Unleashing the Potential of Immuno-Oncology Therapies

December 19, 2024

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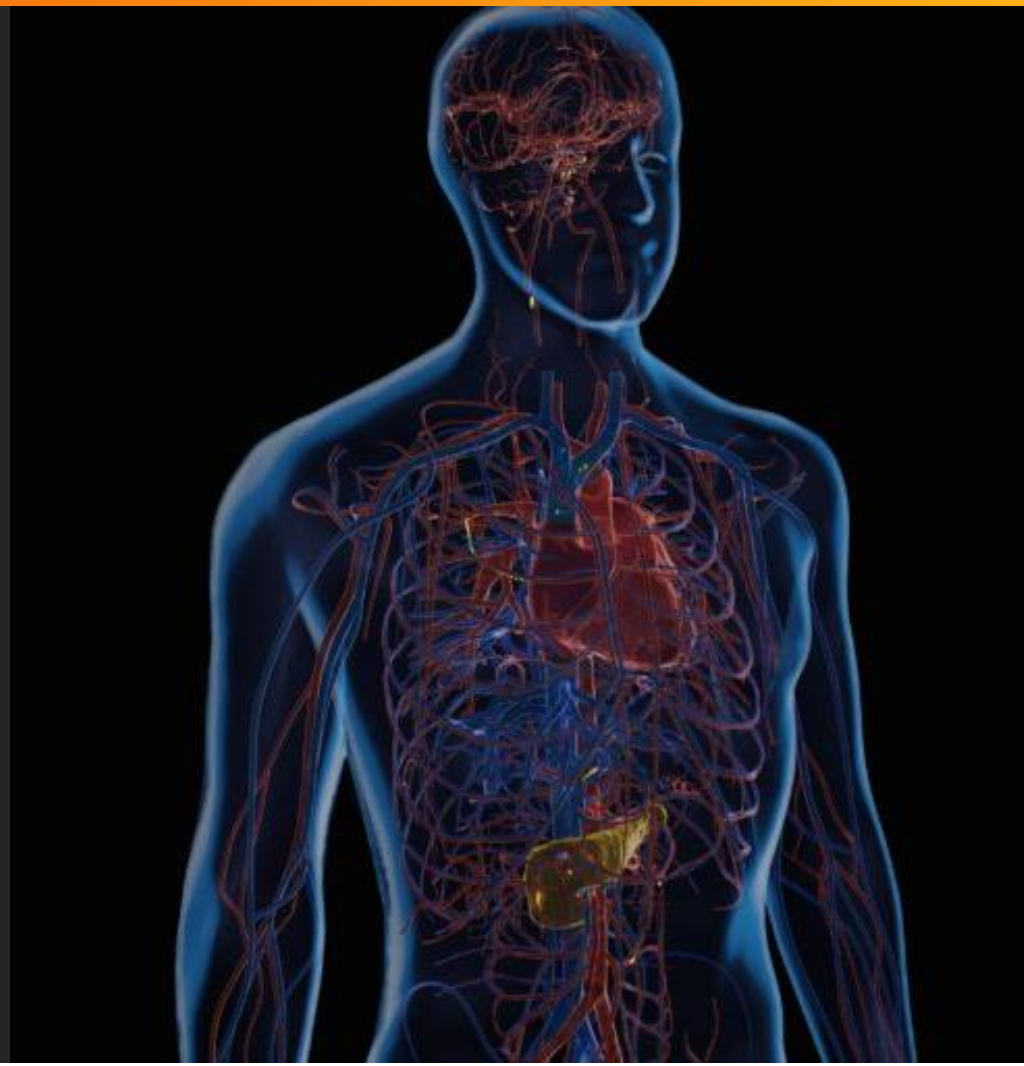
Immuno-Oncology Therapy is the Key to Curative Potential, But Continues to Be Limited by Systemic Toxicity

Xilio believes the next revolution in I-O therapy will **harness the power of the body's immune system** by **leveraging the dysregulated biology of the tumor against itself**

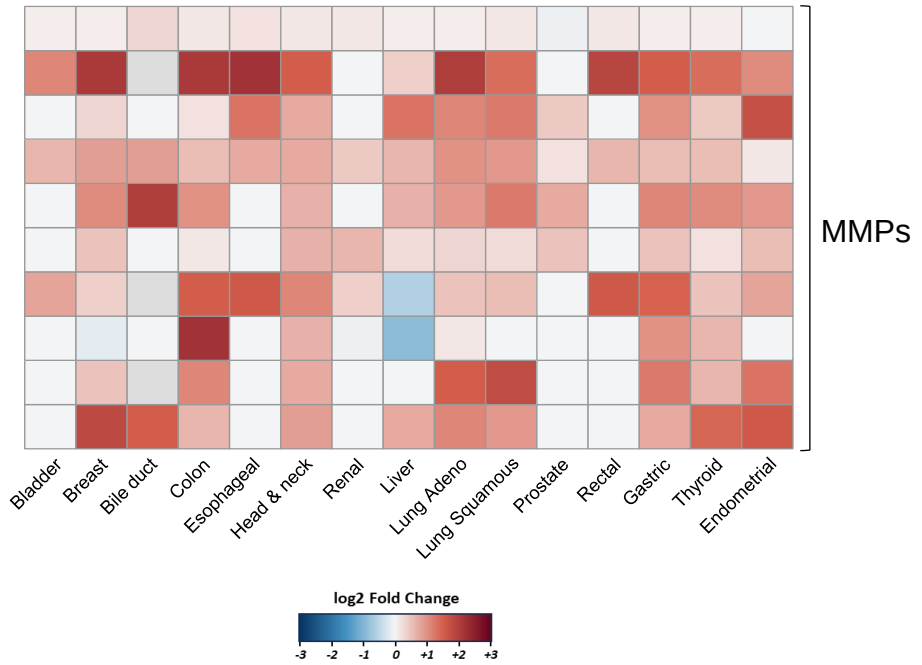


I-O: immuno-oncology

Xilio Exploits Dysregulated MMP Activity, a Hallmark of Invasive Cancer Common Across a Wide Range of Solid Tumors, to Activate Molecules in the Tumor

