Unlocking the Potential of Immuno-Oncology Therapies

August 12, 2026

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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

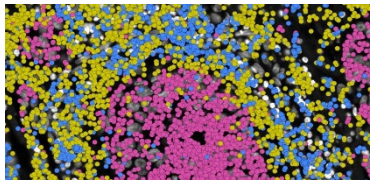
I-O: immuno-oncology

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

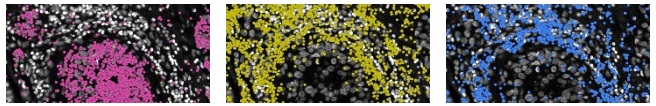
Masking Technology and Capabilities

- ✓ Xilio's masked molecules are activated by tumor-specific proteases (including MMPs)
- ✓ Proprietary masking libraries, custom computational design workflows and translational models

In situ mRNA expression in human breast cancer



Tumor cells (TROP2) | **MMP** (MMP2) | **T cells** (CD4, CD8A)



Clinical Validation and Top-Tier Strategic Partnerships

- ✓ Clinically-validated protease cleavage elements with tumor-selective activation in patients
- ✓ Deep and durable confirmed responses with differentiated safety and tolerability across multiple targets and tumor types

abbvie

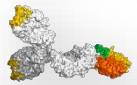
Multi-program collaboration for a masked antibody-based program and option to license masked TCEs

GILEAD

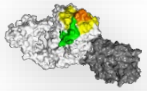
Option to license IL-12

Broad Application Across Architectures and Targets

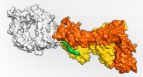
- ✓ Highly developable architectures with low immunogenicity and excellent stability
- ✓ Broad optionality for multi-specific molecule designs and targets



Bispecifics
XTX501
PD-1 / masked IL-2



TCEs
PSMA+STEAP1 and CLDN18.2
Masked TCEs +/- co-stimulation

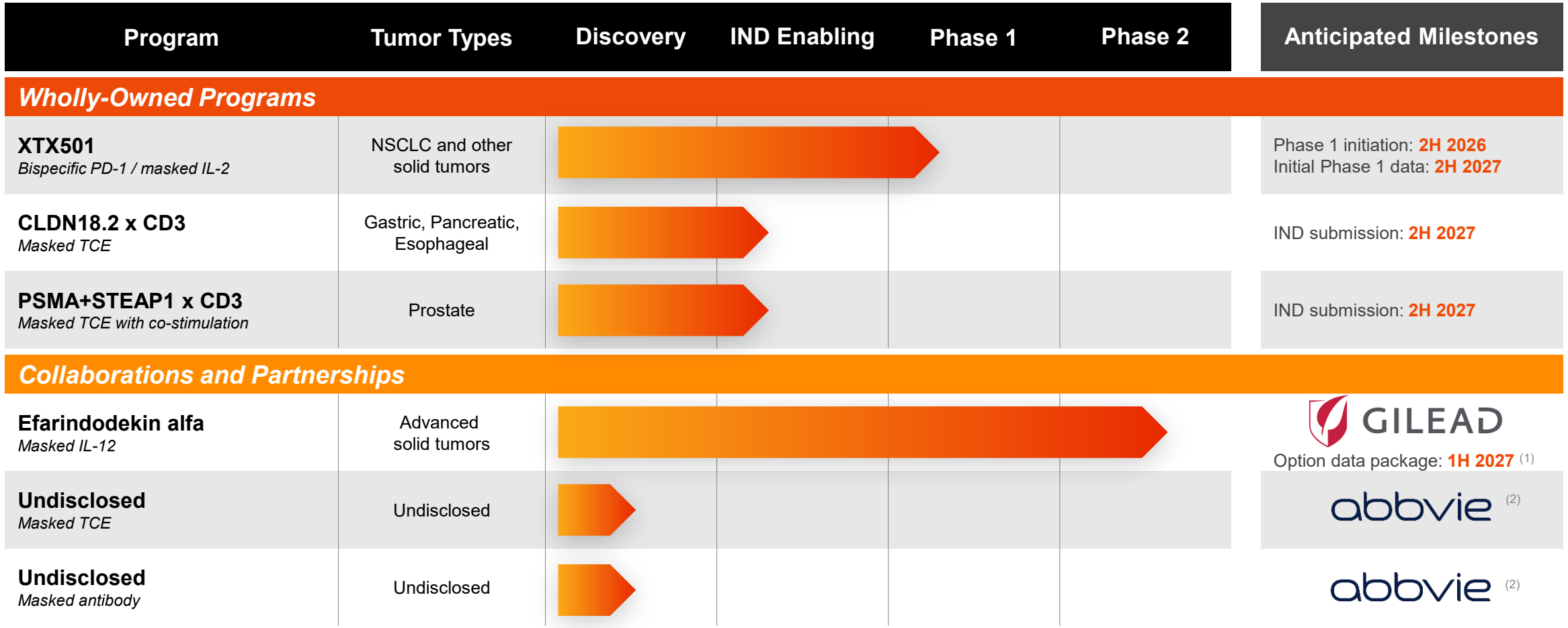


Cytokines
Efarindodekin Alfa
Masked IL-12

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; MMP: matrix metalloproteases; PSMA: prostate-specific membrane antigen; STEAP1: six transmembrane epithelial antigen of prostate 1; T cell engager: TCE

Advancing Pipeline of Potential Best-in-Class Masked I-O Therapies



1. Exclusive global option to license for IL-12 program with Gilead.
2. Collaboration with AbbVie for a licensed masked antibody program and option to license masked TCE program. AbbVie has the right to nominate up to two additional masked TCE programs through February 2028.

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 Into Q1 2028

- **Strong financial position** through top-tier strategic partnerships and equity financings
- **$136.0M in cash and cash equivalents** as of June 30, 2026
- **Multiple opportunities to extend cash runway:**
  - **Up to $36.2M:** additional gross proceeds by end of 2026 if Series C warrants exercised
  - **Up to $31M:** AbbVie development milestones and option fees achievable through 1H 2027
  - **$75M:** potential Gilead option fee in 2027

Achieved and Upcoming Milestones

2026

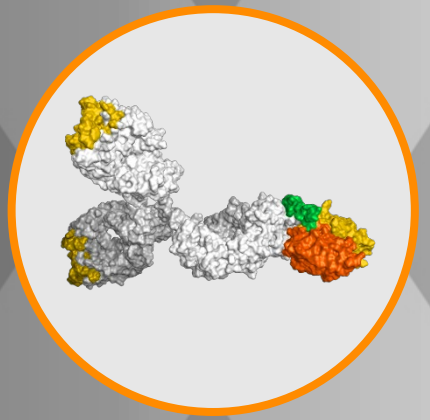
- ✓ **PSMA+STEAP1 x CD3:** initiation of IND-enabling work **(Q2 2026)**
- ✓ **XTX501:** IND submission and clearance by FDA **(mid 2026)**
- ❑ **XTX501:** initiate Phase 1 trial in NSCLC **(2H 2026)**

2027

- ❑ **Efarindodekin alfa:** deliver option data package to Gilead **(1H 2027)**
- ❑ **XTX501:** report initial Phase 1 data in NSCLC **(2H 2027)**
- ❑ **CLDN18.2 x CD3:** IND submission **(2H 2027)**
- ❑ **PSMA+STEAP1 x CD3:** IND submission **(2H 2027)**

XTX501

Bispecific PD-1 / masked IL-2



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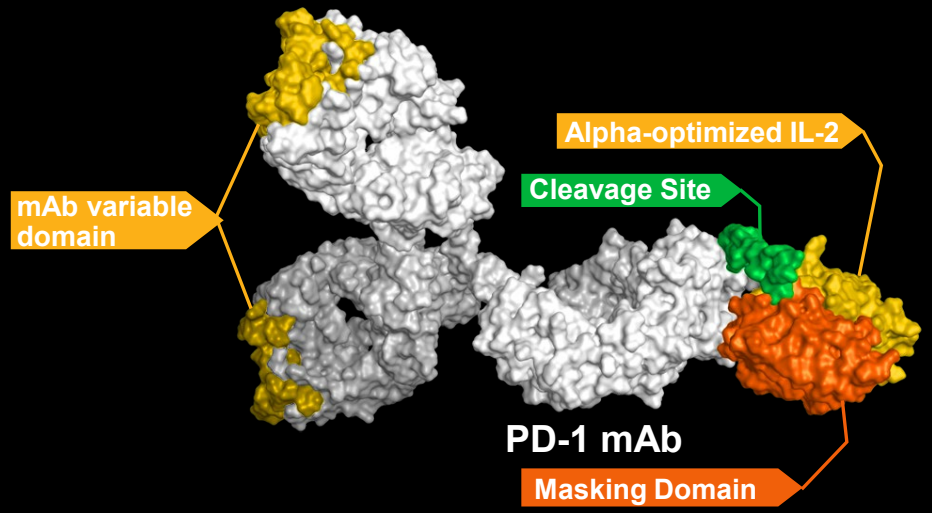
XTX501: Bispecific PD-1 / Masked IL-2 Designed to Enable High Potency IL-2 With Antibody-Like PK and Tolerability

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 to be a foundational backbone therapy** for solid tumors, including for combination treatments with other agents

