Xilio Therapeutics Highlights Portfolio of Differentiated Masked Immunotherapies at Society for Immunotherapy of Cancer (SITC) 40th Annual Meeting

November 7, 2025

Preclinical data support best-in-class potential of masked T cell engager programs and platform utilizing Xilio's ATACR and SEECR formats, including efficient masking, potent anti-tumor activity and broad therapeutic index

Phase 1 data for efarindodekin alfa, a tumor-activated IL-12, demonstrated promising monotherapy anti-tumor activity in patients with advanced solid tumors and generally well-tolerated safety profile

Phase 2 data for vilastobart, a tumor-activated, Fc-enhanced anti-CTLA-4, show potential for ctDNA as an early predictor for response to treatment with vilastobart in combination with atezolizumab in patients with MSS mCRC

WALTHAM, Mass., Nov. 07, 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 new data across its portfolio, including preclinical data highlighting the best-in-class potential for Xilio's masked T cell engager platform and programs, as well as Phase 1 data for efarindodekin alfa, a tumor-activated IL-12, and Phase 2 data related to circulating tumor DNA (ctDNA) for vilastobart, a tumor-activated, Fc-enhanced anti-CTLA-4. The data are being presented in multiple presentations at the Society for Immunotherapy of Cancer (SITC) 40th Annual Meeting, taking place from November 5-9, 2025, in National Harbor, Maryland.

"We are incredibly proud to present data at SITC showcasing the depth of our differentiated pipeline of innovative masked immunotherapies and the broad potential for our proprietary masking technology across a wide range of therapies and modalities," said René Russo, Pharm.D., president and chief executive officer of Xilio. "New preclinical data across multiple targets for our masked T cell engager programs further validate the best-in-class potential of our masking technology to not only meaningfully widen the therapeutic window for T cell engagers, but also add co-stimulation to substantially improve durability of T cell response."

Dr. Russo added, "In addition, data presented for our clinical-stage programs, efarindodekin alfa, our tumor-activated IL-12, and vilastobart, our tumor-activated, Fc-enhanced anti-CTLA-4, highlight the promising clinical profiles for each of these molecules, as well as our continued excellence in clinical execution."

Masked T Cell Engager Programs

Xilio is leveraging its proprietary, clinically validated tumor-activation platform to advance multiple preclinical programs for masked T cell engagers, including wholly owned programs targeting the tumor-associated antigens for PSMA (prostate cancer), CLDN18.2 (gastric, pancreatic, esophageal and lung cancers) and STEAP1 (prostate, colorectal and lung cancers), as well as an additional program in collaboration with AbbVie.

Xilio's masked T cell engager programs include bispecific molecules designed using its advanced tumor-activated cell engager (ATACR) format, which consists of a T cell engager with a masked CD3 targeting domain, and tri-specific molecules designed using its selective effector-enhanced cell engager (SEECR) format. The SEECR format builds upon the ATACR format by adding co-stimulatory signaling designed to further enhance the potency and durability of T cell activation.

Preclinical Data Presented at SITC

Data for Xilio's masked T cell engager programs highlight the potential for the company's masking technology to significantly expand the therapeutic window for T cell engagers and overcome the challenges associated with current, systemically active non-masked T cell engagers.

- By leveraging protease specific activity in the tumor microenvironment, Xilio's masked T cell engager molecules demonstrated potent anti-tumor activity with evidence of reduced systemic toxicity in murine models, supporting the broad applicability and potential best-in-class profile of Xilio's masked T cell engager formats across a diverse range of targets.
- The incorporation of co-stimulatory signaling in Xilio's proprietary SEECR format enhanced durability of anti-tumor activity compared with T cell engager molecules that lacked co-stimulation.

Anticipated Milestones for Masked T Cell Engager Programs

Xilio nominated a development candidate for its PSMA program (ATACR format) in the third quarter of 2025 and anticipates nominating development candidates for its CLDN18.2 program (ATACR format) in the fourth quarter of 2025 and for its STEAP1 program (SEECR format) in the first half of 2026.

Xilio anticipates advancing at least two of these programs into investigational new drug (IND) enabling studies and submitting IND applications for those programs in 2027.

Efarindodekin Alfa: Phase 1 Data in Patients with Advanced Solid Tumors

Efarindodekin alfa is an investigational tumor-activated IL-12 designed to potently stimulate anti-tumor immunity and reprogram the tumor microenvironment (TME) of poorly immunogenic "cold" tumors towards an inflamed or "hot" state. Xilio is evaluating efarindodekin alfa as a monotherapy in an ongoing Phase 1/2 clinical trial in patients with advanced solid tumors.

Phase 1 Data Presented at SITC

As of a data cutoff date of September 2, 2025, 62 patients with advanced solid tumors had been treated with efarindodekin alfa in Phase 1 monotherapy dose escalation. The median age was 66 years (ranging from 43 to 83 years), and patients were heavily pre-treated, with 89% having previously received two or more prior lines of anti-cancer therapy and 81% having received prior immunotherapy.

- In Phase 1, efarindodekin alfa has been administered at doses more than 100-fold greater than the maximum tolerated dose of recombinant human IL-12. At dose levels up to the recommended Phase 2 dose (RP2D), efarindodekin alfa has been generally well-tolerated, and treatment-related adverse events were primarily Grade 1 or 2.

- Efarindodekin alfa also demonstrated encouraging anti-tumor activity, including two partial responses (PRs) in patients with advanced solid tumors consisting of a confirmed PR in a patient with HPV-negative head and neck squamous cell carcinoma (33% decrease in target lesions), with meaningful changes in pharmacodynamic (PD) biomarkers, and an unconfirmed PR in a patient with uveal melanoma (55% decrease in target lesions).