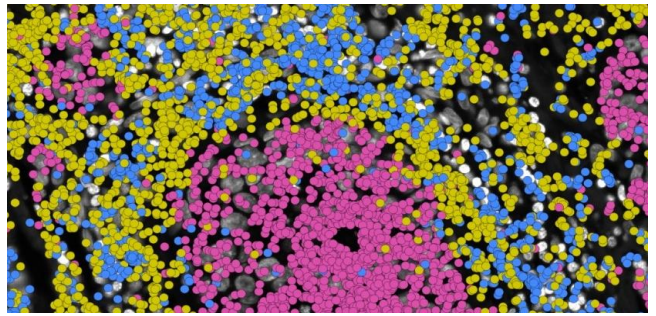
MMPs are dysregulated broadly across solid tumors

MMP mRNA expression in tumor vs. normal tissue

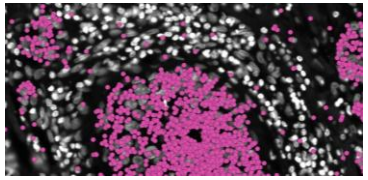


MMPs and immune cells co-localize at the invasive edge of tumors

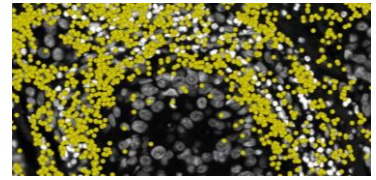
In situ mRNA expression in human breast cancer



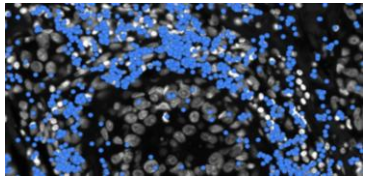
Tumor cells (TROP2)



MMP (MMP2)



T cells (CD4, CD8A)

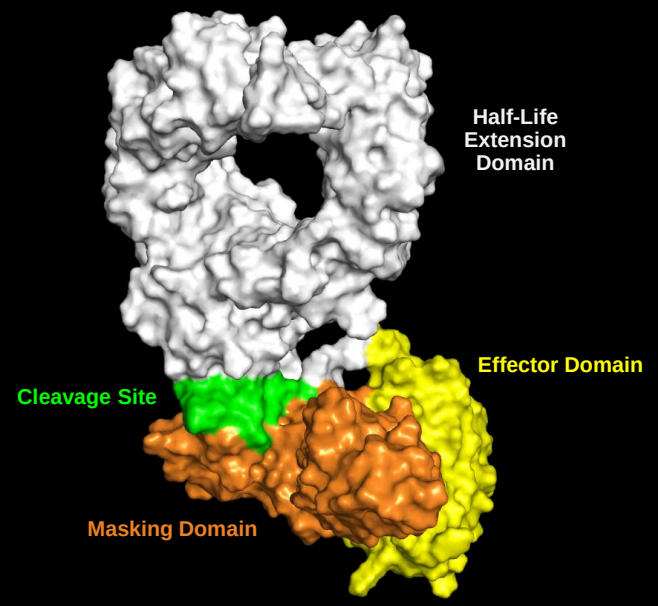


Left panel: Heatmap summarizing RNA expression changes of genes encoding for selected MMPs (bottom) in tumor vs. adjacent normal samples from multiple TCGA studies (x-axis). Color intensity tracks with log2-transformed fold changes (log2FC). Pre-processed TCGA data were obtained from UCSC Xena. **Right 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
MMP: matrix metalloproteases

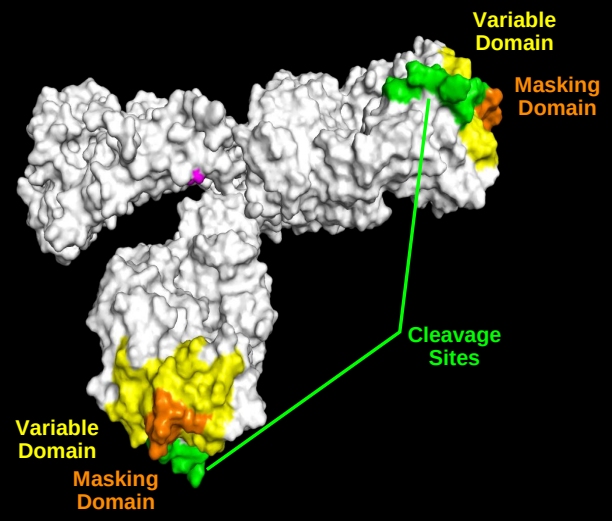
Xilio's Tumor-Activated Approach Has Been Successfully Applied in the Clinic Across Diverse Molecular Architectures

- Initial clinical validation, with >200 patients enrolled to date across clinical programs
- Molecules designed for tumor-selectivity with a masking domain to block interaction with healthy tissue and cells
- Dysregulated MMPs in the TME activate molecules via the protease cleavage site across a wide range of solid tumors (without the need for biomarkers)
- Bank of >1,000 human solid tumor samples informed design and test molecule activation

Cytokine Example



Antibody Example



TME: tumor microenvironment

Advancing Pipeline of Clinical and Preclinical Tumor-Activated Molecules

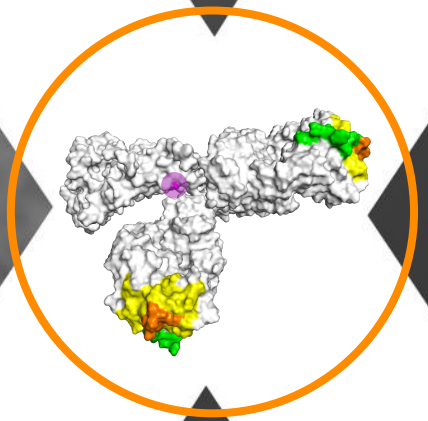
Program	Tumor Types	Mechanism of Action	Discovery	IND-Enabling	Phase 1	Phase 2	Phase 3	Partnerships
Vilastobart (XTX101) in combination with atezolizumab [1]	Metastatic MSS CRC	anti-CTLA-4 + PD-L1						**Clinical collaboration with Roche (with co-funding)**
XTX301 [2]	Advanced Solid Tumors	IL-12						**Exclusive global license with Gilead**
XTX501 [3]	Advanced Solid Tumors	PD-1/IL2 bispecific						
Additional research-stage programs	Undisclosed	Tumor-activated cell engagers						

1. Evaluating vilastobart (XTX101) in combination with atezolizumab (Tecentriq®) in patients with metastatic MSS CRC.
2. Evaluating XTX301 in Phase 1 monotherapy dose escalation and dose expansion for the treatment of advanced solid tumors.
3. Conducting initial IND-enabling activities.