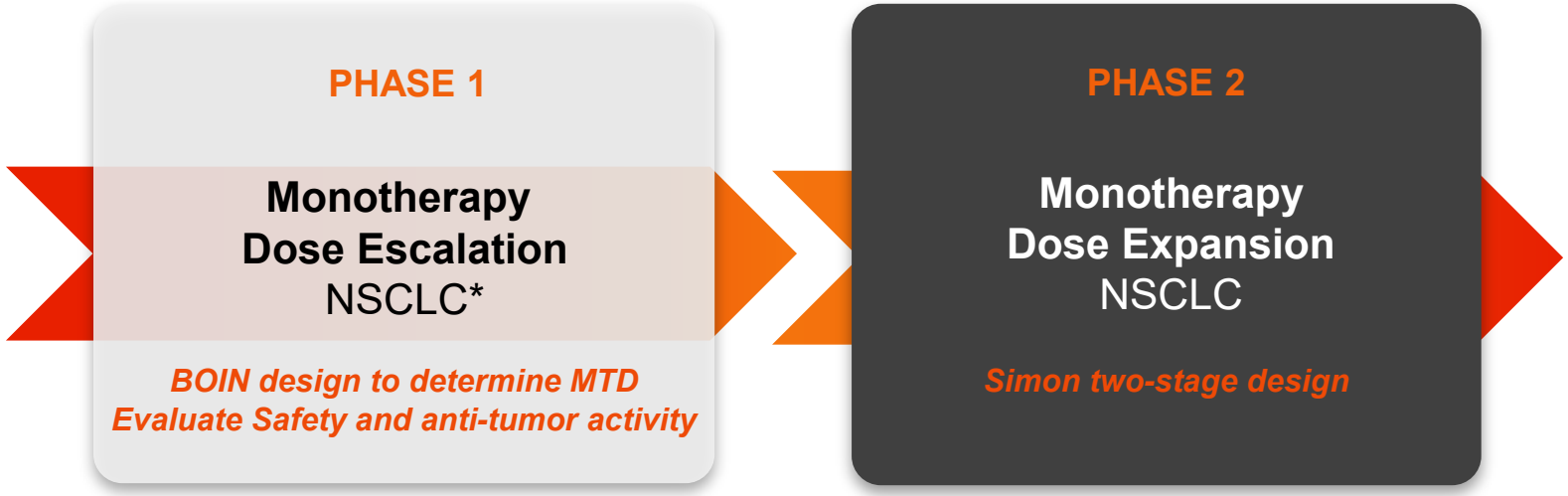
IND cleared by FDA; Phase 1 initiation anticipated 2H 2026
Initial clinical data in NSCLC anticipated 2H 2027

mAb: monoclonal antibody; PK: pharmacokinetics

XTX501 Phase 1/2 Trial Designed for Initial Data in NSCLC in 2H 2027

KEY ELIGIBILITY CRITERIA

- Metastatic NSCLC*
- Prior treatment with anti-PD-1
- Not eligible for targeted therapy
- Patients with CNS metastases that are controlled are eligible to enroll



Initial starting dose of 1 mg/kg

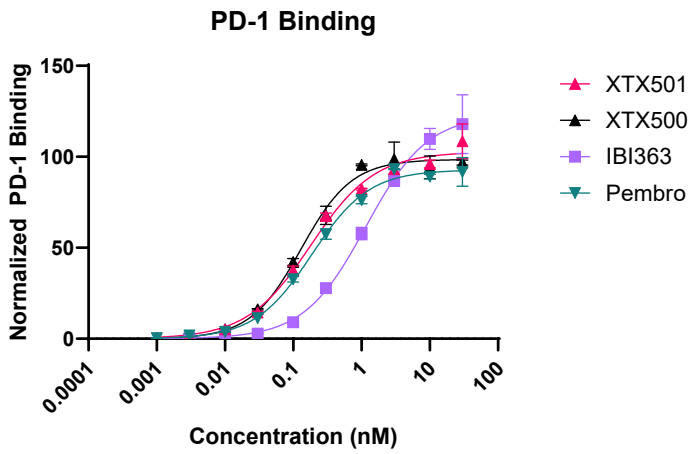
Anticipate enrolling up to ~n=40 patients at multiple sites in the US

Anticipate enrolling up to ~n=80 patients at multiple sites in the US

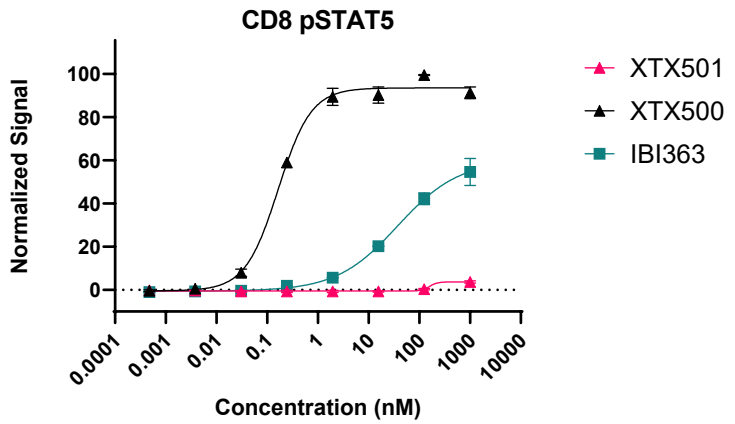
NCT07688577 on www.clinicaltrials.gov for additional details
* In Phase 1, participants with select advanced solid tumors may be enrolled based on scientific or medical rationale
BOIN: Bayesian Optimal Interval; CNS: central nervous system; MTD: maximum tolerated dose; RP2D: recommended phase 2 dose

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



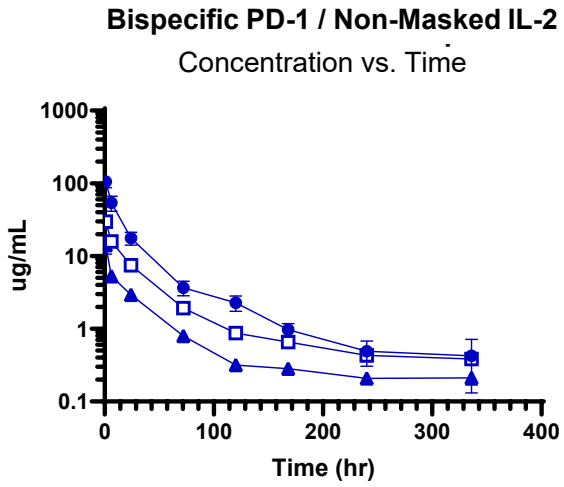
XTX501 Demonstrated Meaningfully Differentiated Overall Preclinical Activity Profile

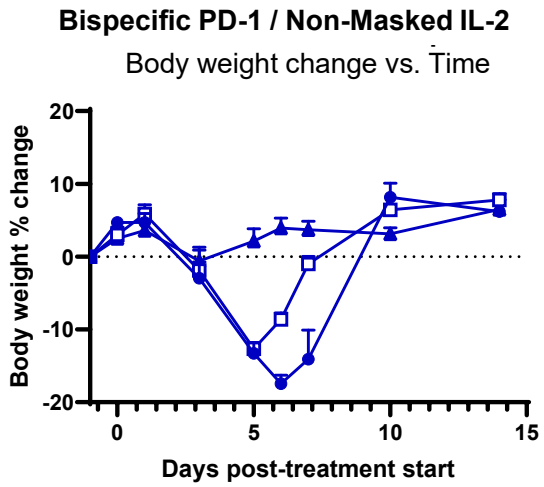
	PD-1 Binding *mean K_d (nM)*	Potency *CD8 T Cell pSTAT5 EC50 (nM)*
XTX501 (masked)	0.165	>1000
XTX500 [1] (non-masked)	0.111	0.168
IBI363	1.025	31

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

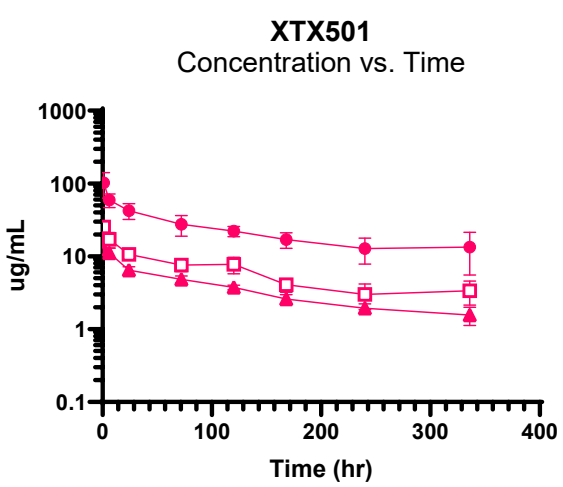


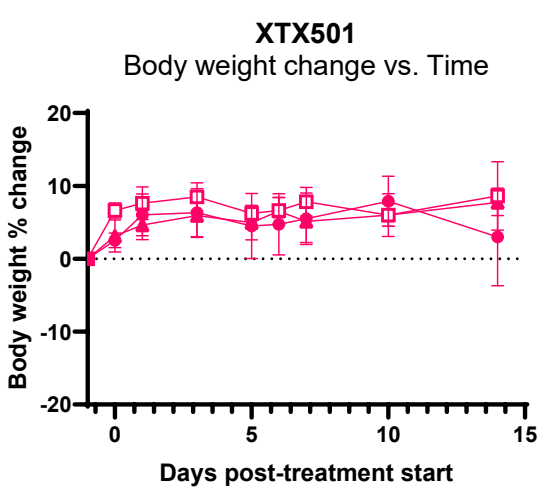


High
Med
Low

Equimolar dosing aligned with XTX501

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



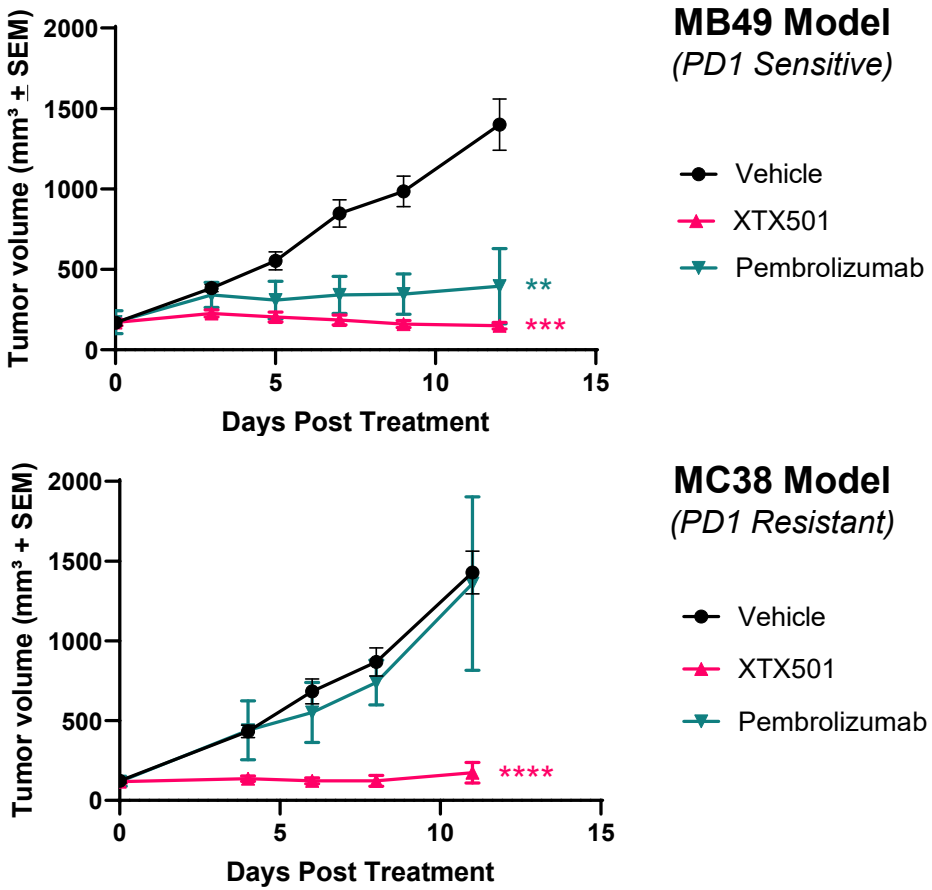


10 mg/kg (High)
3 mg/kg (Med)
1 mg/kg (Low)

