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): **March 9, 2026**

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** (Address of Principal Executive Offices)	**02451** (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 Regulation FD Disclosure.

From time to time, the Company presents or distributes slide presentations to the investment community to provide updates and summaries of its business. The Company is posting a copy of its current corporate investor presentation to the "Investors & Media" portion of its website at https://ir.xiliotx.com. The information contained on, or accessible through, the Company's website is not incorporated by reference into this Current Report on Form 8-K and should not be considered to be a part hereof. A copy of the presentation is furnished as Exhibit 99.1 to this Current Report on Form 8-K.

The information in Item 7.01 of this Current Report on Form 8-K, including Exhibit 99.1, is being furnished and shall not be deemed "filed" for purposes of Section 18 of 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, except as expressly set forth by specific reference in such filing.

Item 9.01 Financial Statements and Exhibits.

(d) Exhibits.

Exhibit No.	Description
99.1	Corporate slide presentation of Xilio Therapeutics, Inc. dated March 9, 2026
104	Cover Page Interactive Data File (embedded within the Inline XBRL document and incorporated as Exhibit 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: March 9, 2026

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

Unlocking the Potential of Immuno-Oncology Therapies

March 9, 2026

Forward-Looking Statements and Disclaimers

This presentation 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: development timelines and anticipated milestones for Xilio's programs; the ultimate safety, efficacy, and potential benefits of any of Xilio's current or future product candidates in any indication; any potential indications or commercial opportunities of our product candidates; the timing and receipt of future payments under Xilio's collaboration or partnership agreements with AbbVie and Gilead; Xilio's preliminary, unaudited, estimated cash balance as of December 31, 2025 and the sufficiency of, and the period in which Xilio expects to have, cash to fund its operations; the availability of additional capital including the timing and potential receipt of cash proceeds upon the exercise of series C warrants; 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 presentation 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 presentation, 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; Xilio's ability to regain and maintain compliance with the Nasdaq listing standards; 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 masked T cell engager programs; initial, preliminary, interim, or retrospective preclinical or clinical data or results, 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; Xilio's need to obtain additional cash resources to fund its operations, 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 presentation 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.

Certain information contained in this presentation relates to or is based on studies, publications, surveys and other data obtained from third-party sources and Xilio's own internal estimates and research. While Xilio believes these third-party studies, publications, surveys and other data to be reliable as of the date of this presentation, Xilio has not independently verified, and makes no representation as to the adequacy, fairness, accuracy or completeness of, any information obtained from third-party sources. In addition, no independent source has evaluated the reasonableness or accuracy of Xilio's internal estimates or research and no reliance should be made on any information or statements made in this presentation relating to or based on such internal estimates and research.

This presentation contains trademarks, trade names and service marks of other companies, which are the property of their respective owners.

Leveraging our **clinically-validated masking technology** to develop **tumor-selective I-O therapies** designed to **unlock the potential for durable efficacy** by focusing anti-tumor activity **within the tumor microenvironment without severe side effects** associated with systemically active I-O agents

x·ilio® THERAPEUTICS

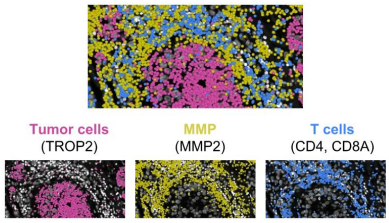
I-O: immuno-oncology

Xilio's Clinically-Validated Masking Technology and Capabilities are Being Applied Across Diverse Mechanisms and Architectures for I-O Therapies

Masking Technology and Capabilities

- ✓ Xilio's masked molecules are activated in the tumor by **matrix metalloproteases (MMP) and other tumor-specific proteases**
- ✓ Proprietary **masking libraries** and **custom computational design workflows**
- ✓ Proprietary **preclinical and clinical translational models**

In situ mRNA expression in human breast cancer



Clinical Validation and Top-Tier Strategic Partnerships

- ✓ **Clinically-validated protease cleavage elements** with demonstrated **tumor-selective activation in patients** (~300 patients treated to date across clinical programs)
- ✓ **Deep and durable confirmed responses** with **differentiated safety and tolerability** demonstrated **in the clinic across multiple tumor types** for vilastobart and efarindodekin alfa

GILEAD

Option to license IL-12

abbvie

Multi-program collaboration for masked antibody-based program and option to license masked cell engagers

Roche

Co-funded clinical trial supply agreement for atezolizumab

Broad Application Across Architectures and Targets

- ✓ **Highly developable architectures** with **low immunogenicity** in the clinic and **excellent stability** enable broad optionality for molecule designs and targets

Bispecifics
XTX501
PD-1 / masked IL-2

T Cell Engagers
PSMA+STEAP1 and CLDN18.2
Masked T cell engagers +/- co-stimulation

Cytokines
Efarindodekin Alfa
Masked IL-12

Antibodies
Vilastobart
Masked, Fc-enhanced anti-CTLA-4

Left panel: Spatial gene expression analysis using Xenium platform (10X Genomics) showing expression of TROP2 (TACSTD2, pink), MMP2 (yellow), CD4 and CD8A (blue) in a human breast cancer sample. https://www.10xgenomics.com/products/xenium-in-situ/human-breast-dataset-explorer; Xenium Explorer Version 1.2.0; Instrument Analysis Version: Xenium- 1.0.1
CLDN18.2: claudin 18.2; PSMA: prostate-specific membrane antigen; STEAP1: six transmembrane epithelial antigen of prostate 1

Advancing Pipeline of Masked I-O Therapies, Including Bispecifics and Multi-Specifics

Program	Tumor Types	Discovery	IND Enabling	Phase 1	Phase 2	Anticipated Milestones
Wholly-Owned Programs						
XTX501 *Bispecific PD-1 / masked IL-2*	NSCLC and other solid tumors					IND submission: **mid 2026** Initial Phase 1 data: **2H 2027** (1)
PSMA+STEAP1 *Multi-specific, masked T cell engager with co-stimulation (SEECR)*	Prostate					DC nomination: **Q2 2026** IND submission: **2027**
CLDN18.2 *Masked T cell engager*	Gastric, pancreatic, esophageal, lung					IND submission: **2027**
Collaborations and Partnerships						
Efarindodekin alfa *Masked IL-12*	Advanced solid tumors					GILEAD Option data package: **1H 2027** (2)
Undisclosed *Masked T cell engager*	Undisclosed					abbvie (3)
Undisclosed *Masked antibody*	Undisclosed					abbvie (3)

1. Subject to clearance of the IND by the FDA.
2. Exclusive global option to license with Gilead.
3. Collaboration with AbbVie for a licensed masked antibody program and option to license masked T cell engager program. AbbVie has the right to nominate up to two additional masked T cell engager programs.