- In addition, treatment with efarindodekin alfa induced sustained, dose-dependent interferon gamma (IFNɣ) signaling without evidence of tachyphylaxis throughout treatment cycles and transformed the TME towards an inflamed state with increased T cell infiltration and differentiation to effector memory.

- PD data for efarindodekin alfa were consistent with IL-12 biology and demonstrated that efarindodekin alfa induced robust immune cell infiltration and PD-1, PD-L1 upregulation in patient tumors.

Development Plans for Efarindodekin Alfa

Xilio has completed enrollment in the Phase 1A monotherapy dose escalation and Phase 1B monotherapy dose expansion portions of the ongoing Phase 1/2 clinical trial, and evaluation of those patients is ongoing.

In the third quarter of 2025, Xilio initiated dosing in the Phase 2 portion of the clinical trial evaluating efarindodekin alfa as a monotherapy in patients with certain advanced solid tumors.

Vilastobart: ctDNA as an Early Biomarker for Response

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 TME. Vilastobart is being evaluated in combination with atezolizumab (Tecentriq®) in Phase 1C (combination dose escalation) in patients with advanced solid tumors and in Phase 2 in patients with microsatellite stable (MSS) metastatic colorectal cancer (mCRC).

Phase 2 ctDNA Data Presented at SITC

New data assessed plasma ctDNA using the Guardant360 Liquid (Infinity) assay and demonstrated the potential of ctDNA as a biomarker predictive of early response to treatment with vilastobart in combination with atezolizumab.

- Radiographic responses were accompanied by deep reductions in ctDNA (≥75% reduction), which generally occurred before radiographic responses, and ctDNA reductions were significantly associated with best overall response in the 23 patients with MSS mCRC without liver metastases who were evaluable for ctDNA and response correlation analysis as of a data cutoff date of May 12, 2025.

- In addition, investigators reported two patients with endoscopic complete responses (CRs) with a lack of detectable tumor in lesion biopsies and a reduction in ctDNA to undetectable levels, as of a data cutoff date of October 20, 2025.

Presentation Details

Xilio's presentations at SITC are listed below, including a separately announced late-breaking poster presentation for its vilastobart program. Copies of these presentations will be available under the "Our Approach—Presentations & Publications" section of the Xilio Therapeutics website at www.xiliotx.com.

- *Poster presentation:* Masked T Cell Engagers Designed to Drive Potent Synthetic Anti-Tumor Immunity with Favorable Tolerability (Abstract # 972; Saturday, Nov. 8, 2025)

- *Poster presentation:* XTX301, a Tumor-Activated Interleukin-12 (IL-12), Demonstrated IL-12 Pharmacology in Patients with Advanced Solid Tumors: Pharmacodynamic Data from First-in-Human Phase 1 Study (Abstract # 567; Friday, Nov. 7, 2025)

- *Poster presentation:* ctDNA as a Potential Surrogate Biomarker for Response to Combination Vilastobart and Atezolizumab in Heavily Pretreated Microsatellite Stable (MSS) Metastatic Colorectal Cancer (mCRC) (Abstract # 541; Friday, Nov. 7, 2025)

- *Late-breaking poster presentation:* Plasma Tumor Mutational Burden (pTMB) Enriched for Response to Vilastobart in Combination with Atezolizumab in Patients with Microsatellite Stable (MSS) Metastatic Colorectal Cancer (mCRC) (Abstract # 1315; Friday, Nov. 7, 2025)

About Efarindodekin Alfa (XTX301) and the Phase 1/2 Clinical Trial

Efarindodekin alfa (XTX301) is an investigational masked IL-12 designed to potently stimulate anti-tumor immunity and reprogram the tumor microenvironment (TME) of poorly immunogenic "cold" tumors towards an inflamed or "hot" state. Xilio is currently evaluating the safety and tolerability of efarindodekin alfa as a monotherapy in patients with advanced solid tumors in the Phase 1 portion of a first-in-human, multi-center, open-label Phase 1/2 clinical trial and the safety and efficacy of efarindodekin alfa as a monotherapy in the Phase 2 portion in patients with advanced solid tumors. The Phase 2 portion of the trial is anticipated to enroll approximately 40 patients in specific tumor types at multiple sites in the United States. Please refer to NCT05684965 on www.clinicaltrials.gov for additional details.

Efarindodekin alfa has not been approved by any regulatory agency, and its efficacy and safety have not been established.

About the Gilead License Agreement for Efarindodekin Alfa

In March 2024, Xilio entered into an exclusive global license agreement with Gilead to develop and commercialize efarindodekin alfa (XTX301), a tumor-activated IL-12, and specified other molecules directed to IL-12.

Xilio is responsible for conducting clinical development for efarindodekin alfa through the initial Phase 2 portion of the ongoing Phase 1/2 clinical trial. Following the delivery by Xilio of a specified clinical data package for efarindodekin alfa related to the Phase 1/2 clinical trial, Gilead can elect to transition responsibilities for the development and commercialization of efarindodekin alfa to Gilead, subject to the terms of the license agreement and payment by Gilead of a $75.0 million transition fee.

If Gilead exercises its option for efarindodekin alfa, Xilio will be eligible to receive up to $500.0 million in specified development, regulatory and sales-based milestones and will be eligible to receive tiered royalties ranging from high single digits to mid-teens on annual global net product sales.

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 microsatellite stable (MSS) metastatic colorectal cancer (mCRC) 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 of Xilio's masked T cell engager programs and platform; the ultimate safety and efficacy of efarindodekin alfa, vilastobart, or any masked T cell engager molecules in any indication; the potential for ctDNA as an early predictor of response to treatment with vilastobart in combination with atezolizumab in patients with MSS CRC; Xilio's development plans and the timing thereof; 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 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.

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