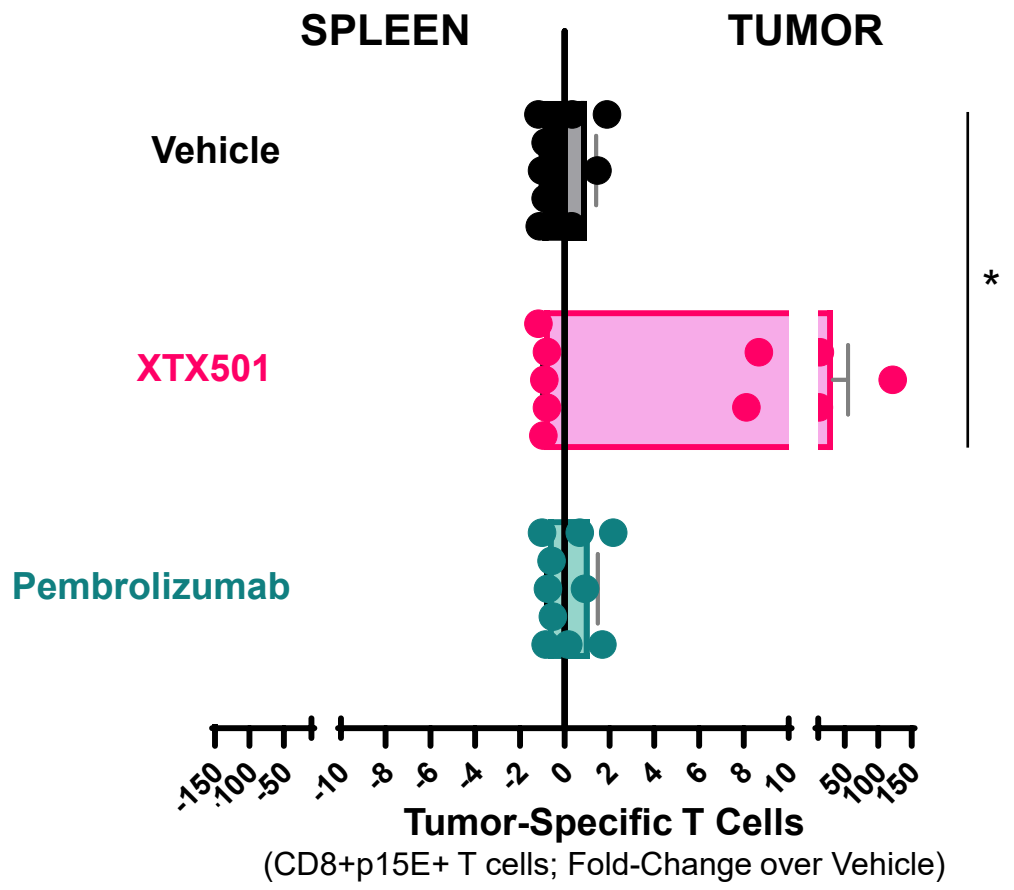
XTX501 exposure after a single 10, 3 or 1 mg/kg intravenous injection in non-tumor bearing C57BL/6-hFcRn mice. Non-masked PD-1/IL-2 exposure after a single equal molar dose of 9.25, 2.75 or 0.92 mg/kg intravenous injection in non-tumor bearing C57BL/6-hFcRn mice. Body weight data are displayed until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

XTX501 Demonstrated Potent Anti-Tumor Activity and Tumor-Specific Pharmacology In Vivo

XTX501 Elicited Robust Anti-Tumor Activity in PD1 Sensitive and PD1 Resistant Models



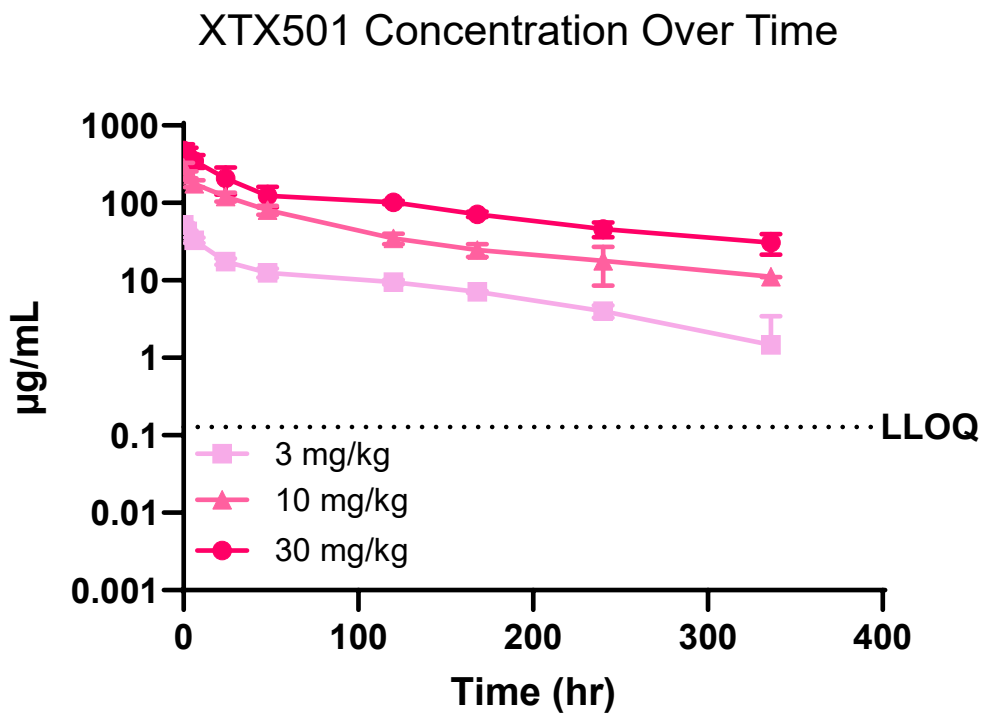
XTX501 Drove Expansion of Tumor-Specific T Cells in Tumor with Minimal Peripheral Activity in Spleen



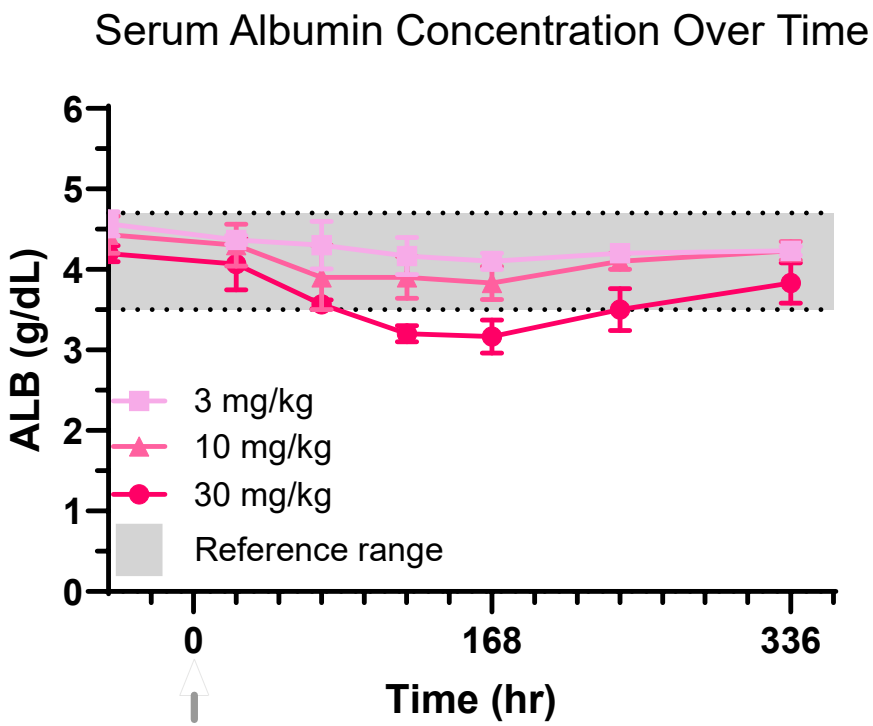
Left panel: B-hPD1-C57BL/6 Tg mice were implanted with either MB49 bladder cancer or MC38 colon cancer cells. Mice with established tumors were treated with the indicated test articles Q5Dx2 (pembrolizumab was matched equimolar to 10 mg/kg XTX501). Tumor volume was plotted as an average ± SEM. N = 10 per group. To determine statistical significance of treatment versus vehicle control, two-way ANOVA was performed with Tukey's multiple comparisons test (***P* <0.005, ****P* ≤ 0.005 on Day 12 compared to the vehicle group). **Right panel:** Changes in tumor or spleen CD8+p15E+ T cells after treatment with XTX501 or pembrolizumab in the MC38 mouse model in B-hPD1-C57BL/6 Tg mice. Average ± SEM is shown as the fold-change over vehicle control. To determine statistical significance of treatment versus vehicle (PBS) control, a one-way ANOVA was performed (*P < 0.05) with nonparametric Dunn's multiple comparison test.