DC: development candidate; IND: investigational new drug application; NSCLC: non-small cell lung cancer

Strong Financial Position and Proven Capabilities to Advance Pipeline of Potential Best-in-Class Masked I-O Therapies

Cash Runway Through End of 2027

- **Strong financial position** through AbbVie, Gilead and Roche collaborations and equity financings
- **$137.5M in estimated cash and cash equivalents as of December 31, 2025** (1)
  - $40M in gross proceeds received in February 2026 from follow-on offering
- **Multiple opportunities to extend cash runway:**
  - Up to $36.2M in additional gross proceeds by end of 2026 if Series C warrants exercised
  - AbbVie development milestones and option fees in 2026 and 2027
  - Gilead option fee in 2027 ($75M)

Upcoming Milestones

2026

- ❑ **PSMA+STEAP1 SEECR:** DC nomination **(Q2 2026)**
- ❑ **XTX501:** IND submission **(mid 2026)**
- ❑ **XTX501:** initiate Phase 1 trial in NSCLC **(2H 2026)** (2)

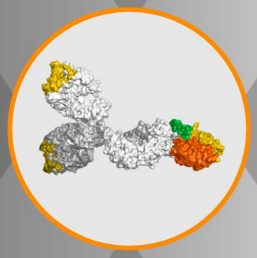
2027

- ❑ **Efarindodekin alfa:** deliver option data package to Gilead **(1H 2027)**
- ❑ **XTX501:** report initial Phase 1 data in NSCLC **(2H 2027)** (2)
- ❑ **PSMA+STEAP1 SEECR:** IND submission **(2027)**
- ❑ **CLDN18.2:** IND submission **(2027)**

1. The cash and cash equivalents information above is a preliminary estimate based on unaudited information and management estimates for the year ended December 31, 2025, is not a comprehensive statement of our financial results as of and for the fiscal year ended December 31, 2025, and may change. Our independent registered public accounting firm has not conducted an audit or review of, and does not express an opinion or any other form of assurance with respect to, this preliminary estimate.
2. Subject to clearance of the IND by the FDA.

XTX501

Bispecific PD-1 / masked IL-2



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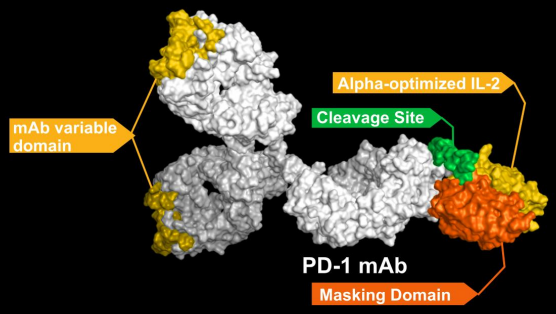
XTX501: Bispecific PD-1 / Masked IL-2 Designed to Enable High Potency IL-2 With Antibody-Like PK and Tolerability

XTX501: Bispecific PD-1 / Masked IL-2



- Designed to direct IL-2 to PD1+ T cells and induce a differentiated, enhanced immune response to cancer compared to PD-(L)1 monotherapy or combination of PD-(L)1 + IL-2
- Non-masked PD-1 in Fc-silenced heterodimeric IgG1 backbone fused to potent alpha-optimized IL-2 with affinity-tuned, VHH-based mask

Masking Optimized IL-2 Enables Potential for Meaningful Differentiation

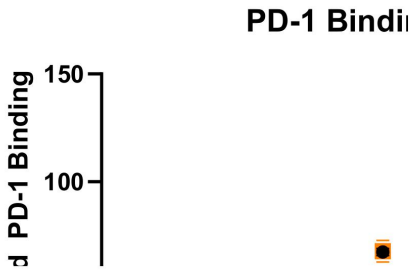
- **Targeted delivery of IL-2 to PD-1+ cells selectively expands tumor-specific CD8+ cells** to increase tumor cell killing efficiency without activating peripheral T cells that drive toxicity
- Incorporates a **high potency IL-2 variant affinity tuned with optimal receptor binding profile** for IL-2 alpha / beta / gamma
- **Plan to evaluate in Phase 1 trial in NSCLC with potential to expand in other tumor types**
- **Potential for XTX501 be a foundational "backbone" therapy** for combination treatment

IND submission anticipated mid 2026
Initial clinical data anticipated 2H 2027

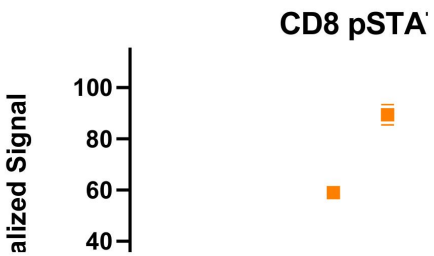
Expected timing for initial clinical data for XTX501 is subject to clearance of the IND by the FDA.
mAb: monoclonal antibody; PK: pharmacokinetics

XTX501 Exhibited a Potential Best-in-Class Profile Based on Preclinical Data

XTX501 and XTX500 (1) Bind PD-1 With Higher Affinity Than Other PD-1 Bispecifics



XTX501 was Effectively Masked and XTX500 (Unmasked XTX501) was Most Potent Activator of T Cells



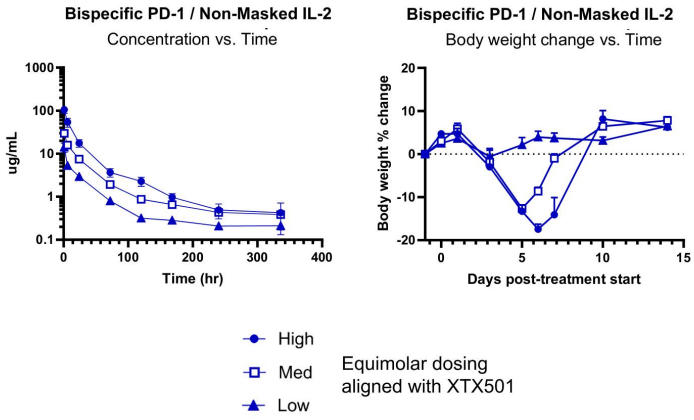
XTX501 Demonstrated Meaningfully Differentiated Overall Preclinical Activity Profile

	PD-1 Binding *mean K_d (nM)*	Potency *CD8 T Cell pSTAT5 EC50 (nM)*
XTX501 (masked)	0.165	>1000
XTX500 (1) (non-masked)	0.111	0.168
IBI363	1.025	31

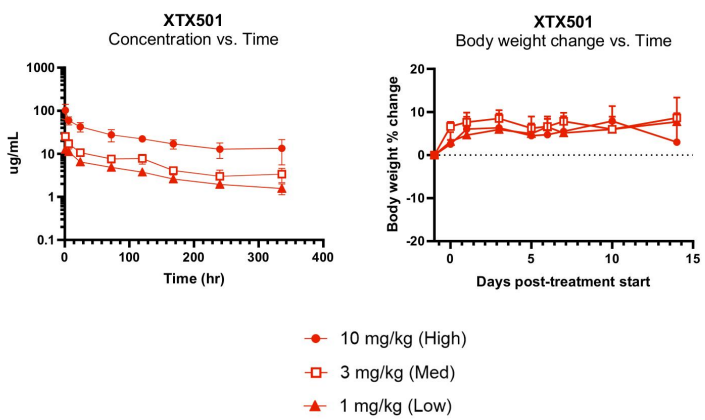
1. XTX500 is XTX501 without a mask.
2. Preclinical data based on analogues of IBI363 generated by Xilio for research use only.

