UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
WASHINGTON, D.C. 20549

FORM 8-K

CURRENT REPORT
Pursuant to Section 13 or 15(d)
of the Securities Exchange Act of 1934

Date of report (Date of earliest event reported): **November 7, 2025**

Xilio Therapeutics, Inc.
(Exact Name of Registrant as Specified in Charter)

Delaware	**001-40925**	**85-1623397**
(State or Other Jurisdiction of Incorporation)	(Commission File Number)	(IRS Employer Identification No.)

828 Winter Street, Suite 300 **Waltham, Massachusetts**	**02451**
(Address of Principal Executive Offices)	(Zip Code)

Registrant's telephone number, including area code: **(857) 524-2466**

Not applicable
(Former Name or Former Address, if Changed Since Last Report)

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions (*see* General Instruction A.2. below):

☐ Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)

☐ Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)

☐ Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))

☐ Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

Securities registered pursuant to Section 12(b) of the Act:

Title of each class	Trading symbol(s)	Name of each exchange on which registered
Common stock, par value $0.0001 per share	**XLO**	**Nasdaq Capital Market**

Indicate by check mark whether the registrant is an emerging growth company as defined in Rule 405 of the Securities Act of 1933 (§230.405 of this chapter) or Rule 12b-2 of the Securities Exchange Act of 1934 (§240.12b-2 of this chapter).

Emerging growth company ☒

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. ☐

Item 7.01. Other Events.

On November 7, 2025, Xilio Therapeutics, Inc. (the "Company") issued a press release announcing new data related to high plasma tumor mutational burden from its ongoing Phase 2 clinical trial evaluating vilastobart in combination with atezolizumab in patients with microsatellite stable metastatic colorectal cancer, a copy of which is furnished as Exhibit 99.1 to this Current Report on Form 8-K.

Also on November 7, 2025, the Company issued a press release announcing updated data across its portfolio, including preclinical data for the Company's masked T cell engager platform and programs, as well as updated Phase 1 data for efarindodekin alfa, and Phase 2 data related to circulating tumor DNA for vilastobart, a copy of which is furnished as Exhibit 99.2 to this Current Report on Form 8-K.

These data are presented in poster presentations at the Society for Immunotherapy of Cancer (SITC) 40thAnnual Meeting. The information in Item 7.01 of this Current Report on Form 8-K, including Exhibit 99.1 and Exhibit 99.2, is being furnished and shall not be deemed "filed" for purposes of Section 18 of the Securities Exchange Act of 1934, as amended (the "Exchange Act"), or otherwise subject to the liabilities of that section, nor shall it be deemed incorporated by reference in any filing under the Exchange Act or the Securities Act of 1933, as amended, except as expressly set forth by specific reference in such filing.

Item 9.01. Financial Statements and Exhibits.

(d) Exhibits.

Exhibit Number	Description
99.1	Press release issued by Xilio Therapeutics, Inc. on November 7, 2025
99.2	Press release issued by Xilio Therapeutics, Inc. on November 7, 2025
104	Cover Page Interactive Data File (formatted as Inline XBRL with applicable taxonomy extension information contained in Exhibits 101)

SIGNATURES

Pursuant to the requirements of the Securities Exchange Act of 1934, as amended, the registrant has duly caused this report to be signed on its behalf by the undersigned hereunto duly authorized.

XILIO THERAPEUTICS, INC.

Date: November 7, 2025

By: /s/ Caroline Hensley
Caroline Hensley
Chief Legal Officer

Xilio Therapeutics Announces Late-Breaking Phase 2 Data for Vilastobart in Patients with MSS mCRC and High Plasma Tumor Mutational Burden at Society for Immunotherapy of Cancer (SITC) 40th Annual Meeting

40% ORR in heavily pre-treated patients with MSS mCRC without liver metastases and with high plasma tumor mutational burden (TMB)

Estimate 55% of patients with MSS CRC have high plasma TMB, representing a meaningful population with high unmet need

Company to host conference call and webcast on Monday, November 10, 2025, at 4:30 p.m. ET with leading cancer experts to review the data