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 Has Potential to Become a Foundational Backbone Therapy for Solid Tumors

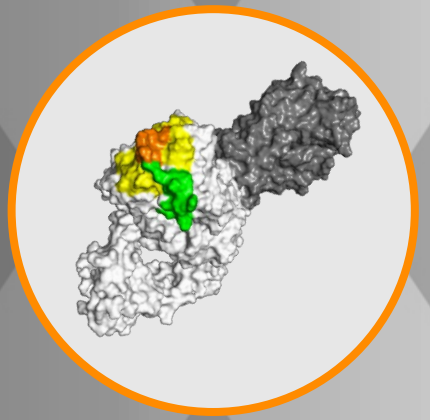
Potential Best-in-Class Profile	• XTX501 incorporates a **high potency IL-2 variant affinity tuned with optimal receptor binding profile** for IL-2 alpha / beta / gamma • **Masking IL-2** to **direct activity to the tumor microenvironment, improve therapeutic index and optimize PK profile**
Clinical Development Plans	• **IND cleared by FDA**; Phase 1 initiation anticipated in 2H 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 solid tumors, including for combination treatments with other agents

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

CONFIDENTIAL

Masked T Cell Engagers



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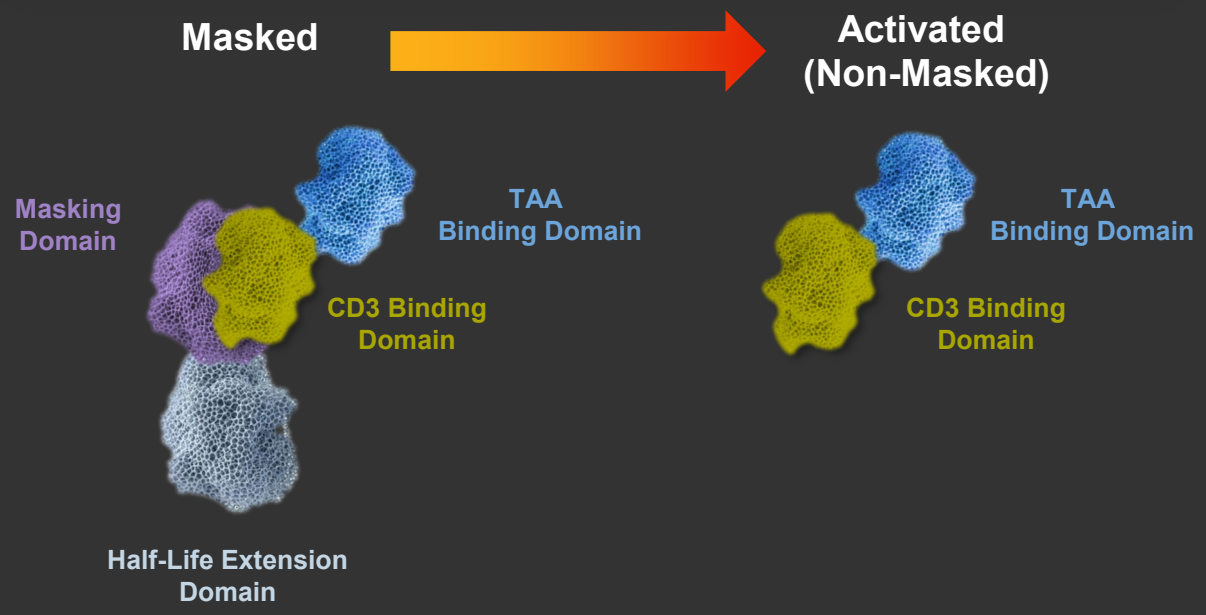
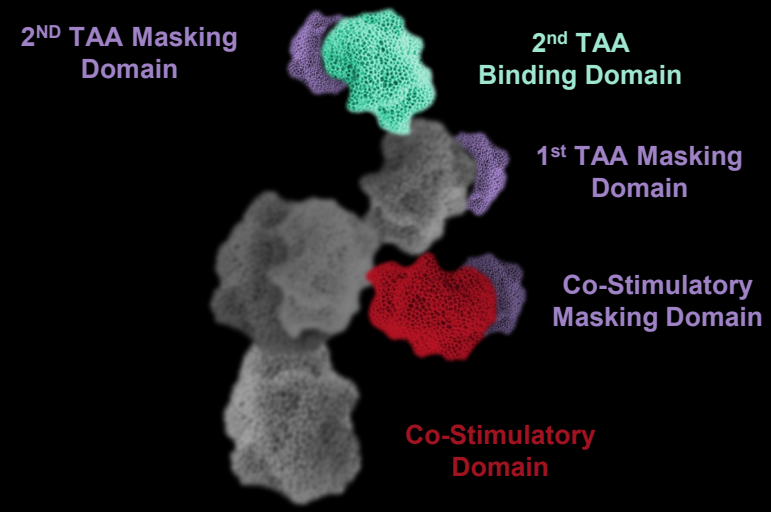
Xilio's Modular Architecture Enables Optimal T Cell Engager Designs Tailored to Maximize Tumor Exposure While Minimizing T Cell Engagement in Healthy Tissue

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

TAA: tumor-associated antigen

PSMA+STEAP1 x CD3

Dual-TAA targeted, masked TCE with co-stimulation

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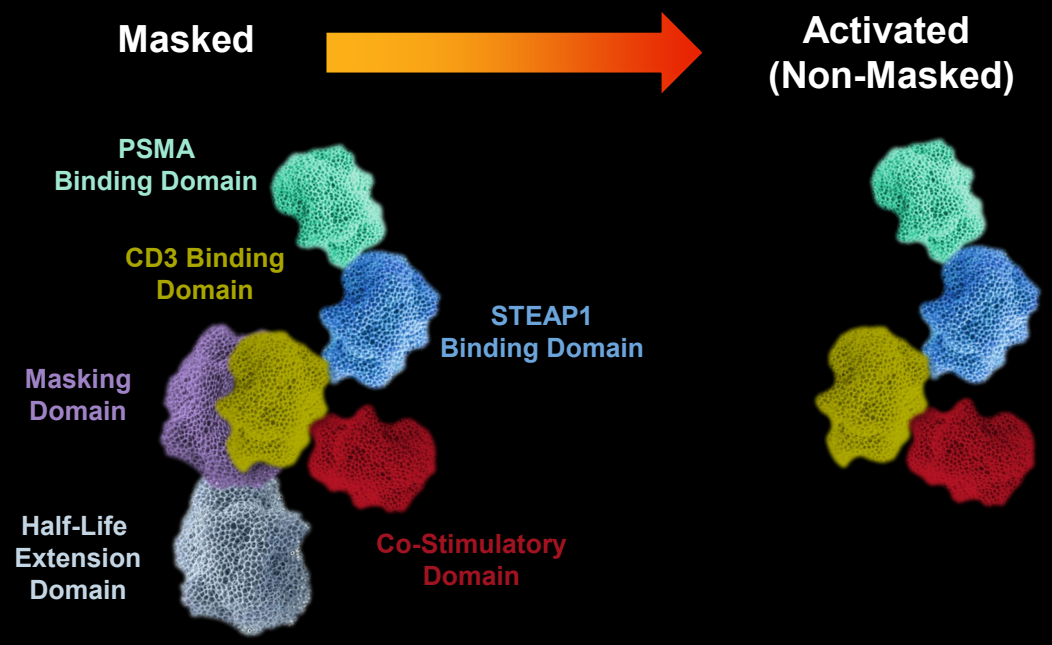
PSMA+STEAP1 x CD3: Dual-TAA Targeted Masked TCE Has Best-in-Class Potential for Prostate Cancer

PSMA+STEAP1 x CD3 with Co-Stimulation



- ***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 cancer cells expressing PSMA or STEAP1, designed to **avoid resistance due to antigen escape**
  - 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** 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 2H 2027

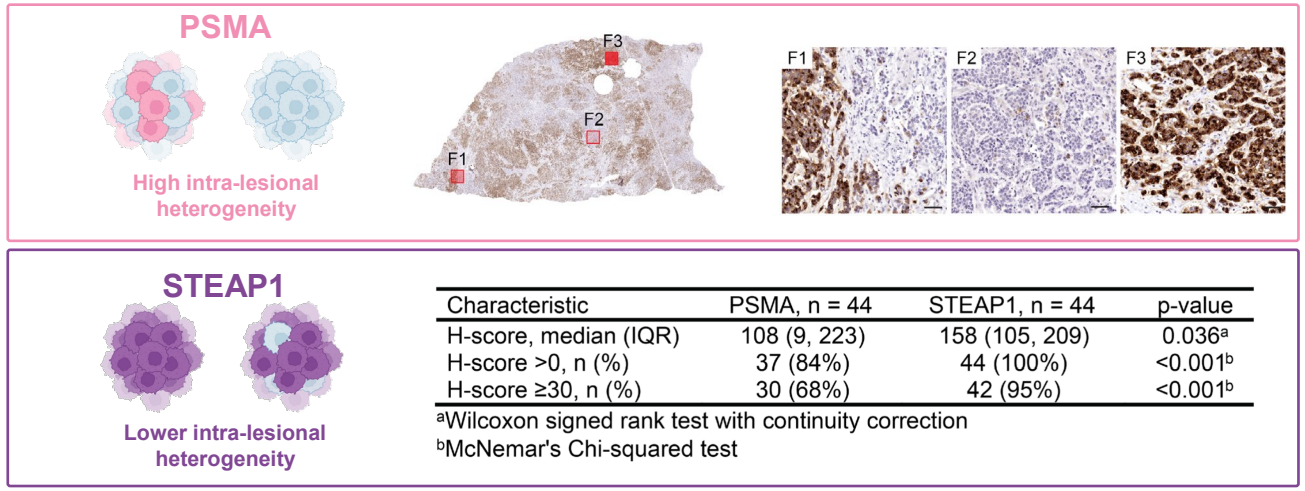
CRPC: castration-resistant prostate cancer; Q3W: once every three weeks

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%

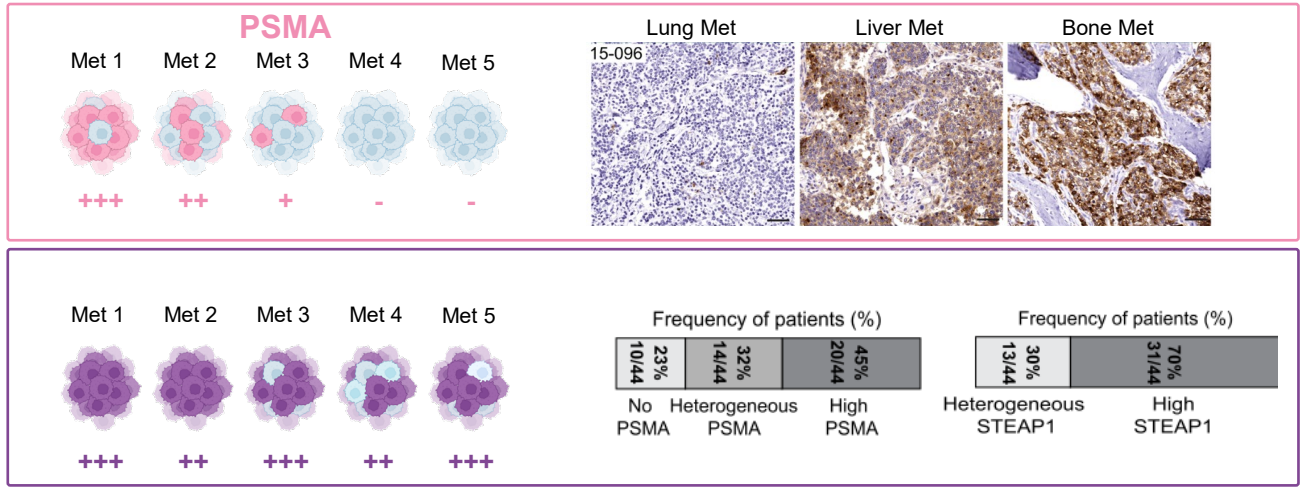
Intra-Lesional Heterogeneity — Expression Variability Within a Single Metastatic Site