CRC: colorectal cancer; MSS: microsatellite stable

Vilastobart (XTX101)

Tumor-Activated, Fc-enhanced Anti-CTLA-4



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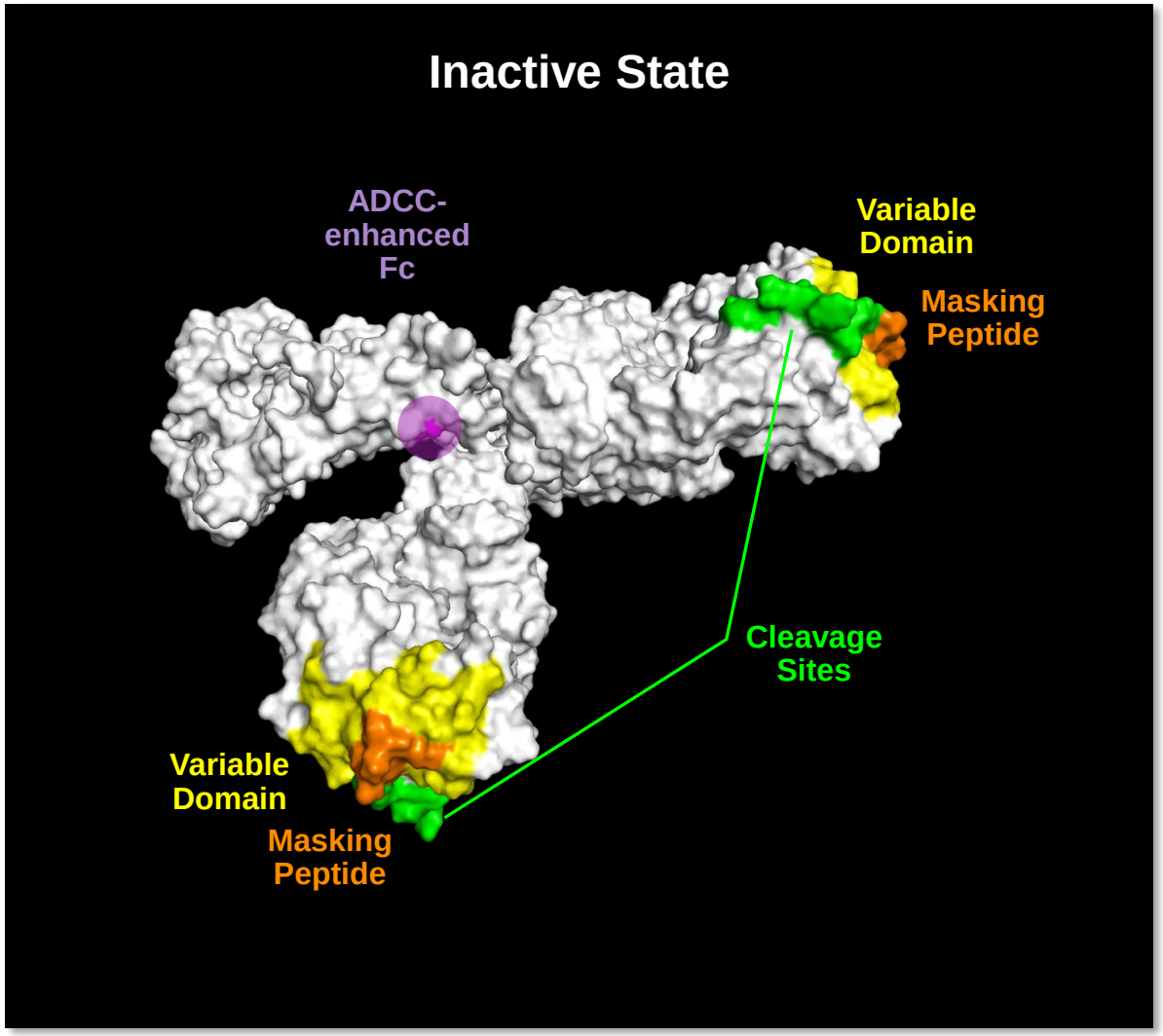
Vilastobart: Tumor-Activated, High Affinity Binding, Fc-Enhanced Anti-CTLA-4



Vilastobart Incorporates Multiple Differentiating Design Features for a Potential Best-in-Class Profile

- High affinity binding, 10x potency of ipilimumab in preclinical studies*
- Fc mutations for enhanced effector function (ADCC), improved T cell priming and Treg depletion
- On-treatment biopsies in Phase 1 monotherapy demonstrated >70% activated molecule in tumor with <15% activated molecule in periphery
- Generally well-tolerated in Phase 1 monotherapy, consistent with tumor-activated design
- Confirmed PR observed with monotherapy in Phase 1 in a PD-L1 negative NSCLC patient, including resolution of innumerable liver metastases
- Confirmed PR observed with combination in Phase 1 in MSS CRC patient, including full resolution of liver metastasis

* Ipilimumab analog used for preclinical studies
ADCC: antibody-dependent cell-mediated cytotoxicity; NSCLC, non-small lung cancer; PR: partial response; Treg: regulatory T cells

Vilastobart (anti-CTLA-4) Advancing in Phase 2 Proof-of-Concept Trial for MSS CRC in Co-Funded Clinical Collaboration with Roche