XTX501 Demonstrated Antibody-Like PK and Favorable Tolerability Preclinically

Bispecific PD-1 / Non-Masked IL-2 Was Rapidly Cleared and Poorly Tolerated



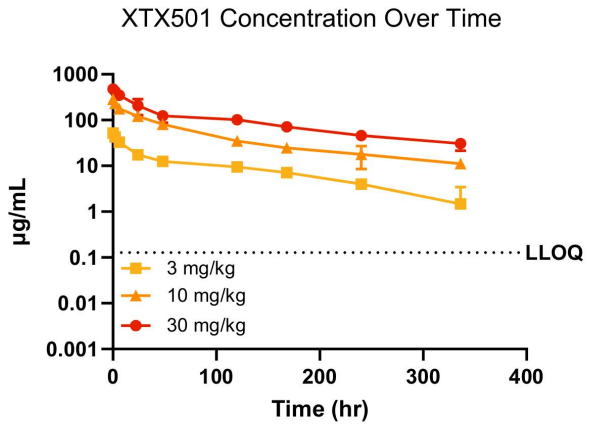
XTX501 Achieved Antibody-Like Exposures and Was Well-Tolerated Even at High Doses



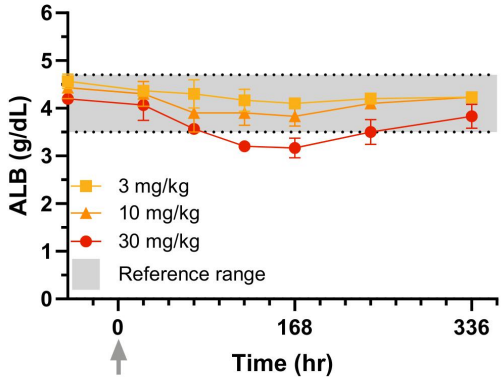
XTX501 exposure after a single 10, 3 or 1 mg/kg intravenous injection in non-tumor bearing C57BL/6-hFcRn mice. Non-masked PD-1/IL-2 exposure after a single equal molar dose of 9.25, 2.75 or 0.92 mg/kg intravenous injection in non-tumor bearing C57BL/6-hFcRn mice. Body weight data are displayed until day 14, the last time point measured.

XTX501 Demonstrated Favorable Tolerability in NHP

Single Dose PK Study in NHP Tolerable Up to 30 mg/kg



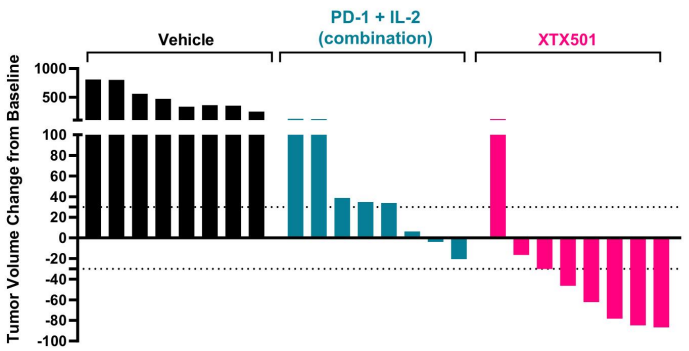
Minimal Effects of XTX501 on Serum Albumin (i.e., No Signs of Vascular Leak Syndrome)



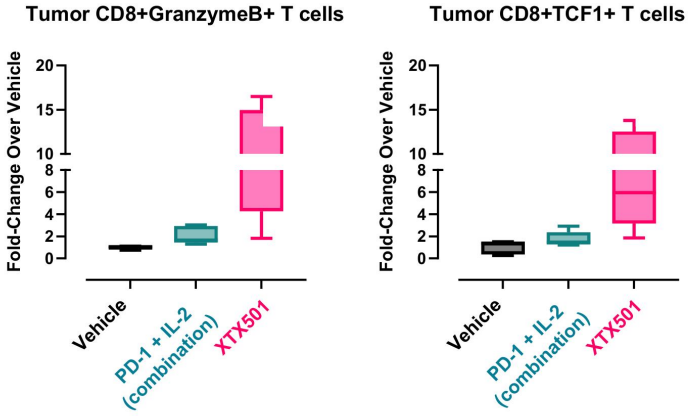
Female cynomolgus monkeys were given a single 30-minute intravenous infusion of XTX501 at 3, 10, and 30 mg/kg and samples were collected for PK and clinical pathology analysis. **Left panel:** PK analysis demonstrated dose-proportional exposure and linear elimination across all doses tested. **Right panel:** Albumin remained within normal ranges in animals receiving 3 and 10 mg/kg PD-1/IL-2 and was transiently decreased in animals receiving 30 mg/kg XTX501. There were no observed adverse clinical observations, and transaminase levels remained within normal ranges for all animals. Data generated with analogue of XTX501 with minimal variance in amino acid sequence.
LLOQ: lower limit of quantification; NHP: non-human primates

XTX501 Demonstrated Differentiated Preclinical Pharmacology Compared to PD-1 and Combination of PD-1 + IL-2, Suggesting Enhanced Anti-Tumor Immunity

XTX501 Demonstrated Enhanced Robust Preclinical Activity Compared to Combination of PD-1 + IL-2



XTX501 Demonstrated Increased Intra-Tumoral Cytotoxic and TCF1+ Stem-Like T Cells



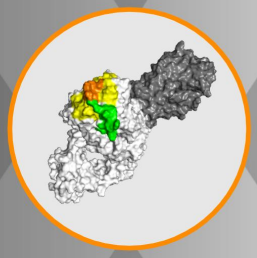
Left panel: Female C57BL/6 hPD-1 mice (n=8 in each treatment group) were inoculated with MB49 tumor cells. On day 0, 5 mice received vehicle or equimolar doses of anti-PD1 antibody (pembrolizumab) plus masked βγIL-2 or XTX501. Tumor volume change on day 12 post treatment relative to baseline is shown as a waterfall plot. **Right panel:** Female C57BL/6 hPD-1 mice (n=5 in each treatment group) were inoculated with MB49 tumor cells. On day 0, 5 mice received vehicle or equimolar doses of anti-PD1 antibody (pembrolizumab) plus masked βγIL-2 or XTX501. Tumors were harvested on day 7 post initial treatment and tumor infiltrating lymphocytes were phenotyped using flow cytometry. Fold-over mean vehicle is shown for the treatment arms for CD8+/GranzymeB positive and CD8+/TCF1+ T cells.
Data generated with analogue of XTX501 with minimal variance in amino acid sequence.

XTX501 Has Potential for Increased Therapeutic Index with Meaningfully Differentiated Anti-Tumor Activity and Safety Profile

Potential Best-in-Class Profile	• XTX501 incorporates a **high potency IL-2 variant affinity tuned with optimal receptor binding profile** for IL-2 alpha / beta / gamma • **Masking IL-2** to **direct activity to the tumor microenvironment, improve therapeutic index and optimize PK profile**
Clinical Development Plans	• **IND submission** anticipated **mid 2026** • **Phase 1 trial planned in post-PD-1 NSCLC** with opportunity to expand into other tumor types • **Initial clinical data** anticipated in **2H 2027**
Significant Opportunity	• **Clinical efficacy and survival benefits demonstrated for the PD-1 / IL-2 mechanism,** including immunotherapy-resistant NSCLC and cold tumors (1) • **Significant opportunity in PD-1 insensitive tumors** including MSS CRC and prostate cancer • **Potential for XTX501 be a foundational "backbone" therapy** for combination treatment

1. Clinical data reported by Innovent Biologics, Inc. for IBI363, a PD-1/IL-2 α-bias bispecific antibody fusion protein (non-masked), in immunotherapy-resistant NSCLC and cold tumors such as acral, mucosal melanoma and MSS CRC.
MSS CRC: microsatellite stable colorectal cancer