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

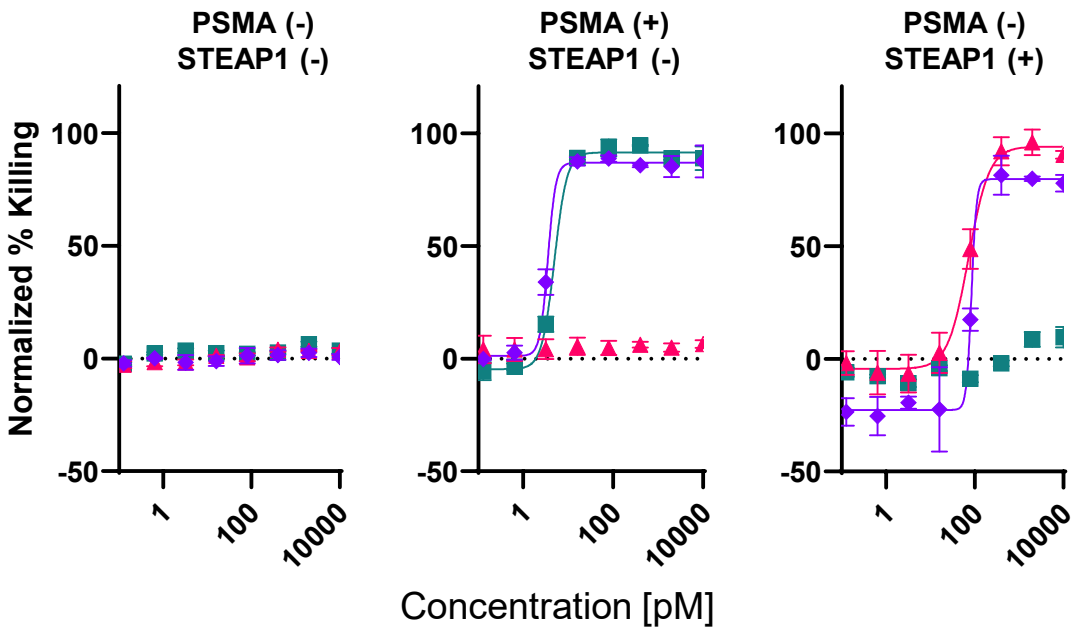
Inter-Lesional Heterogeneity — Expression Variability Across Different Metastatic Sites



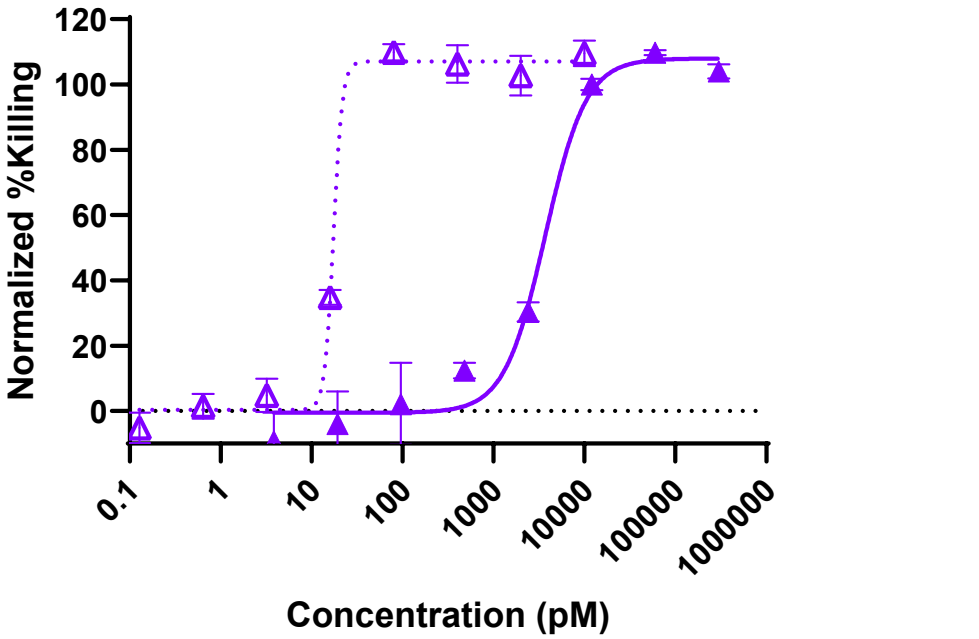
Figures and tables generated and adapted based on: Bhatia et al. Nat Commun 2023; Sayar et al. JCI Insight 2023; Paschalis et al. Eur Urol 2019; Westerman et al. JCO 2023 (CASCADE); Mulati et al. Sci Rep 2025

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

Able to Kill Both PSMA+ Cells and STEAP1+ Cells



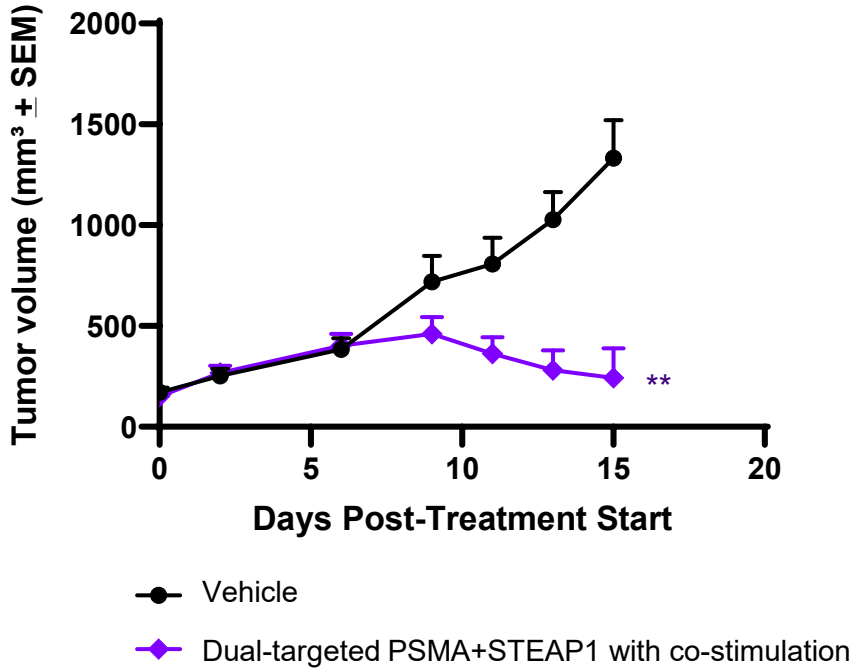
Robust Window Between Masked and Activated State



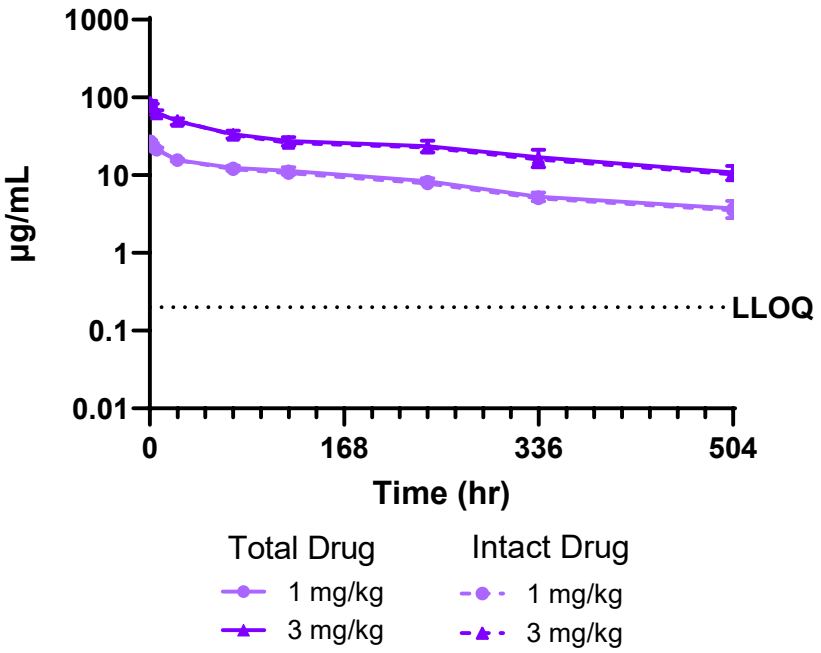
Left panel: Isogenic cells lines engineered to either express PSMA or STEAP1 (or remain target-negative) were co-cultured with primary human T cells. Target cell killing in response to indicated titrations of test articles was evaluated using a luciferase-based cell viability readout. **Right panel:** 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 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

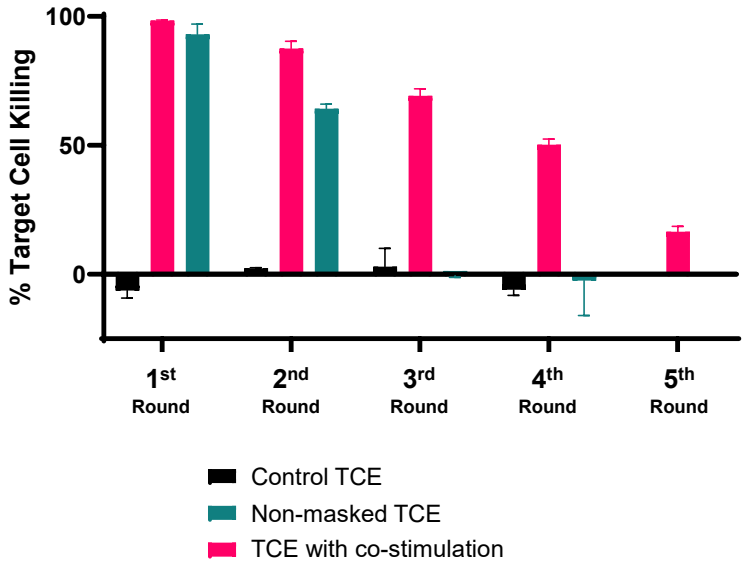


- No clinical signs and no CRS at either dose level
- Minimal peripheral cleavage with antibody-like PK predicted to enable at least Q3W or less frequent dosing