Phase 2 Combination Proof-of-Concept Trial

Metastatic MSS CRC patients with and without liver metastases

vilastobart at 100 mg Q6W + atezolizumab at 1200 mg Q3W

Currently Enrolling

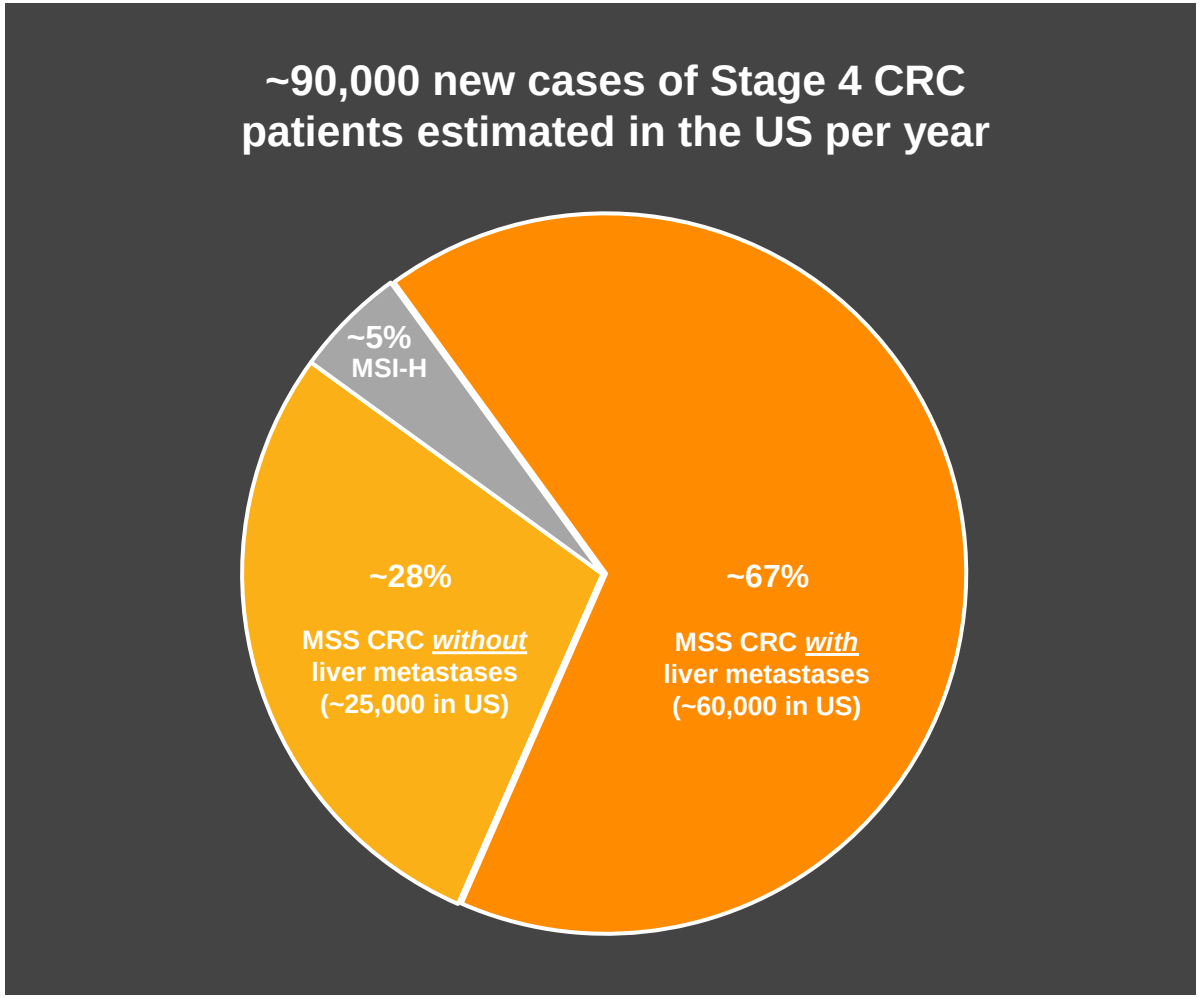
Anticipated Near-Term Phase 2 Data Milestones

- Plan to report initial Phase 2 data (n = ≥20 total) in MSS CRC at ASCO GI in January 2025
- Plan to report additional Phase 2 data (n = ~40 total) in MSS CRC in mid 2025

Q3W: once every three weeks; Q6W: once every six weeks

CRC Incidence is Increasing, Particularly In Young Adults: Majority of Patients with Stage 4 MSS CRC Have Liver Metastases

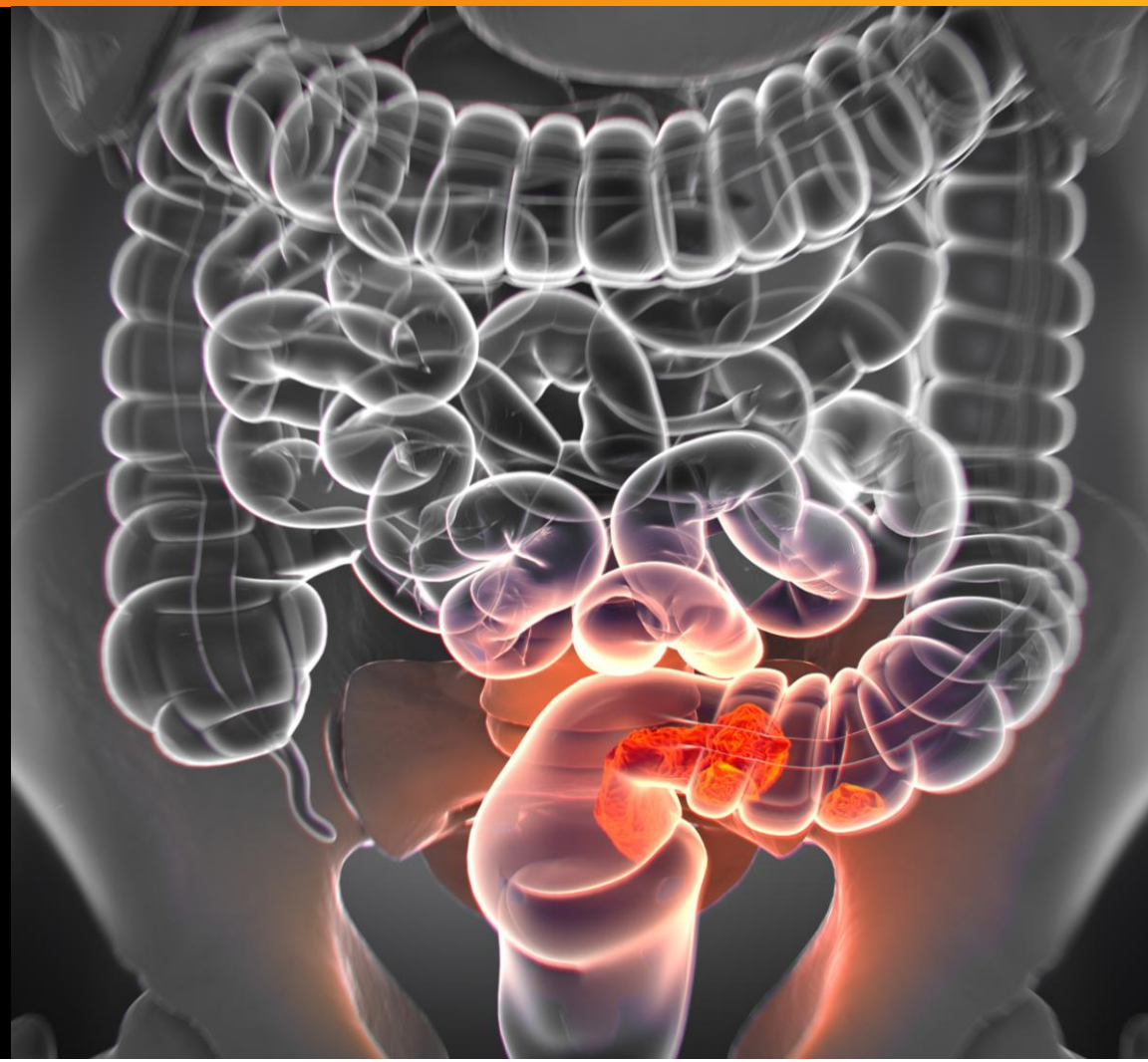
- CRC is 2nd in cancer-related deaths in the US and leading cause of cancer-related death in men younger than 50 in the US (1)
- CRC is 3rd in total annual new cases globally, with ~1.9M new cases and ~900,000 deaths related to CRC globally (2)
- >65% of Stage 4 CRC patients present with liver metastases, which are associated with poor outcomes (3)