Masked T Cell Engagers



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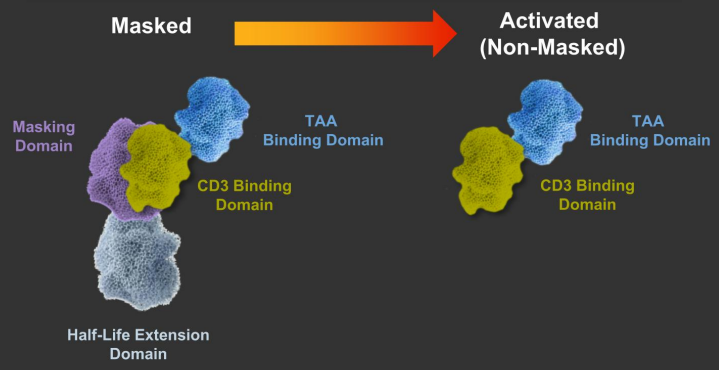
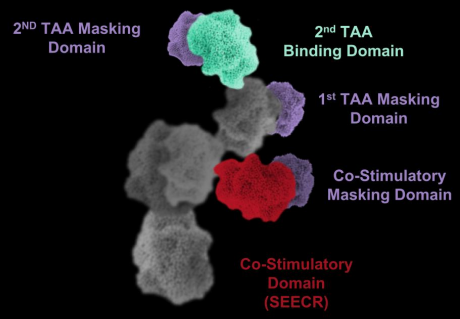
Xilio's Modular Architecture Enables Optimal T Cell Engager Designs Tailored to Maximize Tumor Exposure While Minimizing T Cell Engagement in Healthy Tissue

Core Components



- ***Highly effective CD3 mask:*** with clinically-validated cleavage element design
- ***Conditional half-life modulation:*** designed to release mask and half-life extension domain upon activation resulting in antibody-like half-life in masked state, short half-life once activated
- ***Multiple proprietary CD3 binding domains:*** with a range of affinities

Flexibility to Add Additional Components



- ***Ability to incorporate co-stimulatory domain:*** to enhance T cell activation and durability of T cell response
- ***Compatible with masking each domain:*** TAA, CD3, co-stimulatory domains
- ***Modular architecture:*** enables dual-TAA targeting, bivalent TAA targeting

SEECR: selective effector-enhanced cell engager (masked T cell engager with co-stimulation); TAA: tumor-associated antigen

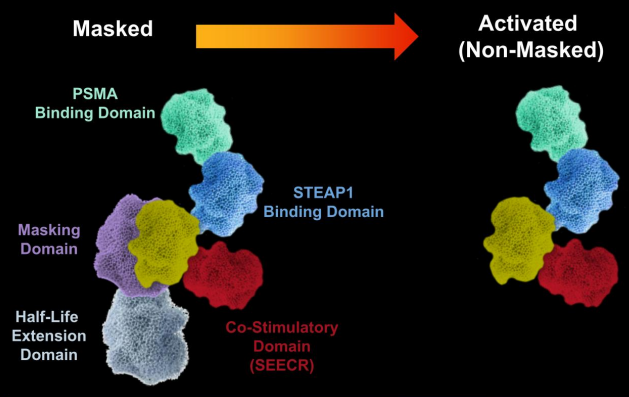
PSMA+STEAP1

Dual-TAA targeted, masked T cell engager with co-stimulation (SEECR)

xilio THERAPEUTICS®

PSMA+STEAP1 (SEECR): Dual-TAA Targeted Masked T Cell Engager Has Best-in-Class Potential for Prostate Cancer

PSMA+STEAP1 (SEECR)



- ***Multifunctional fusion protein design:*** incorporating masked CD3 binding domain, co-stimulatory domain, half-life extension domain and two TAA targeting domains
- ***Conditional half-life modulation:*** designed to release mask and half-life extension domain upon activation resulting in antibody-like half-life in masked state, short half-life once activated

Designed to Address Key Limitations of Other Prostate Cancer T Cell Engagers in Development

- By targeting PSMA+STEAP1, designed to **avoid resistance due to antigen escape and sub-clonal selection**
  - Dual-TAA targeting designed to **address heterogeneity of PSMA and STEAP1 expression** across prostate tumors
  - Significant opportunity, with **PSMA and/or STEAP1 expressed in ~95% of metastatic CRPC**
- **Co-stimulation built into single molecule** (SEECR format) designed to enable **enhanced T cell activation, proliferation and durability of response**
- **Designed for optimized masking** leveraging Xilio's **clinically-validated masking approach** and **potential best-in-class masking efficiency**
- PK data support **potential for Q3W or less frequent dosing**

IND submission for PSMA+STEAP1 anticipated in 2027

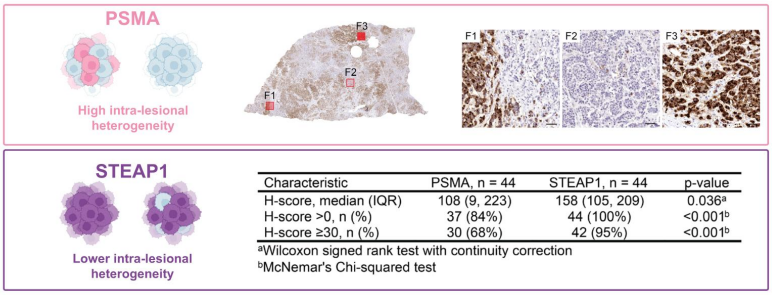
CRPC: castration-resistant prostate cancer; Q3W: once every three weeks

Dual-TAA Targeting Supported by Heterogeneous Patterns of PSMA and STEAP1 Expression in Advanced Prostate Cancer

- PSMA and STEAP1 are validated T cell engager targets in prostate cancer
- However, a significant proportion of advanced stage prostate tumors display heterogenous PSMA or STEAP1 expression
- Heterogenous expression patterns could allow for resistance to T cell engagers targeting a single antigen
- Dual-TAA targeting of PSMA and STEAP1 has the potential to expand activity and reduce resistance

Expression Pattern	PSMA	STEAP1
Intra-tumoral heterogeneity	High	Low
Heterogeneous across sites	32–44%	32%
Negative at all sites	23–25%	0%

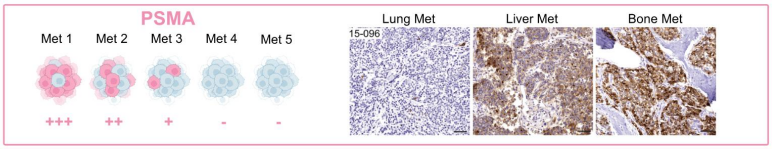
Intra-Lesional Heterogeneity — Expression Variability Within a Single Metastatic Site

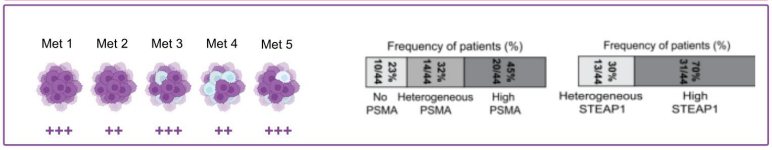


Characteristic	PSMA, n = 44	STEAP1, n = 44	p-value
H-score, median (IQR)	108 (9, 223)	158 (105, 209)	0.036[a]
H-score >0, n (%)	37 (84%)	44 (100%)	<0.001[b]
H-score ≥30, n (%)	30 (68%)	42 (95%)	<0.001[b]

[a]Wilcoxon signed rank test with continuity correction
[b]McNemar's Chi-squared test

Inter-Lesional Heterogeneity — Expression Variability Across Different Metastatic Sites