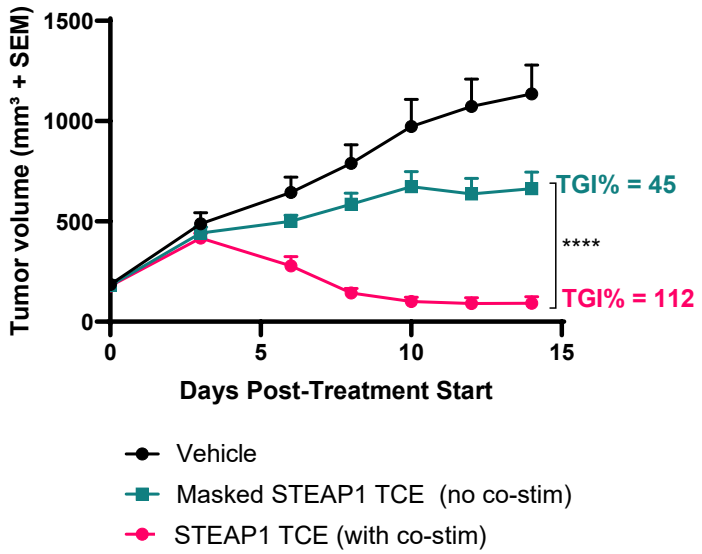
Left panel: C4-2 prostate cancer tumor cells were inoculated in NSG mice engrafted with human T cells. Anti-tumor activity in response to indicated test articles was evaluated over time. Two-way ANOVA followed by Dunnett's multiple comparisons test was used for statistical analysis (**P < 0.01). **Right 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-Stimulation Enabled Enhanced Anti-Tumor Activity and Increased Durability of Response

Co-Stimulation Enabled Sustained Tumor Cell Killing in Repeat Stimulation Assay

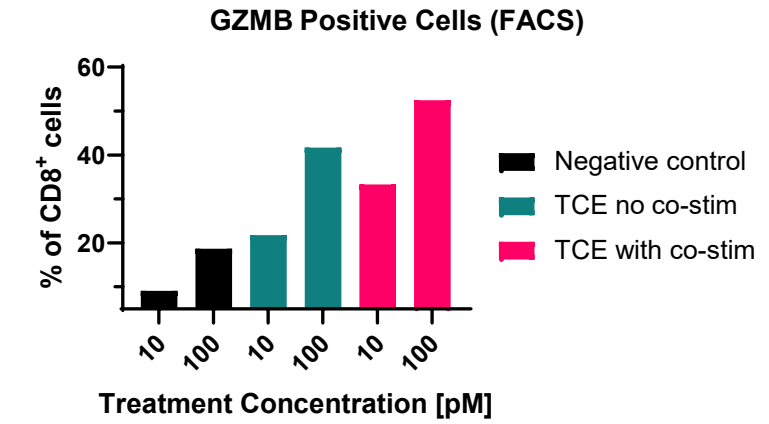


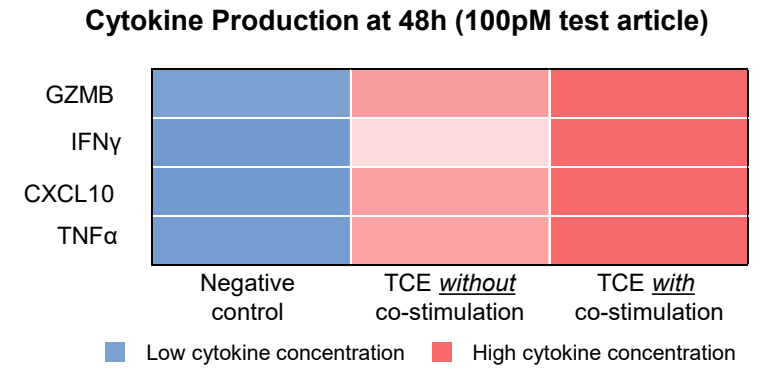
STEAP1 With Co-Stimulation Demonstrated Enhanced Potency and TGI *In Vivo*



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

Co-Stimulation 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 A375 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). .

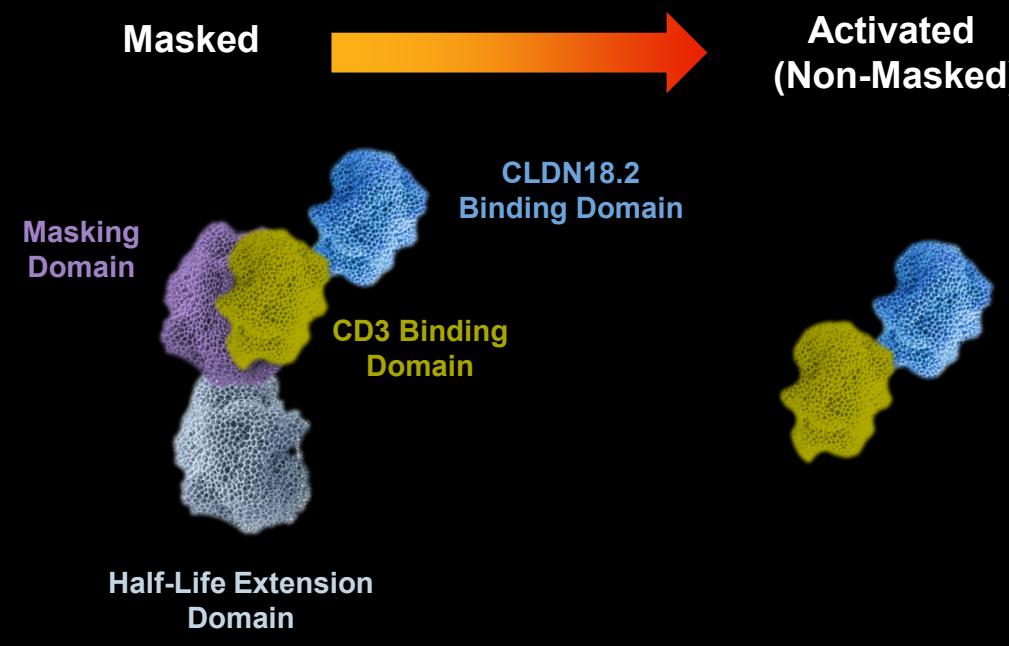
CLDN18.2 x CD3

Masked TCE

x·ilio THERAPEUTICS®

CLDN18.2 x CD3: Potential First-in-Class Masked TCE for Gastrointestinal Cancers

XTX601: Masked T Cell Engager



- ***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

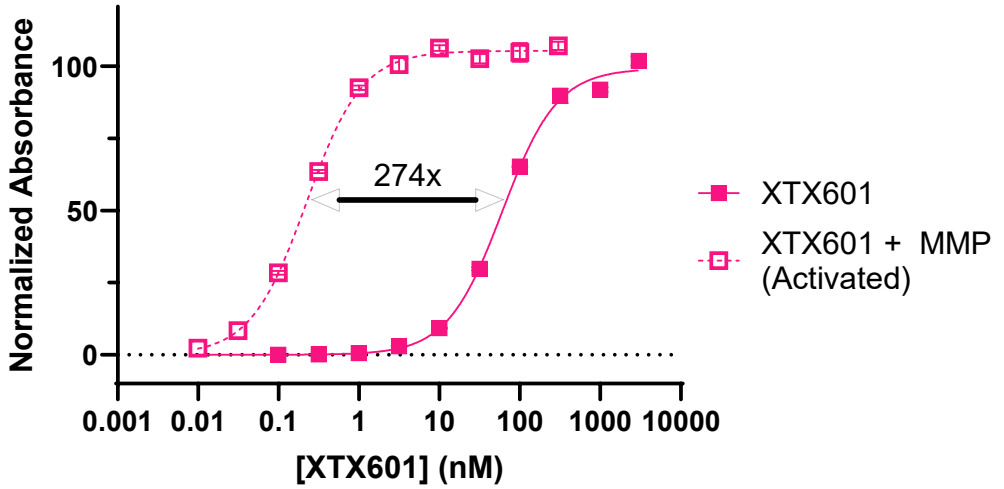
- Xilio design uses **high affinity CLDN18.2 isoform-selective binder**
- CLDN18.2 is a **validated target expressed across gastrointestinal cancers** (gastric, pancreatic, esophageal) **and lung cancer**
- Potential for **significantly expanded therapeutic index with masking** – non-masked T cell engagers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

IND submission anticipated in 2H 2027

GI: gastrointestinal

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

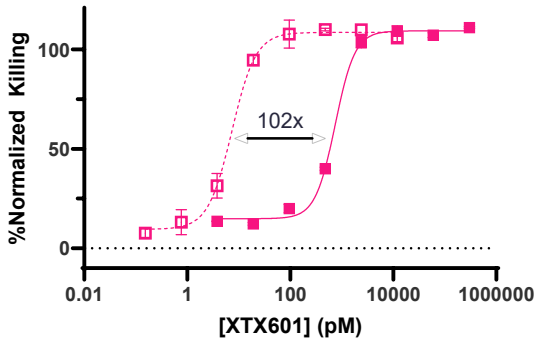
Protease-Dependent Binding to CD3

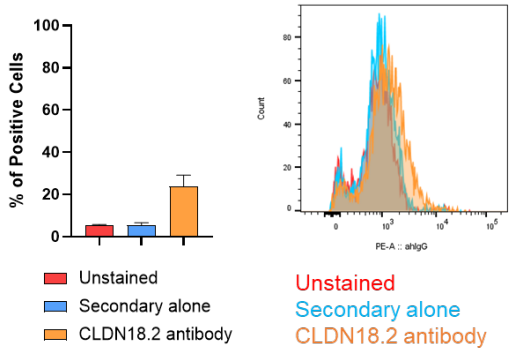


Test Condition	K_d (nM)	Fold- Masking
XTX601	60.31	**274**
XTX601 + MMP (Activated)	0.22	