1. Siegel. CA Cancer J Clin.2023;73:233. 2. Bray. CA Cancer J Clin 2024;74:229. 3. Kawazoe. J Clin Oncol. 2024;42:2918.
MSI-H: microsatellite instability-high

I-O Therapies Have Shown Little to No Efficacy in MSS CRC to Date

- Majority of patients diagnosed with metastatic disease are not eligible for surgery and primary treatment includes chemotherapy and/or radiation [1]
- Treatment for advanced MSS CRC typically includes chemotherapy +/- TKI, [1] followed by clinical trials or late-line therapies with minimal benefit (OS: ~6-9 months) [2]
- Immune checkpoint inhibitors (pembrolizumab/ nivolumab) approved in MSI-H CRC have no meaningful efficacy in patients with MSS CRC (0-3% ORR) [3]



1. Eng. Lancet. 2024;404:294.
2. Grothey. Lancet. 2013;381:303; Mayer. N Engl J Med. 2015;372:1909; Li. JAMA. 2018;319:2486; Dasari. Lancet. 2023;402:41; Kawazoe. J Clin Oncol. 2024;42:2918.
3. Sahin. Am Soc Clin Oncol Educ Book. 2022:42:1
ORR: objective response rate; OS: overall survival; TKI: tyrosine kinase inhibitor

Vilastobart (anti-CTLA-4)

Phase 1C Combination Dose Escalation Data
Vilastobart + Atezolizumab

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Vilastobart (anti-CTLA-4) Advancing in Phase 2 Proof-of-Concept Trial for MSS CRC in Co-Funded Clinical Collaboration with Roche

Phase 1C Combination Dose Escalation	*Phase 2 Combination Proof-of-Concept*
Advanced solid tumors vilastobart at 75, 100 and 150 mg Q6W + atezolizumab at 1200 mg Q3W	**Metastatic MSS CRC patients with and without liver metastases** vilastobart at 100 mg Q6W + atezolizumab at 1200 mg Q3W
Currently enrolling	*Currently enrolling*

Combination of Vilastobart (anti-CTLA-4) and Atezolizumab Was Generally Well-Tolerated with Minimal irAEs

AE Category / Term ***All TRAEs with ≥10% incidence in any category or any Grade 3 TRAE***	**All Phase 1C Patients (n=17) vilastobart (75, 100 or 150 mg Q6W) + atezolizumab (1200 mg Q3W)**	
	Any	**Grade 3**
ALT increased	3 (18%)	2 (12%)
Blood ALP increased	2 (12%)	1 (6%)
Diarrhea	2 (12%)	1 (6%)
Colitis	1 (6%)	1 (6%)
Infusion related reaction (1)	10 (59%)	0
AST increased	3 (18%)	0
Lipase increased	3 (18%)	0
Fatigue	2 (12%)	0
Dose reduction due to TRAE	1	
Treatment discontinuation due to TRAE (2)	1	

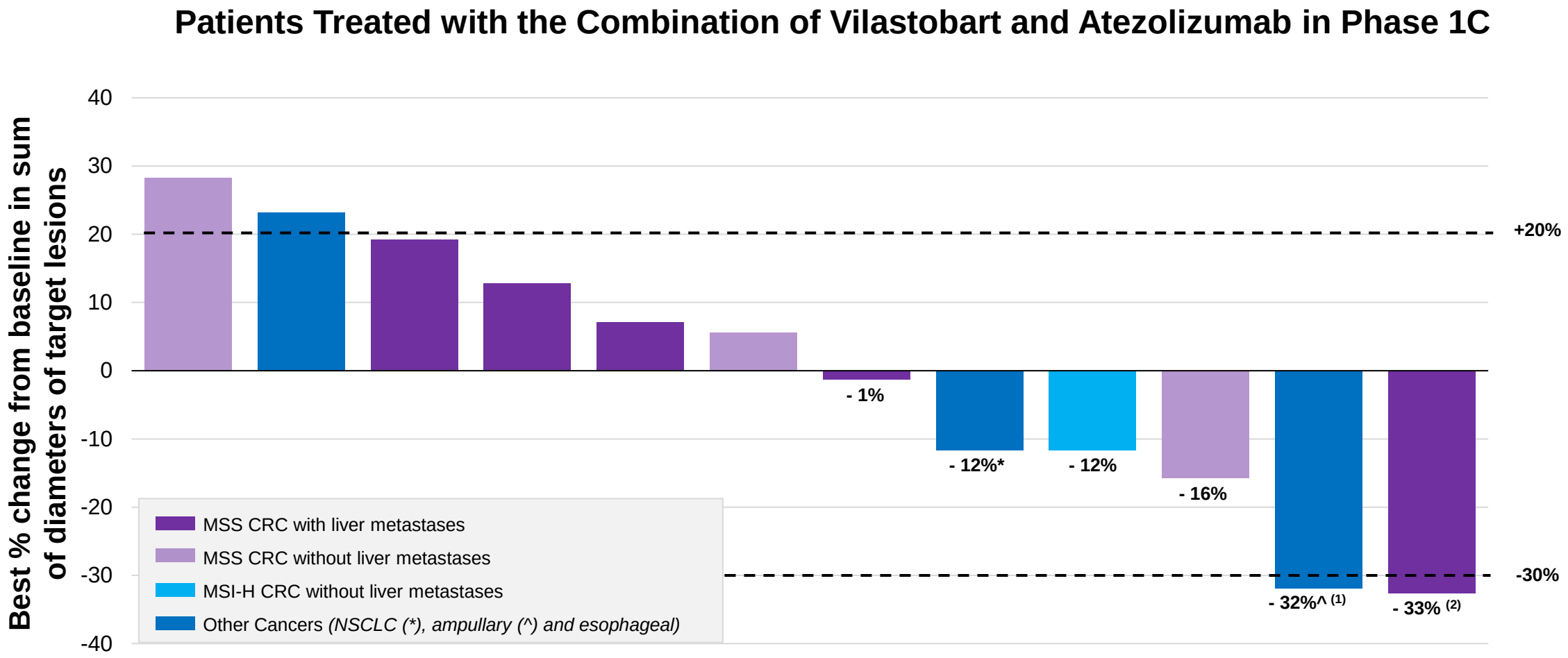
- ***No Grade 4 or Grade 5 TRAEs at any dose level***
- ***Only 3 patients experienced Grade 3 TRAEs, of these 2 experienced DLTs (150 mg dose level of vilastobart)*** (3)
- ***No endocrine irAEs and limited skin irAEs***
- ***Selected initial RP2D of vilastobart (100 mg Q6W) + atezolizumab (1200 mg Q3W)***