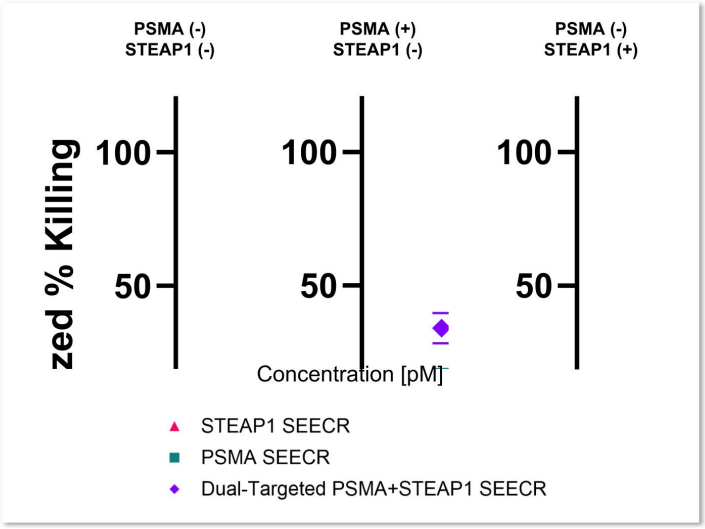




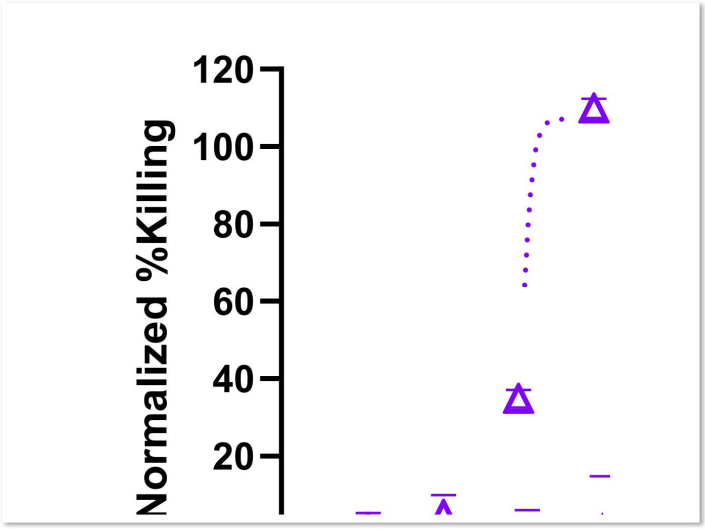
Figures and tables generated and adapted based on: Bhatia et al. Nat Commun 2023; Sayar et al. JCI Insight 2023; Paschalis et al. Eur Urol 2019; Westerman et al. JCO 2023 (CASCADE); Mulati et al. Sci Rep 2025

PSMA+STEAP1 (SEECR): Demonstrated Target-Dependent Activity and Effective Masking

Able to Kill Both PSMA+ Cells and STEAP1+ Cells



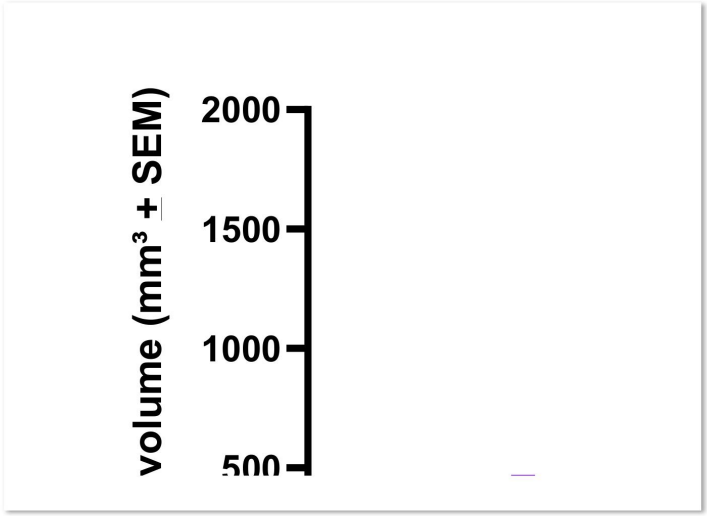
Robust Window Between Masked and Activated State



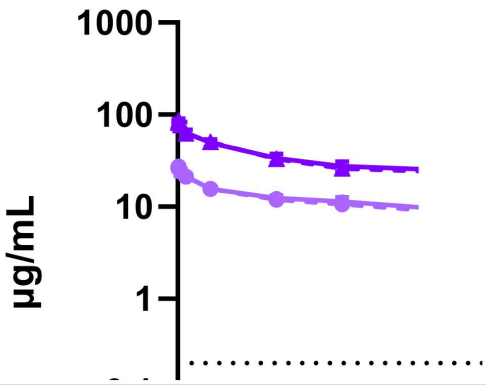
Left panel: Isogenic cells lines engineered to either express PSMA or STEAP1 (or remain target-negative) were co-cultured with primary human T cells. Target cell killing in response to indicated titrations of test articles was evaluated using a luciferase-based cell viability readout. **Right panel:** T cells were co-cultured with C4-2 prostate cancer and test article (masked molecule or pre-activated molecule) were titrated across the plate. Target cell killing was determined using a luciferase-based readout.

PSMA+STEAP1 (SEECR) Demonstrated Robust Anti-Tumor Activity in Prostate Cancer Model with Favorable Tolerability and PK in NHPs

Tumor Regressions in C4-2 Prostate Cancer Model



Antibody-Like PK and Well-Tolerated ≥3 mg/kg in NHPs

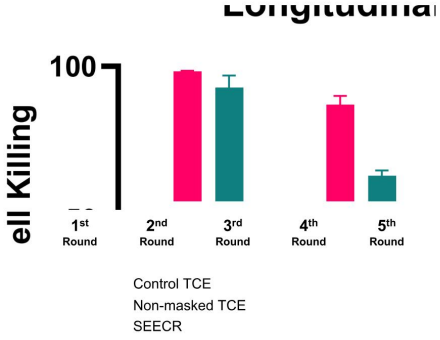


- No clinical signs and no CRS at either dose level
- Minimal peripheral cleavage with antibody-like PK predicted to enable at least Q3W or less frequent dosing

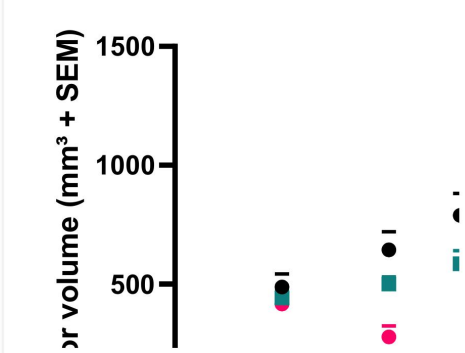
Left panel: C4-2 prostate cancer tumor cells were inoculated in NSG mice engrafted with human T cells. Anti-tumor activity in response to indicated test articles was evaluated over time. Two-way ANOVA followed by Dunnett's multiple comparisons test was used for statistical analysis (**P < 0.01). **Right panel:** Male cynomolgus monkeys were infused with indicated test article at either 1 mg/kg or 3 mg/kg and drug exposure was measured over time alongside clinical observations. Sera were collected for cytokine analysis and clinical pathology.
CRS: cytokine release syndrome

Co-Stimulatory Signaling (SEECR Format) Enabled Enhanced Anti-Tumor Activity and Increased Durability of T Cell Response

SEECR Format Enabled Sustained Tumor Cell Killing in Repeat Stimulation Assay

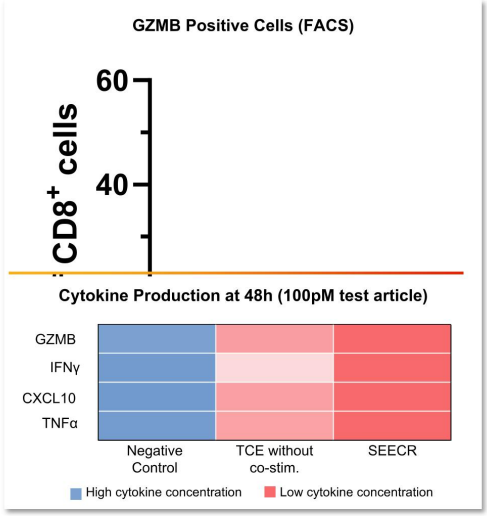


SEECR Format Demonstrated Enhanced Potency and TGI *In Vivo*



Tumor growth inhibition (TGI) achieved for STEAP1 without co-stimulation, but complete regressions observed for STEAP1 with co-stimulation (SEECR)