WALTHAM, Mass., November 7, 2025 -- 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 from its ongoing Phase 2 clinical trial evaluating vilastobart, a tumor-activated, Fc-enhanced anti-CTLA-4, in combination with atezolizumab (Tecentriq®) in patients with microsatellite stable (MSS) metastatic colorectal cancer (mCRC). A 40% objective response rate (ORR) was demonstrated in heavily pre-treated patients with MSS mCRC without liver metastases and with high plasma TMB (≥10 mutations/Mb), as well as a statistically significant correlation between plasma TMB status and response. These new clinical data are being presented in a late-breaking poster presentation (Abstract # 1315) today at the Society for Immunotherapy of Cancer (SITC) 40th Annual Meeting, taking place from November 5-9, 2025, in National Harbor, Maryland.

“These compelling new Phase 2 data for vilastobart in combination with atezolizumab demonstrated a 40% objective response rate in heavily pre-pretreated patients with MSS mCRC without liver metastases and with high plasma TMB, signifying an important advance in our understanding of response to novel immunotherapy in MSS mCRC,” said Katarina Luptakova, M.D., chief medical officer of Xilio. “In addition, these data showed a statistically significant correlation between plasma-based TMB and response. We estimate that approximately 55% of patients with MSS CRC have high plasma TMB, representing a meaningful patient population who could ultimately benefit from combination treatment with vilastobart and a substantially greater prevalence of patients with high TMB than previously estimated using traditional tissue-based assays.”

“These new data highlight the potential to use plasma TMB as a predictive biomarker and identify patients with MSS mCRC who may benefit from treatment with vilastobart, a tumor-activated anti-CTLA-4, in combination with a PD-(L)1,” said Diwakar Davar, M.D., Associate Professor of Medicine, Clinical Director of the Melanoma Program and Medical Oncologist/Hematologist at the UPMC Hillman Cancer Center. “This biomarker guided approach, utilizing a feasible and reproducible biomarker, together with vilastobart’s differentiated safety profile, continue to support the promising opportunity for vilastobart in combination with PD-(L)1 or PD1-VEGF in MSS mCRC, as well as other tumor types.”

Promising Opportunity for Plasma-Based TMB as a Biomarker Predictive of Response to Combination Treatment with Vilastobart in Patients with MSS mCRC

Tissue-based TMB has demonstrated potential as a biomarker predictive of response to immune checkpoint inhibitors in many tumor types. However, tissue-based TMB assays have not shown predictive utility in MSS mCRC historically, and these tissue-based assays may underestimate the mutational burden in patients. In particular, tissue-based assays are limited to evaluating mutations in a single-site biopsy

specimen, which is typically taken once at the time of diagnosis, and cannot account for tumor heterogeneity or changes in TMB over time.

Newer plasma-based assays show potential to better assess TMB status and be used as a biomarker predictive of response in patients with MSS mCRC. These plasma-based assays are more sensitive than traditional tissue-based assays in that plasma-based TMB assays provide a comprehensive assessment of mutational load and account for tumor heterogeneity. In addition, plasma can be readily obtained from blood samples throughout the course of treatment, accounting for changes in TMB over time without the need for invasive procedures.

Approximately 55% of non-MSI-H CRC patients were plasma TMB high (>10 mutations/Mb) based on an analysis of the GuardantINFORM real-world clinical-genomic database in approximately 8,000 patients who received the Guardant360 Liquid (Infinity) assay and who had non-MSI-H disease and a reportable TMB result. In contrast, historical data for tissue-based TMB assays have suggested <10% of patients with MSS mCRC were TMB-high.

These data support the meaningful opportunity to use plasma-based TMB as a biomarker predictive of response to combination treatment with vilastobart in patients with MSS mCRC.

New Data from Phase 2 Trial for Vilastobart in Combination with Atezolizumab in Patients with MSS mCRC Without Liver Metastases and with High Plasma TMB

As of a data cutoff date of May 12, 2025, 44 patients with MSS mCRC 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), including 27 patients without liver metastases. Patients were heavily pre-treated, with 80% having previously received three or more prior lines of anti-cancer therapy.