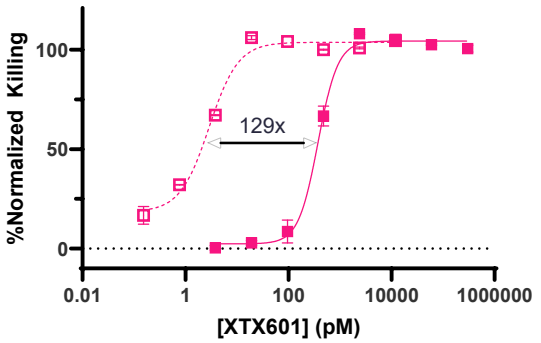
Protease-Dependent Tumor Cell Killing in CLDN18.2 High and Low Cell Lines

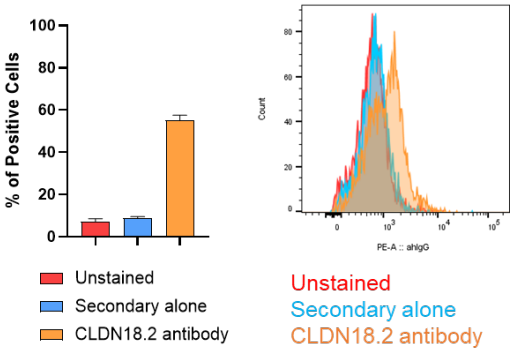
Low CLDN18.2 Expression: GSU





High CLDN18.2 Expression: OE19

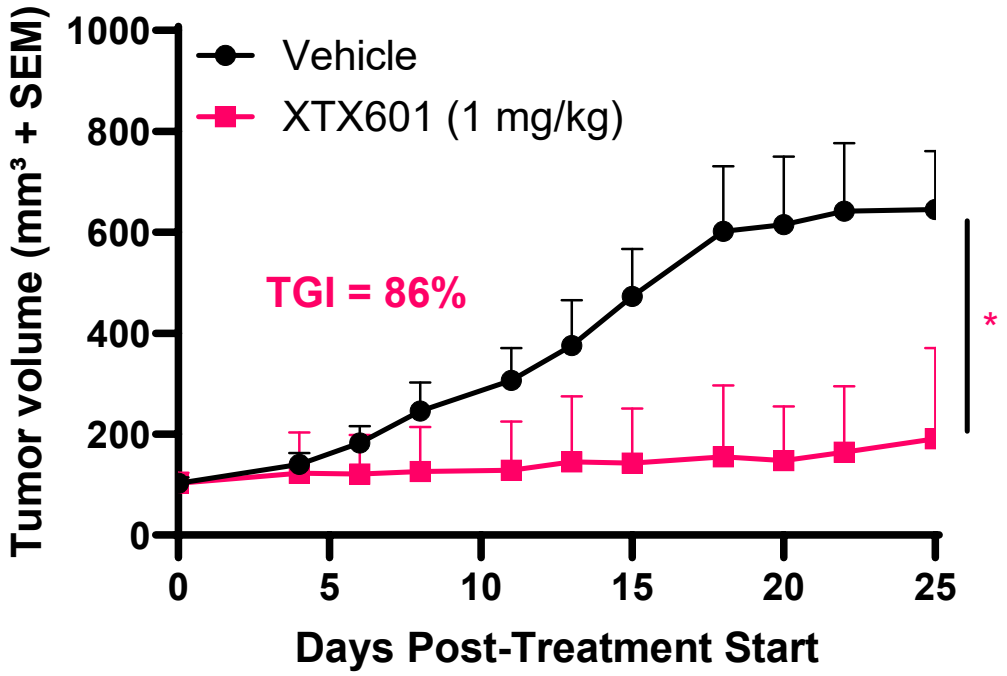




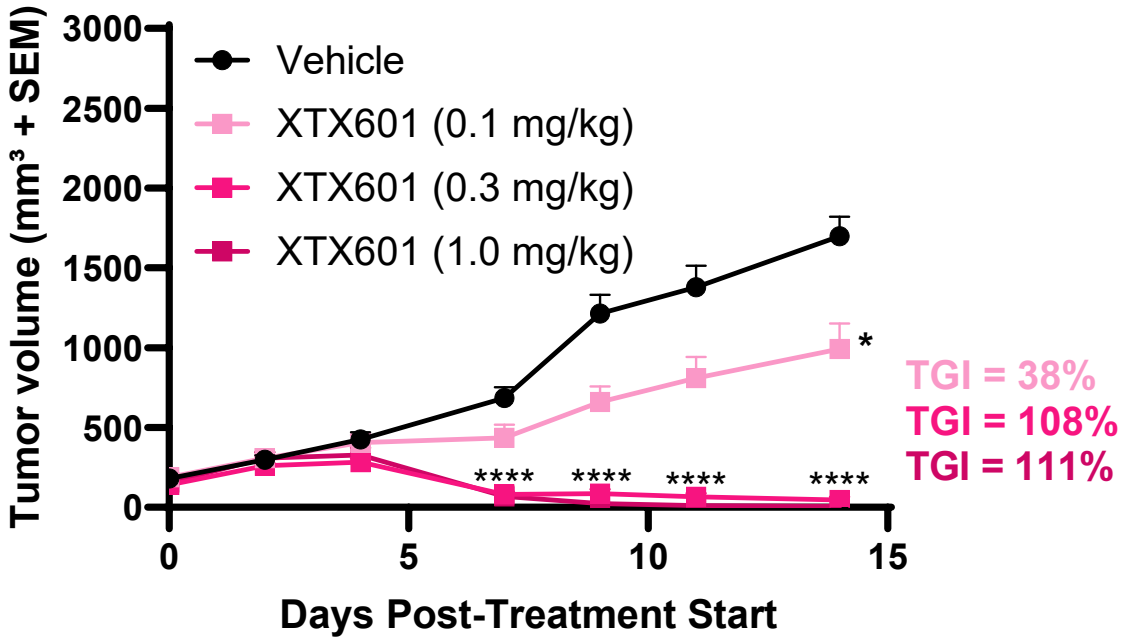
Left panel: CLDN18.2 molecule binding to recombinant human CD3 delta/epsilon either in intact form or pre-activated using recombinant MMP. Analysis performed using ELISA.
Right panel top: Human T cell/cancer cell line co-culture assay evaluating tumor cell killing by either intact CLDN18.2 or CLDN18.2 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.

Robust, Dose-Dependent Anti-Tumor Activity in Multiple *In Vivo* Murine CDX Models

Potent Anti-Tumor Activity in GSU Gastric Cancer Model

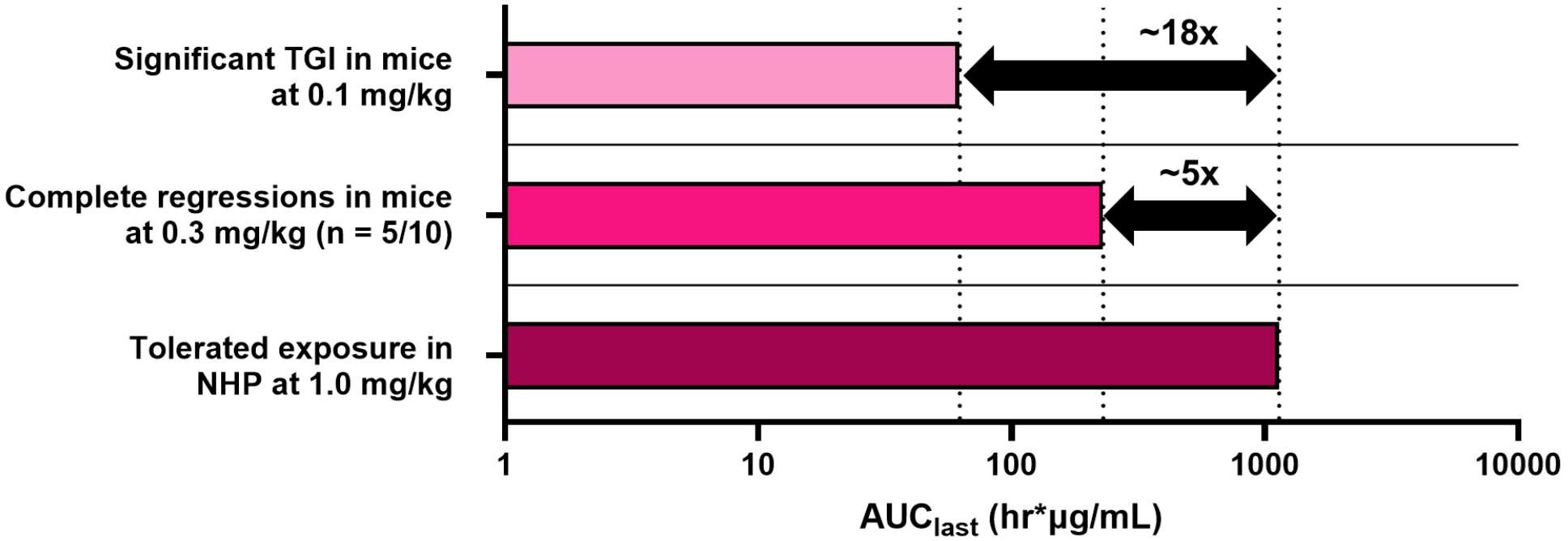


Complete Tumor Regressions in OE19 Esophageal Cancer Model at Doses ≥ 0.3 mg/kg



Left panel: GSU cells were inoculated in NSG mice engrafted with human T cells. Anti-tumor activity change in response to a dose of 1.0 mg/kg XTX601 was evaluated over time. A 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 the indicated dose levels of XTX601 was evaluated over time. A 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 Demonstrated a 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