SEECR Format Enhanced T Cell Activation and Polyfunctionality in Primary Tumor *Ex Vivo* Culture



Left panel: Human T cells were incubated over five consecutive rounds with indicated test articles and A431 cancer cells and percent tumor cell killing was assessed using a luminescence readout. **Middle panel:** C4-2 prostate cancer tumor cells were inoculated in NSG mice engrafted with human T cells. Anti-tumor activity in response to indicated test articles was evaluated over time. Two-way ANOVA followed by Dunnett's multiple comparisons test was used for statistical analysis (P=0.0001). **Right panel:** Representative primary human squamous cell carcinoma of the head and neck was obtained and dissociated for 48h ex vivo culture with indicated treatments followed by flow cytometry (fluorescence activated cell sorting: FACS) measuring indicated markers. Culture media from this ex vivo tumor culture were collected after 48h incubation with indicated test articles and cytokine concentrations were measured using MSD (Mesoscale Discovery).
TAA: tumor associated antigen; TCE: T cell engager (regular CD3 only, not effector enhanced). .

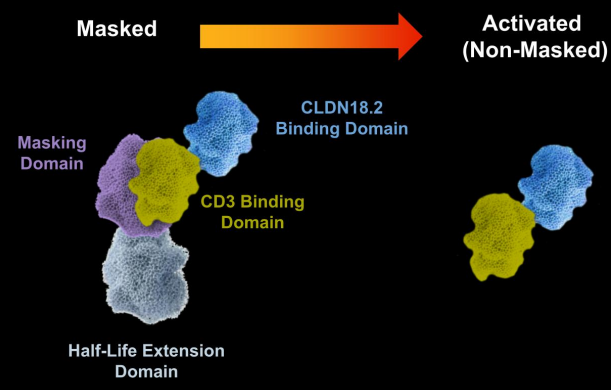
CLDN18.2

Masked T cell engager

xilio THERAPEUTICS®

CLDN18.2: Potential First-in-Class Masked T Cell Engager for Gastrointestinal Cancers

CLDN18.2: Masked T Cell Engager (ATACR)



- ***Masked T cell engager design:*** incorporating masked CD3 binding domain, half-life extension domain and CLDN18.2 targeting domain
- ***Conditional half-life modulation:*** designed to release mask and half-life extension domain upon activation resulting in antibody-like half-life in masked state, short half-life once activated

Designed to Improve Therapeutic Index Relative to Non-Masked CLDN18.2 Agents in Development

- Xilio design uses **high affinity CLDN18.2 isoform-selective binder**
- CLDN18.2 is a **validated target expressed across gastrointestinal cancers** (gastric, pancreatic, esophageal) **and lung cancer**
- Potential for **significantly expanded therapeutic index with masking** – non-masked T cell engagers targeting CLDN18.2 limited by severe GI toxicity
- Xilio's modular architecture enables evaluation of **dual-masking and/or co-stimulation (SEECR format) designs in parallel** with current molecule design

IND submission anticipated in 2027

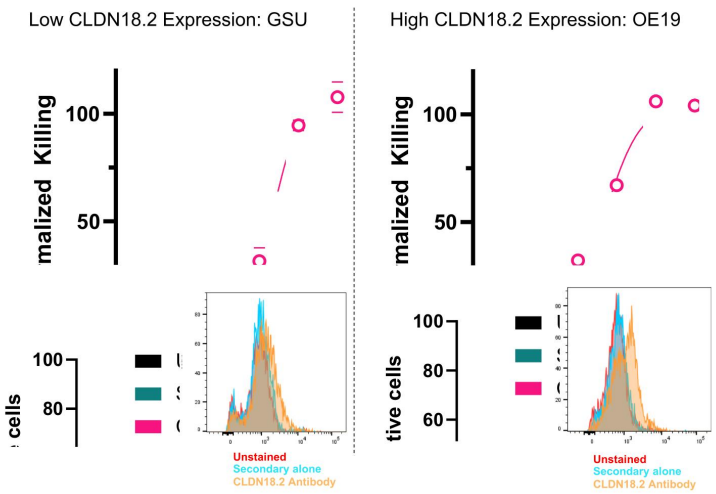
GI: gastrointestinal

CLDN18.2 (ATACR) Demonstrated Protease-Dependent CD3 Binding and Tumor Cell Killing in High and Low Expression Settings for CLDN18.2

Protease-Dependent Binding to CD3

Test Condition	K_d (nM)	Fold- Masking
CLDN18.2 ATACR	60.31	274
CLDN18.2 ATACR + MMP (Activated)	0.22	

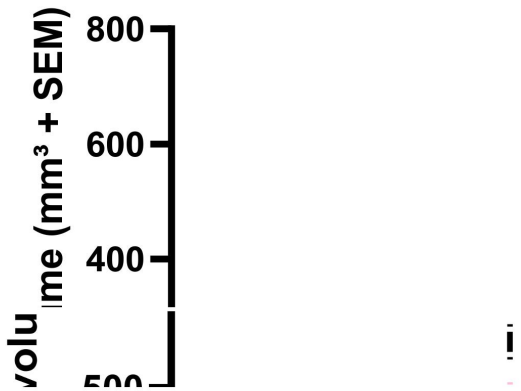
Protease-Dependent Tumor Cell Killing in CLDN18.2 High and Low Cell Lines



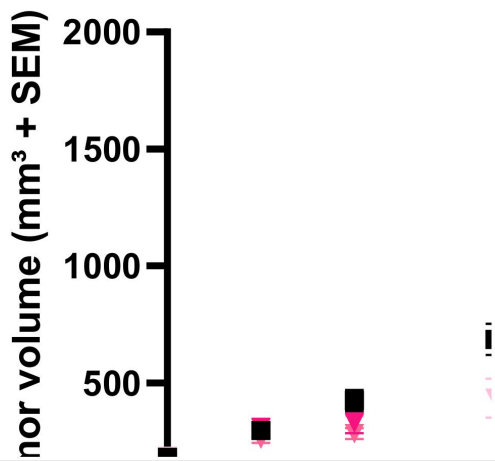
Left panel: CLDN18.2 ATACR molecule binding to recombinant human CD3 delta/epsilon either in intact form or pre-activated using recombinant MMP. Analysis performed using ELISA. **Right panel top**: Human T cell/cancer cell line co-culture assay evaluating tumor cell killing by either intact CLDN18.2 ATACR or CLDN18.2 ATACR molecule pre-activated using recombinant MMP. Experiments performed using either GSU (gastric cancer) or OE19 (esophageal cancer) cell lines. **Right panel bottom:** Flow cytometry analysis showing expression of CLDN18.2 on GSU or OE19 cells.

