented in a poster session (abstract #3553) today at the American Society of Clinical Oncology (ASCO) Annual Meeting in Chicago.

“These Phase 2 data for the combination of vilastobart and atezolizumab demonstrate a meaningfully differentiated safety and tolerability profile for an anti-CTLA-4 combination therapy, together with a preliminary 26% objective response rate in patients with late-line metastatic MSS CRC without liver metastases,” said Katarina Luptakova, M.D., chief medical officer of Xilio. “Responses were deep and durable for up to 37 weeks and were accompanied by substantial decreases in tumor biomarkers such as circulating tumor DNA and improvements in clinical symptoms. Currently, no immunotherapy treatment options are available for patients with MSS CRC, an immunologically cold tumor type that is rising in incidence. We are very encouraged by these data demonstrating the potential of vilastobart, a next generation anti-CTLA-4, as a combination therapy not only for patients with MSS CRC but also a range of other tumor types traditionally resistant to treatment with immunotherapy.”

“These data further highlight the potential for vilastobart, a tumor-activated anti-CTLA-4, in combination with PD-(L)1 inhibitors to provide a meaningful clinical benefit for patients with metastatic MSS CRC without liver metastases, an area of significant and increasing unmet need, especially in younger people,” said Marwan G. Fakih, M.D., Professor in the Department of Medical Oncology and Therapeutics Research and Division Head, GI Medical Oncology at City of Hope. “I am particularly excited to see the depth and durability of responses in these late-line patients, as well as the low incidence of colitis and other immune-related adverse events that are common dose-limiting adverse events for other anti-CTLA-4 agents. Beyond MSS CRC, I believe these data support the potential for vilastobart as a combination therapy across a range of tumor types, including those where toxicity has limited the significant opportunity for anti-CTLA-4 to date.”

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

As of a data cutoff date of May 12, 2025, 44 patients with metastatic MSS CRC had been treated with the combination of vilastobart at 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 80% having previously received three or more prior lines of anti-cancer therapy.

Anti-Tumor Activity Data

In patients with metastatic MSS CRC without liver metastases, the preliminary objective response rate (ORR) was 26% with seven partial responses (PRs), including six confirmed PRs. Responses were deep and durable and were accompanied by substantial decreases in tumor biomarker levels, as well as improvements in clinical symptoms.

As of the data cutoff date, 44 patients were evaluated for response (per RECIST version 1.1 criteria), consisting of 27 patients without liver metastases and 17 patients with liver metastases.

In patients with metastatic MSS CRC without liver metastases:

- Investigators reported a preliminary ORR of 26% consisting of seven PRs (six confirmed, including two confirmed after the data cutoff, and one unconfirmed), with six of these patients still on treatment as of the data cutoff date. Responders included a patient with peritoneal metastases as well as patients with both *KRAS* mutant and *KRAS* wild type tumors. In addition, investigators reported stable disease in five patients without liver metastases, with three of these patients

remaining on treatment as of the data cutoff date.

- Responses were deep and durable, with reductions in target lesions of up to 71% from baseline and responders ongoing on treatment for up to 37 weeks as of the data cutoff date.

- Responses were accompanied by substantial decreases in tumor biomarkers for circulating tumor DNA (ctDNA) and carcinoembryonic antigen (CEA) levels. In addition, investigators observed improvements in clinical symptoms.

In patients with metastatic MSS CRC with liver metastases, investigators reported stable disease in three patients, each of whom was still on treatment as of the data cutoff date.

Safety Data

The combination of vilastobart and atezolizumab continued to demonstrate a differentiated and well-tolerated safety profile, consistent with the tumor-selective design for vilastobart. Patients experienced a low incidence of immune-mediated adverse events (imAEs), including only three patients (7%) experiencing colitis.

As of the data cutoff date, 44 patients were evaluable for safety. Across all patients treated, the combination of vilastobart at 100 mg Q6W and atezolizumab at 1200 mg Q3W was generally well-tolerated:

- Only three patients (7%) experienced colitis (one patient with Grade 1 colitis and two patients with Grade 3 colitis). In addition, only 11 patients (25%) required steroids or other immunosuppression for imAEs.
- Only two patients (5%) discontinued treatment for the combination of vilastobart and atezolizumab due to a treatment-related adverse event (AE).
- The most common treatment-related AEs (≥10% incidence) of any grade reported by investigators were fatigue (30%); infusion-related reactions (23%); diarrhea (18%); aspartate aminotransferase (AST) increase (14%); alanine aminotransferase (ALT) increase (11%); pruritus (11%); and pyrexia (11%).
- The only Grade 3 treatment-related AEs reported by investigators in more than one patient were the following (2 patients each (5%)): colitis; AST increase; ALT increase; infusion-related reactions; and white blood cell decrease.
- As previously reported, there were no Grade 5 treatment-related AEs and investigators reported only two Grade 4 treatment-related AEs (laboratory abnormalities of thrombocytopenia and neutropenia, one patient each) both of which resolved.

Phase 1C (Combination Dose Escalation) Updates

In the ongoing Phase 1C, the 150 mg Q6W dose level was recently cleared for vilastobart, and evaluation of patients enrolled in Phase 1C is ongoing.

In addition, as previously reported, an MSS CRC patient with a metastatic liver lesion enrolled in Phase 1C achieved a confirmed partial response, including full resolution of the liver lesion. As of the data cutoff date, this patient was still on treatment after more than 14 months.

Clinical Development Plans for Vilastobart

In the ongoing Phase 2 trial, Xilio recently began enrolling a cohort of patients with metastatic MSS CRC at the 150 mg Q6W dose level for vilastobart. Xilio anticipates initially enrolling approximately 10 patients with metastatic MSS CRC without liver metastases in the Phase 2 trial at the 150 mg Q6W dose level for vilastobart, with the goal of further evaluating the efficacy and safety of the combination at this higher dose level. Xilio anticipates reporting additional data from the Phase 2 trial in the first half of 2026, including data for patients at the 150 mg Q6W dose level for vilastobart.

Based on the encouraging Phase 1/2 data for vilastobart in patients with metastatic MSS CRC, Xilio is seeking opportunities to partner the vilastobart program to accelerate and expand further development.

About Vilastobart 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 efficacy and safety of the combination in Phase 2 in patients with metastatic microsatellite stable colorectal cancer (MSS CRC) 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, or masked, 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 leveraging its proprietary platform to advance a pipeline of novel, tumor-activated I-O molecules that are designed to optimize the therapeutic index by localizing anti-tumor activity within the tumor microenvironment. 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 the potential for vilastobart to provide benefit as a combination therapy in any indication or at any

dose level; the development plans for vilastobart and the timing thereof; the timing of clinical data for vilastobart; the ultimate efficacy and safety profile of vilastobart; the ability to partner the vilastobart program; 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 related to general market conditions and geopolitical uncertainties; 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 ability to advance multiple early stage masked T cell engager programs; initial, preliminary or interim preclinical or clinical data or results 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 may not support further development of such product candidates; actions of regulatory agencies 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 need to obtain additional cash resources to fund its operations beyond the first quarter of 2026, including to advance its pipeline of tumor-activated I-O molecules; the impact of international trade policies on Xilio's business, including U.S. and China trade policies; and Xilio's ability to maintain its collaboration or partnership agreements with AbbVie, Gilead and Roche. 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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