Data cutoff date: October 7, 2024

1. Of the 10 patients with infusion related reactions, 4 experienced reactions related to vilastobart, 3 experienced reactions related to atezolizumab and 3 experienced reactions related to the combination.
2. Reflects discontinuation of both vilastobart and atezolizumab.
3. DLTs at the 150 mg dose level of vilastobart were experienced by one patient with Grade 3 colitis and diarrhea and one patient with grade 3 ALT and blood ALP elevation.

AE: adverse event; ALP: alkaline phosphatase; ALT: alanine aminotransferase; AST: aspartate transaminase; DLT: dose-limiting toxicity; irAE: immune-related adverse event; RP2D: recommended Phase 2 dose; TRAE: treatment-related adverse event

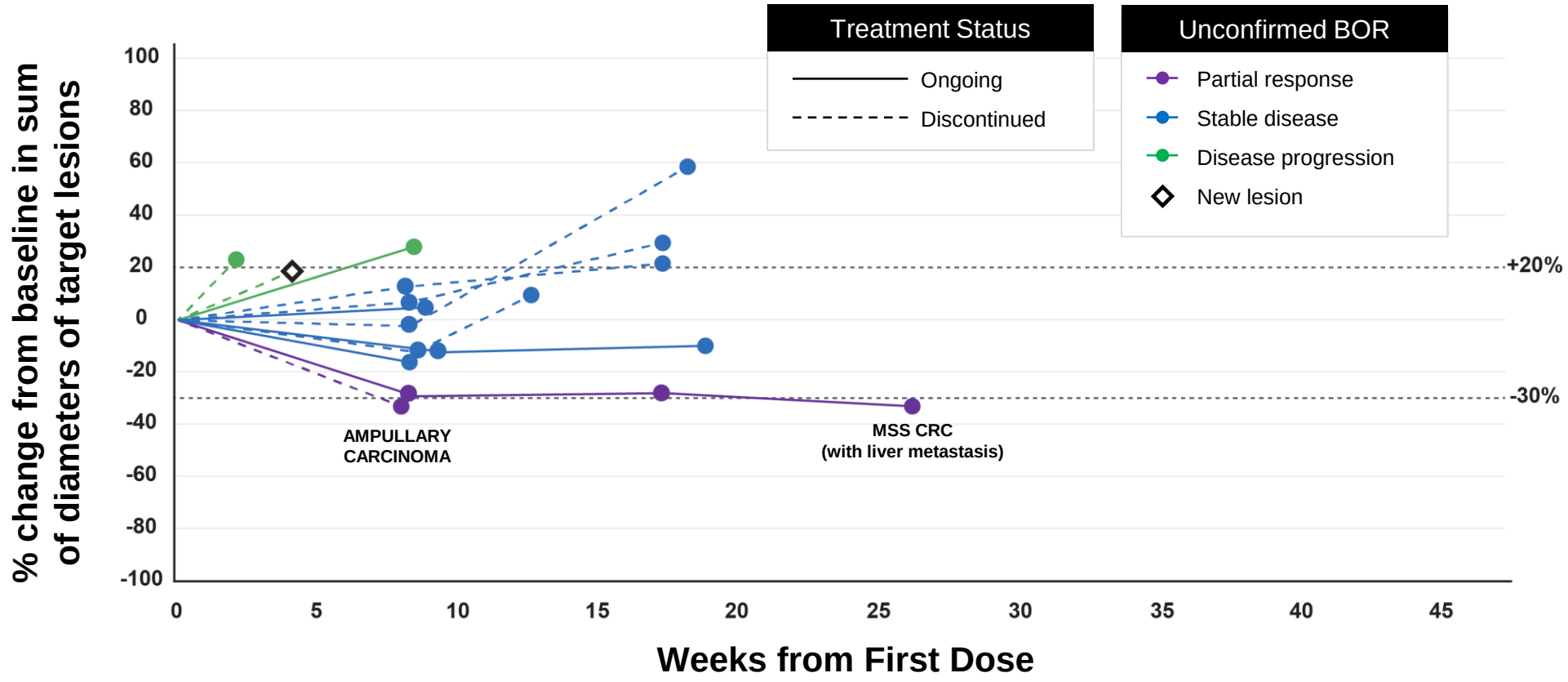
Combination of Vilastobart (anti-CTLA-4) and Atezolizumab Demonstrated Anti-Tumor Activity in Cold Tumors, Including a Sustained Tumor Reduction in a MSS CRC Patient with Metastatic Liver Disease



Data cutoff date: October 7, 2024. n=12 response-evaluable patients.
1. PR (unconfirmed), patient withdrew consent prior to confirmatory scan.
2. PR confirmed after the data cutoff date.