CLDN18.2 (ATACR) Demonstrated Robust, Dose-Dependent Anti-Tumor Activity in Multiple Murine Cancer Models

Potent Anti-Tumor Activity in GSU Gastric Cancer Model



Complete Tumor Regressions in OE19 Esophageal Cancer Model at Doses ≥ 0.3 mg/kg

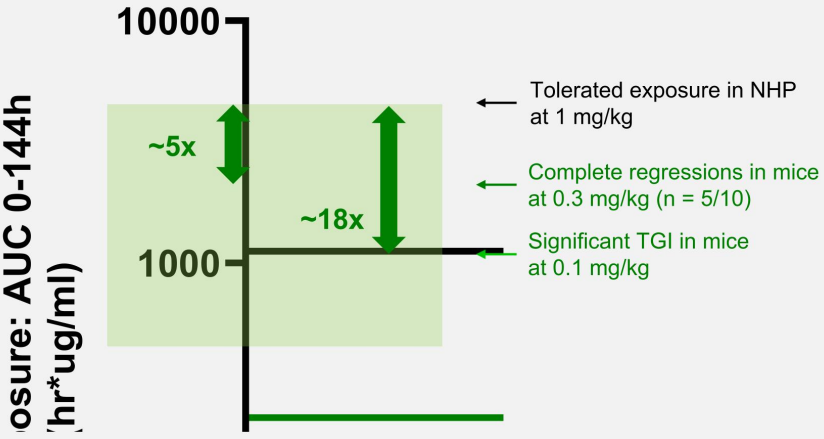


Left panel: GSU cells were inoculated in NSG mice engrafted with human T cells. Anti-tumor activity change in response to indicated test articles was evaluated over time. Two-way ANOVA followed by Dunnet's multiple comparisons test was used for statistical analysis: p<0.05(*). **Right panel**: OE19 cells were inoculated in NSG mice engrafted with human T cells. Anti-tumor activity change in response to indicated test articles was evaluated over time. Two-way ANOVA followed by Šídák's multiple comparisons test was used for statistical analysis: p<0.05(*), p<0.0001(****).

Integration of Murine Activity and NHP Tolerability Data for CLDN18.2 (ATACR) Indicative of Favorable, Positive Therapeutic Index Consistent with Masked Design

- ✓ Well-tolerated in NHP at 1 mg/kg
  - No evidence of CRS
  - Liver function markers within reference range
- ✓ Antibody-like PK of intact molecule
- ✓ No evidence of peripheral cleavage
  - Percent cleaved molecule below LLOQ

Demonstrated Positive Exposure-Based Therapeutic Index in Preclinical Studies



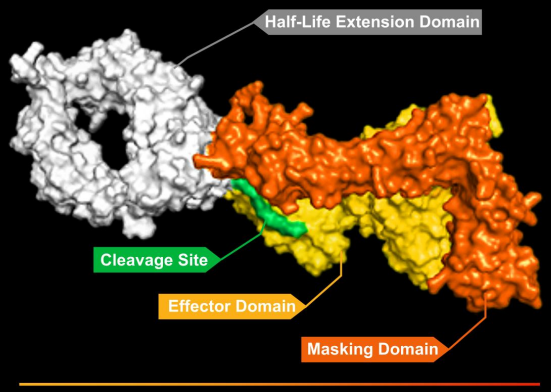
Efarindodekin Alfa

Masked IL-12

x·ilio THERAPEUTICS®

Efarindodekin Alfa Designed to Overcome Limitations of Systemic Recombinant Human IL-12

Efarindodekin alfa: masked IL-12



- Designed to have optimized short half-life IL-12 in the active state (half-life extension domain not retained)

Untapped Potential of IL-12

- **IL-12 has highly compelling biology for cancer immunotherapy**
  - Potent stimulator of NK and T cell cytotoxicity drives cellular immunity against infection and cancer
  - Robust INFγ signaling remodels the TME towards a more immune-permissive environment
- **Severe toxicity has limited systemic administration of IL-12** to date; currently **no approved IL-12 agents**
- **IL-12 has potential to turn "cold" tumors to "hot" tumors**, including HNSCC, NSCLC, ovarian cancer, CRPC and TNBC

HNSCC: head and neck squamous cell carcinoma; INFγ: interferon gamma; NK: natural killer; TNBC: triple-negative breast cancer

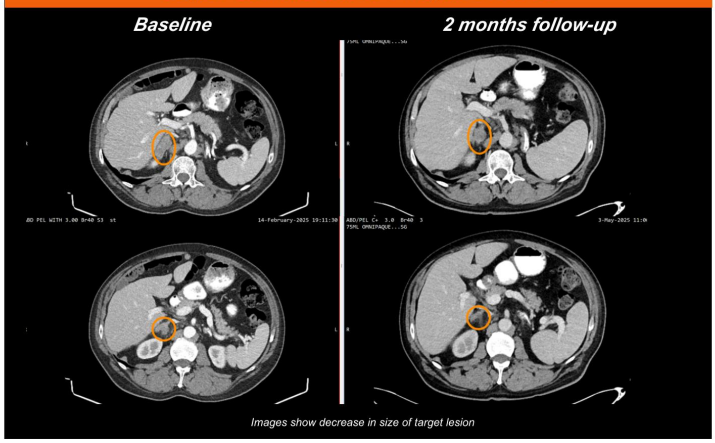
Efarindodekin Alfa Demonstrated Promising Monotherapy Clinical Efficacy in Phase 1, Including Two PRs in Patients With I-O Refractory Advanced Solid Tumors

PRs in Patients with I-O Refractory Tumors

HPV-negative HNSCC patient
- 5 prior lines of therapy; no response to pembrolizumab-based therapy
- Confirmed PR (33% decrease)
- Accompanied by robust changes in PD biomarkers

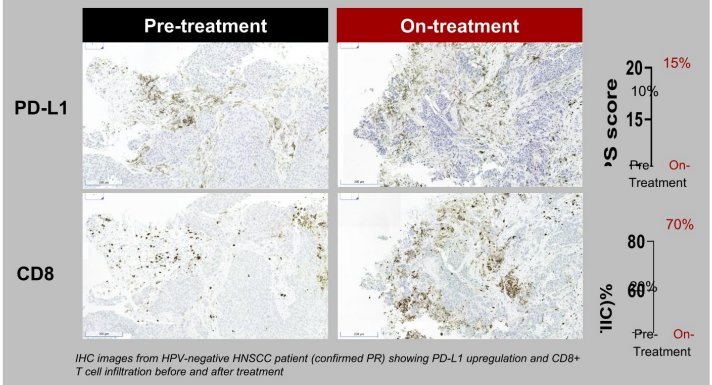
Uveal melanoma patient
- 2 prior lines of therapy
- Unconfirmed PR (55% decrease)*

66-year-old male with HPV-negative HNSCC



Images show decrease in size of target lesion

Efarindodekin alfa induced PD-L1 upregulation and CD8+ T cell infiltration



IHC images from HPV-negative HNSCC patient (confirmed PR) showing PD-L1 upregulation and CD8+ T cell infiltration before and after treatment

Responses represent decrease in sum of diameters by RECISTv1.1
* Patient discontinued treatment due to Grade 3 immune system activation AE that subsequently resolved. There was no evidence of further tumor growth through the 90-day follow-up, suggesting duration of response of at least 2 months.
HPV: human papillomavirus; HNSCC: head and neck squamous cell carcinoma; IHC: immunohistochemistry

Presented in poster presentation at SITC on November 7, 2025

Advancing Efarindodekin Alfa in Partnership with Gilead Across a Range of Solid Tumors

Promising Clinical Efficacy with Monotherapy PRs	• **Monotherapy anti-tumor activity, including two PRs** in patients with advanced solid tumors* • **Sustained, dose-dependent IFNɣ signaling** with repeat dosing **without tachyphylaxis** • **Robust immune cell infiltration and PD-L1 upregulation demonstrated in patient tumors**
Well-Tolerated Clinical Profile with Minimal, Low-Grade AEs	• Generally **well-tolerated** up to the RP2D with **treatment-related AEs primarily Grade 1 or 2** • **At the RP2D, no DLTs and no dose reductions due to treatment-related AEs**
Advancing in Partnership with Gilead	• **Phase 2 initiated** in Q3 2025 in multiple tumor types (anticipate n=~40 patients) • Achieved **$17.5M development milestone** in Q3 2025 in connection with initiation of Phase 2