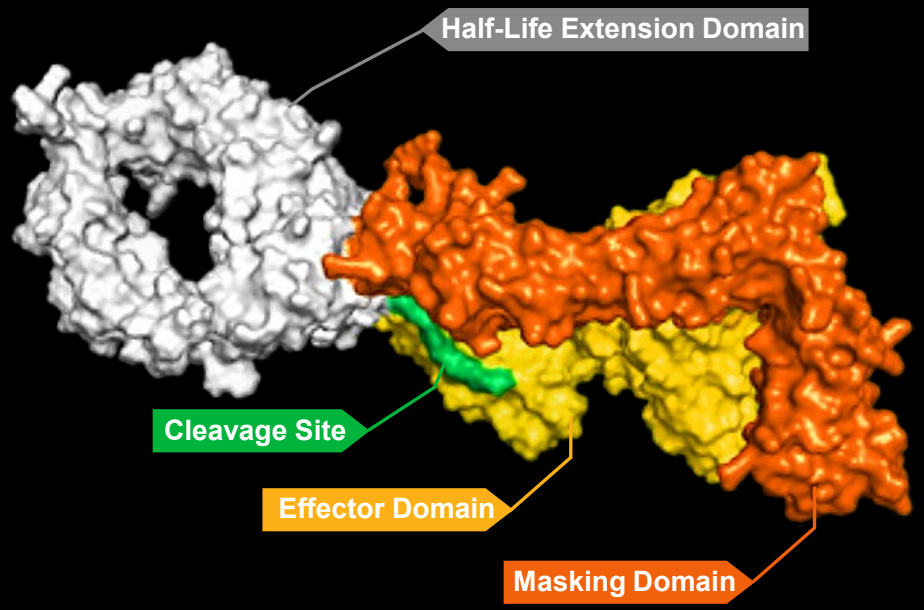
Efarindodekin alfa

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

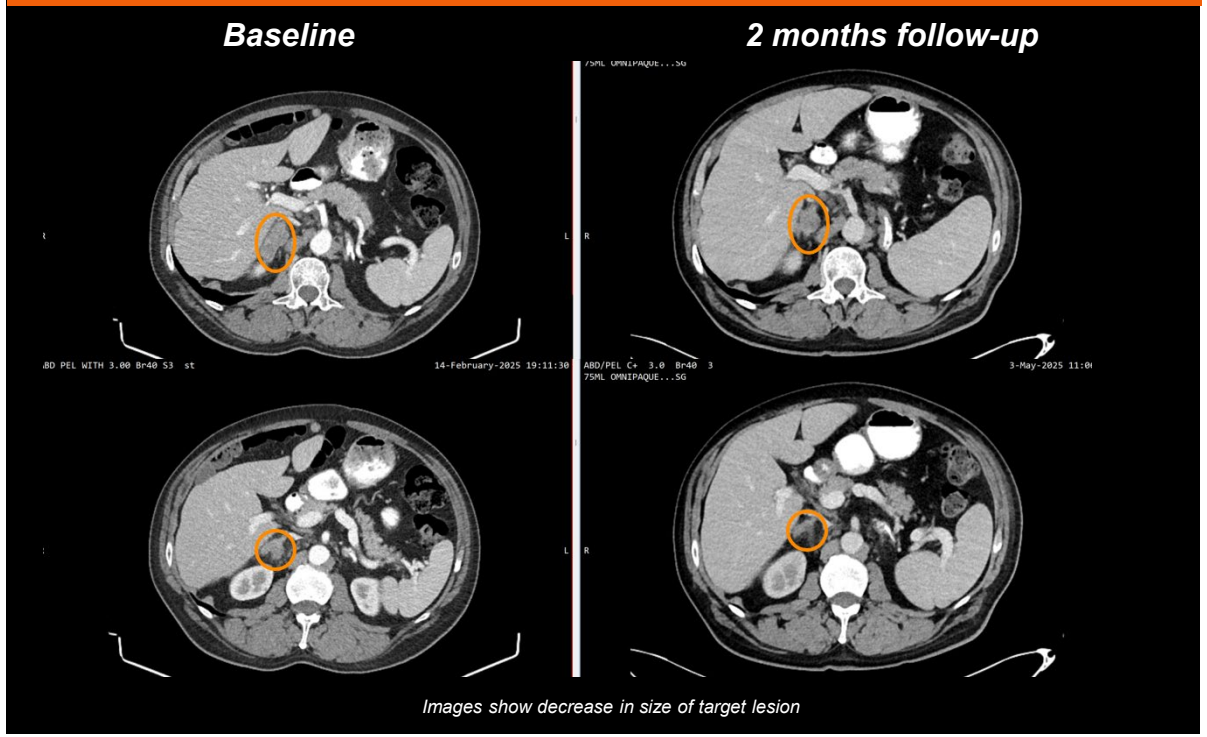
Efarindodekin Alfa Demonstrated Promising Monotherapy Clinical Efficacy in Phase 1, Including Two PRs in Patients With I-O Refractory Advanced Solid Tumors

PRs in Patients with I-O Refractory Tumors

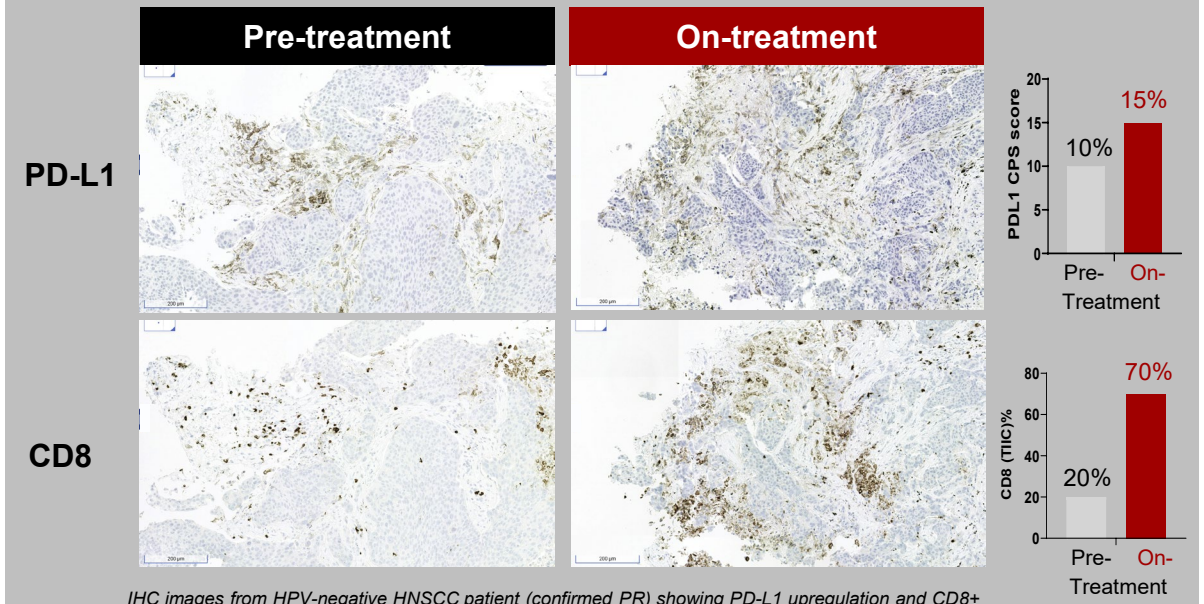
HPV-negative HNSCC patient
- 5 prior lines of therapy; no response to pembrolizumab-based therapy
- Confirmed PR (33% decrease)
- Accompanied by robust changes in PD biomarkers

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

66-year-old male with HPV-negative HNSCC



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

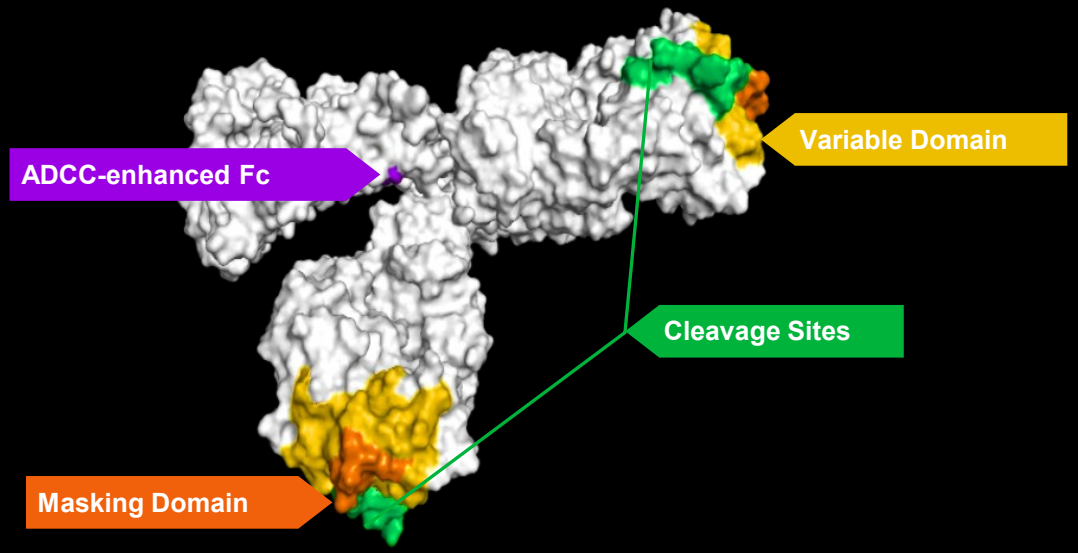
Vilastobart

Masked, Fc-enhanced anti-CTLA-4

xilio 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** (>50% of MSS CRC patients of have 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** • **Real-word data** in ~8,000 patients with MSS CRC showed **~55% have high plasma TMB** (1) • **63% of patients** in Phase 2 had **high plasma TMB**, **including all TMB-evaluable responders**

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

Recent Financial Results and Management Overview

xilio THERAPEUTICS®

Q2 2026 Financial Results and Summary Capitalization
Anticipate Cash Runway Into Q1 2028 (1)

Balance Sheet

	June 30, 2026
Cash and Cash Equivalents	$136.0M

Statement of Operations

	Three Months Ended June 30, 2026
Collaboration and License Revenue	$18.7M
R&D Expenses	$14.6M
G&A Expenses	$7.6M
Total Operating Expenses	$22.2M
Net Loss	$(6.4M)

Summary Capitalization

	June 30, 2026
Common Stock	6,580,149
Prefunded Warrants for Common Stock	13,107,620
Series A Common Stock Warrants	4,762,533
Series C Common Stock Warrants	3,443,388
Total Common Stock Warrants	8,205,921
Total Common Stock + Prefunded Warrants + Common Stock Warrants	27,893,690

1. Unaudited. This cash runway estimate (i) includes $6.0 million development milestone achieved in Q2 2026 and received in Q3 2026, and (ii) excludes up to $36.2 million in additional gross proceeds in the second half of 2026 if all outstanding Series C warrants are exercised at their current exercise price and any potential additional milestone payments, option-related fees or other contingent payments under our collaboration and license agreements with AbbVie and Gilead.

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

SCOTT COLEMAN, PH.D.
Chief Development Officer

NATE MCBRIDE
Chief Information Officer

BEN HARSHBARGER
Chief Legal Officer

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