Combination of Vilastobart (anti-CTLA-4) and Atezolizumab Demonstrated Anti-Tumor Activity in Cold Tumors, Including a Sustained Tumor Reduction in a MSS CRC Patient with Metastatic Liver Disease

Patients Treated with the Combination of Vilastobart and Atezolizumab in Phase 1C



Data cutoff date: October 7, 2024. n=12 response-evaluable patients.
BOR: best overall response

Confirmed PR in MSS CRC Patient, Including Full Resolution of Metastatic Liver Lesion

MSS CRC and Liver Metastasis

- 69 year-old female
- 5 prior lines of therapy:
  - FOLFOX-Avastin
  - FOLFIRI-Avastin
  - Cetuximab
  - Lonsurf
  - FOLFIRI-Panitumamab
- Administered vilastobart (150 mg Q6W) + atezolizumab (1200 mg Q3W)

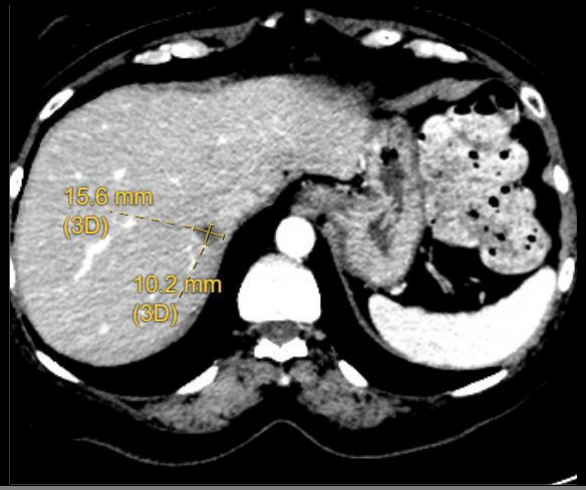
	Screening	1st follow-up (9 weeks)	2nd follow-up (18 weeks)	3rd follow-up (27 weeks)	4th follow-up (36 weeks)
Sum of diameters	98.4 mm	70.5 mm	71.0 mm	66.3 mm	63.8 mm
Change		**- 28%**	**- 28%**	**- 33%**	**-35%**

Including full resolution of target lesion in the liver

Data cutoff date: October 7, 2024
PR confirmed at 36 weeks, after the data cutoff.

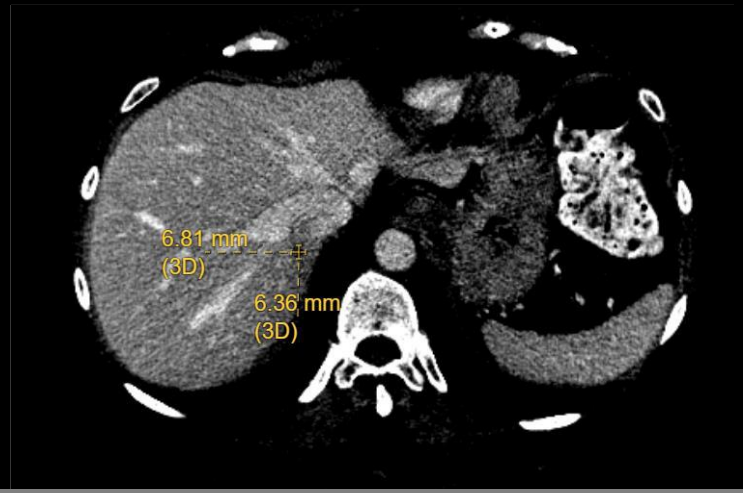
Confirmed PR in MSS CRC Patient, Including Full Resolution of Metastatic Liver Lesion

Target Liver Lesion – Baseline



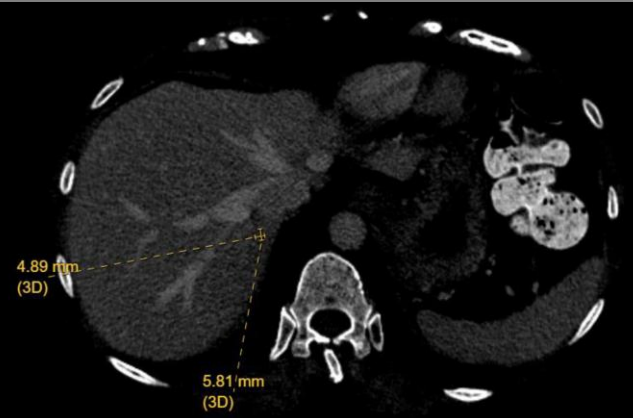
15.6 mm

Target Liver Lesion – After 9 Weeks



6.8 mm

Target Liver Lesion – After 18 Weeks



5.8 mm

Target Liver Lesion – After 27 and After 36 Weeks

No visible lesion

Data cutoff date: October 7, 2024.
Patient administered vilastobart (150 mg Q6W) and atezolizumab (1200 mg Q3W)
PR confirmed at 36 weeks, after the data cutoff date.

PR (Unconfirmed)* in Patient with Ampullary Carcinoma (Cold Tumor) After Single Cycle of Combination of Vilastobart (anti-CTLA-4) and Atezolizumab

Malignant Neoplasm of Ampulla of Vater

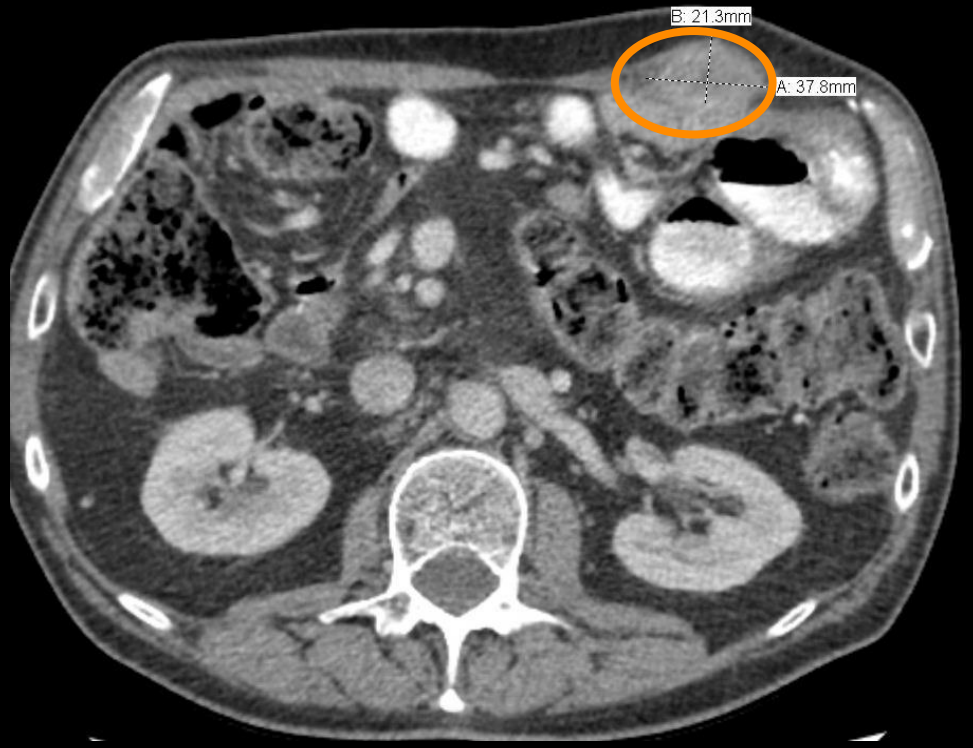
- 76 year-old male
- 2 prior lines of therapy:
  - Gemcitabine + nab-Paclitaxel
  - 5-fluorouracil + Irinotecan Liposome + Leucovorin
- Administered vilastobart (150 mg Q6W) + atezolizumab (1200 mg Q3W)
- Significant CA 19-9 decrease after a single cycle of the combination