In a retrospective analysis, 24 patients without liver metastases were evaluable for plasma TMB status. Baseline plasma TMB was assessed using the Guardant360 Liquid (Infinity) assay, and patients with TMB ≥10 mutations/Mb were defined as having high plasma TMB.

Clinical Efficacy Data

40% ORR in patients with MSS mCRC without liver metastases and high plasma TMB, with statistically significant correlation (p=0.05) between plasma TMB status and response.

- 40% ORR in plasma TMB-high patients, consisting of six partial responses (PRs), with five confirmed PRs (with one confirmed after the data cutoff date) and one unconfirmed PR.
- In patients evaluable for plasma TMB status, 62.5% were TMB-high. All responders who were evaluable for plasma TMB status were TMB-high, and the correlation between plasma TMB status and response was statistically significant (p=0.05).
- As previously reported, responses were deep and durable, with reductions in target lesions of up to 71% from baseline.

Safety Data

Vilastobart in combination with atezolizumab continued to demonstrate a differentiated and generally well-tolerated safety profile. Treatment-related adverse events (AEs) were primarily Grade 1 or 2, consistent with the tumor-activated design for vilastobart.

As previously reported, across all patients treated as of a data cutoff date of May 12, 2025 (n=44), the combination of vilastobart at 100 mg Q6W and atezolizumab at 1200 mg Q3W was generally well-tolerated. Treatment-related AEs were primarily Grade 1 or 2. Only two patients (5%) discontinued treatment for the combination of vilastobart and atezolizumab due to a treatment-related AE, and only three patients (7%) experienced colitis of any grade.

Clinical Development Plans for Vilastobart

Based on the promising clinical activity and safety profile demonstrated by vilastobart as a combination therapy, including in patients who had high plasma TMB, Xilio is actively seeking a partner to develop vilastobart in combination with PD-(L)1 or PD1-VEGF in MSS CRC and other tumor types.

Investor Conference Call Information

Xilio will host a conference call and webcast on Monday, November 10, 2025, at 4:30 p.m. ET. The webcast will feature a discussion with expert clinicians Aparna Parikh, M.D., Associate Professor of Medicine, Harvard Medical School, Program Director, GI Medical Oncology, Colorectal, Anal, and Neuroendocrine, Director of the MGB Global Cancer Care Program, Mass General Brigham Cancer Institute, Boston, MA, and Diwakar Davar, M.D., Associate Professor of Medicine, Clinical Director of the Melanoma Program and Medical Oncologist/Hematologist at the UPMC Hillman Cancer Center, Pittsburgh, PA. During the webcast, Xilio will discuss the new Phase 2 combination data for vilastobart and the promising opportunity to use high plasma TMB as a predictive biomarker for response, as well as briefly highlight additional data updates presented at SITC across the company's portfolio of differentiated masked immunotherapies.

Viewers can access the webcast by using this link. 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 ir.xiliotx.com. A replay of the webcast will be archived on the website for 30 days following the presentation.

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 for plasma-based TMB as a predictive biomarker for response in patients with MSS mCRC; the potential for vilastobart to provide benefit as a combination therapy in patients with MSS mCRC or any other indication; the ultimate efficacy and safety profile of vilastobart; the plans and 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, interim, or retrospective 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.

This press release contains hyperlinks to information that is not deemed to be incorporated by reference in this press release.

Tecentriq® is a registered trademark of Genentech USA, Inc., a member of the Roche Group.

Investor Contact
Alex Lobo, Precision AQ
alex.lobo@precisionaq.com

Media Contact
Josie Butler, 1AB
josie@1abmedia.com

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

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., November 7, 2025 -- 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.

This press release contains hyperlinks to information that is not deemed to be incorporated by reference in this press release.

Tecentriq® is a registered trademark of Genentech USA, Inc., a member of the Roche Group.

Investor Contact
Alex Lobo, Precision AQ
alex.lobo@precisionaq.com

Media Contact
Josie Butler, 1AB
josie@1abmedia.com