- ***Delivery of Phase 1/2 option data package to Gilead anticipated in 1H 2027***
- ***Xilio will receive a $75M option fee if Gilead exercises its option to the IL-12 program***

Data cutoff date: September 2, 2025. All doses and schedules (n=62) and RP2D (n=13).
* 1 confirmed PR, 1 unconfirmed PR
AE: adverse event; DLT: dose-limiting toxicity; PR: partial response; RP2D: recommended Phase 2 dose

Presented in poster presentation at SITC on November 7, 2025

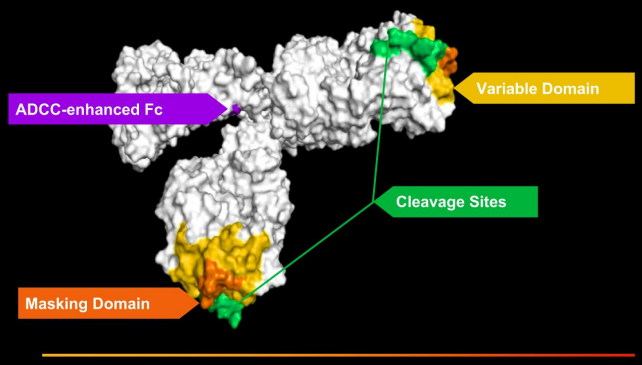
Vilastobart

Masked, Fc-enhanced anti-CTLA-4

x·ilio THERAPEUTICS®

Vilastobart is a Next Generation anti-CTLA-4 With Meaningful Clinical Efficacy and Differentiated Safety Supporting a Significant Opportunity in MSS mCRC and Other Tumors

Vilastobart: masked, Fc-enhanced anti-CTLA-4



- High affinity binding, 10x potency of ipilimumab in preclinical studies[1]
- Fc mutations for enhanced effector function (ADCC), improved T cell priming and Treg depletion
- Tumor-selective activation with >70% activated molecule measured in patient tumors and <15% activated molecule in peripheral blood in patients

Significant Opportunity for Vilastobart to Expand Reach of Validated I-O Mechanism

- CTLA-4 established as most potent immune checkpoint regulating T cell priming with complementary biology to PD-1
- Systemic toxicity has limited clinical potential of non-masked CTLA-4 agents
- Masked, Fc-enhanced design of vilastobart validated by durable clinical efficacy as monotherapy and in combination with PD-(L)1 with generally well-tolerated safety profile
- Dual mechanism of action for vilastobart is ideally suited to promote T cell responses against lower quality neoantigens:

1. CTLA-4 blockade and co-stimulation lower the threshold for priming naïve T cells against lower quality neoantigens
2. Depletion of regulatory T cells reduces immune suppressive signaling during priming and drives potent, polyclonal CD8 T cell expansion including for weaker antigens

1. Ipilimumab analog used for preclinical studies.
ADCC: antibody-dependent cell-mediated cytotoxicity

Vilastobart in Combination with Atezolizumab Demonstrated Highly Differentiated Clinical Efficacy and Safety in Patients with MSS mCRC

Promising clinical efficacy	• **Deep and durable responses** for vilastobart + atezolizumab combination in **heavily pre-treated MSS mCRC patients without liver metastases** ▪ **26% ORR** in patients **regardless of plasma TMB status** ▪ **40% ORR** in patients with **high plasma TMB**
Differentiated and well-tolerated safety profile	• **Treatment-related AEs primarily Grade 1 or 2, consistent with tumor-selective activation** (>70% activated molecule in tumor and <15% activated molecule in periphery[2]) • **Low incidence of colitis** of any grade (7%) or other imAEs, which have limited the potential of other anti-CTLA-4 agents in combination; **low discontinuation rate** (5%)
Plasma-based TMB as a biomarker predictive of response	• **Statistically significant correlation** (p=0.05) between **plasma TMB status and response** • **63% of patients** in Phase 2 had **high plasma TMB**, **including all TMB-evaluable responders** • **Real-word data** in ~8,000 patients with MSS CRC showed **~55% have high plasma TMB** [1]

Actively seeking a partner to advance development – well-suited for combinations, including PD-(L)1, PD-1/IL-2, PD1-VEGF and/or ADCs

Data cutoff date: May 12, 2025.

1. ~55% of non-MSI-H CRC patients were plasma TMB high (>10 mut/Mb) based on an analysis of the GuardantINFORM real-world clinical-genomic database in ~8,000 patients who received the Guardant360 Liquid (Infinity) assay and who had non-MSI-H disease and a reportable TMB result.
2. Measurement of tumor-selective activation presented in Phase 1 data presentation at 2023 ESMO Immuno-Oncology Congress

ADC: antibody-drug conjugate; imAE: immune-mediated adverse event; mCRC: metastatic CRC; TMB: tumor mutational burden

Presented in late-breaking presentation at SITC on November 7, 2025

Corporate Summary

xilio THERAPEUTICS®

Strong Financial Position and Proven Capabilities to Advance Pipeline of Potential Best-in-Class Masked I-O Therapies

Cash Runway Through End of 2027

- **Strong financial position** through AbbVie, Gilead and Roche collaborations and equity financings
- **$137.5M in estimated cash and cash equivalents as of December 31, 2025** (1)
  - $40M in gross proceeds received in February 2026 from follow-on offering
- **Multiple opportunities to extend cash runway:**
  - Up to $36.2M in additional gross proceeds by end of 2026 if Series C warrants exercised
  - AbbVie development milestones and option fees in 2026 and 2027
  - Gilead option fee in 2027 ($75M)

Upcoming Milestones

2026

- ❑ **PSMA+STEAP1 SEECR:** DC nomination **(Q2 2026)**
- ❑ **XTX501:** IND submission **(mid 2026)**
- ❑ **XTX501:** initiate Phase 1 trial in NSCLC **(2H 2026)** (2)

2027

- ❑ **Efarindodekin alfa:** deliver option data package to Gilead **(1H 2027)**
- ❑ **XTX501:** report initial Phase 1 data in NSCLC **(2H 2027)** (2)
- ❑ **PSMA+STEAP1 SEECR:** IND submission **(2027)**
- ❑ **CLDN18.2:** IND submission **(2027)**

1. The cash and cash equivalents information above is a preliminary estimate based on unaudited information and management estimates for the year ended December 31, 2025, is not a comprehensive statement of our financial results as of and for the fiscal year ended December 31, 2025, and may change. Our independent registered public accounting firm has not conducted an audit or review of, and does not express an opinion or any other form of assurance with respect to, this preliminary estimate.
2. Subject to clearance of the IND by the FDA.

Deep Expertise to Build a Transformational Immuno-Oncology Company

RENÉ RUSSO, PHARM.D.
Chief Executive Officer and President, Director

CHRIS FRANKENFIELD
Chief Financial and Operating Officer

ULI BIALUCHA, PH.D.
Chief Scientific Officer

KATARINA LUPTAKOVA, M.D.
Chief Medical Officer

SCOTT COLEMAN, PH.D.
Chief Development Officer

NATE MCBRIDE
Chief Information Officer

CAROLINE HENSLEY
Chief Legal Officer

Experienced Leadership Team with Proven Track Record in Biotech and Pharma Developing Novel Therapies