	Screening		8 weeks after C1D1
Sum of diameters	60.5 mm		41.2 mm
Change			**- 32%**
Serum tumor marker	**Screening**	**C1D1**	**6 weeks after C1D1**
CA 19-9 (U/mL)	**575.0**	**700.2**	**40.8**

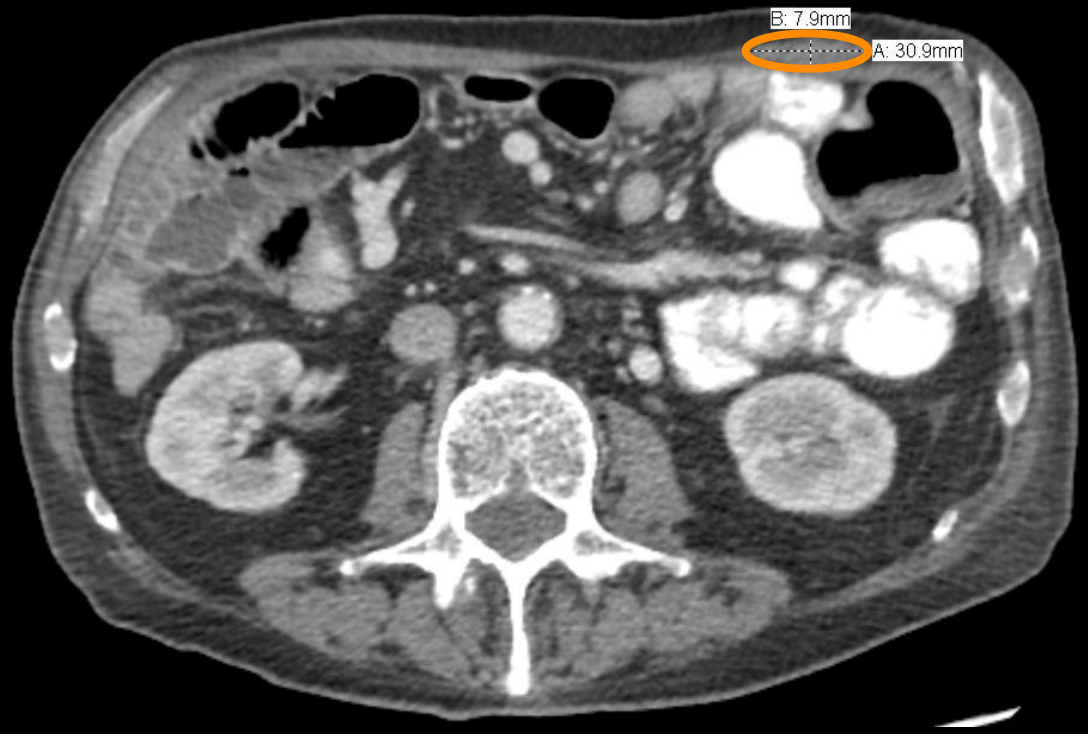
Data cutoff date: October 7, 2024
* Patient withdrew consent prior to confirmatory scan.
C1D1: cycle 1, day 1

PR (Unconfirmed)* in Patient with Ampullary Carcinoma (Cold Tumor) After Single Cycle of Combination of Vilastobart (anti-CTLA-4) and Atezolizumab

Target Lesion At Screening



Target Lesion After 8 weeks



Data cutoff date: October 7, 2024. Patient administered vilastobart (150 mg Q6W) and atezolizumab (1200 mg Q3W).
* PR (unconfirmed) at week 8 (32% reduction in sum of diameters). Patient withdrew consent prior to confirmatory scan.

Encouraging Initial Evidence of Combination Activity in Phase 1C; Plan to Present Initial Phase 2 Combination Proof-of-Concept Data at ASCO GI in January 2025

Initial Phase 1C Data for Combination of Vilastobart and Atezolizumab

- Generally well-tolerated with minimal irAEs
- Initial evidence of anti-tumor activity in cold tumors, including a confirmed PR in a patient with MSS CRC with complete resolution of liver metastasis

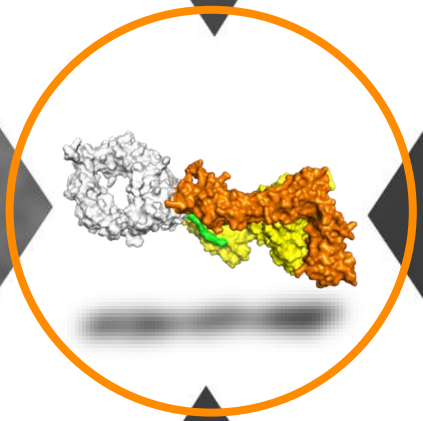
Anticipated Near-Term Phase 2 Data Milestones

- ❑ Plan to report initial Phase 2 data (n = ≥20 total) in MSS CRC at ASCO GI in January 2025
- ❑ Plan to report additional Phase 2 data (n = ~40 total) in MSS CRC in mid 2025

Data cutoff date: October 7, 2024
PR confirmed after data cutoff date.

XTX301

Tumor-Activated IL-12



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The Compelling Potential of IL-12 as a Therapeutic Agent

- IL-12 has significant potential as a potent I-O therapeutic agent in cold tumors
- Poor tolerability has limited its clinical progress for decades
- No currently approved IL-12 agents

IL-12 Has Highly Compelling Biology for I-O Applications

Exquisitely potent stimulator of NK and T cell cytotoxicity and INFγ production

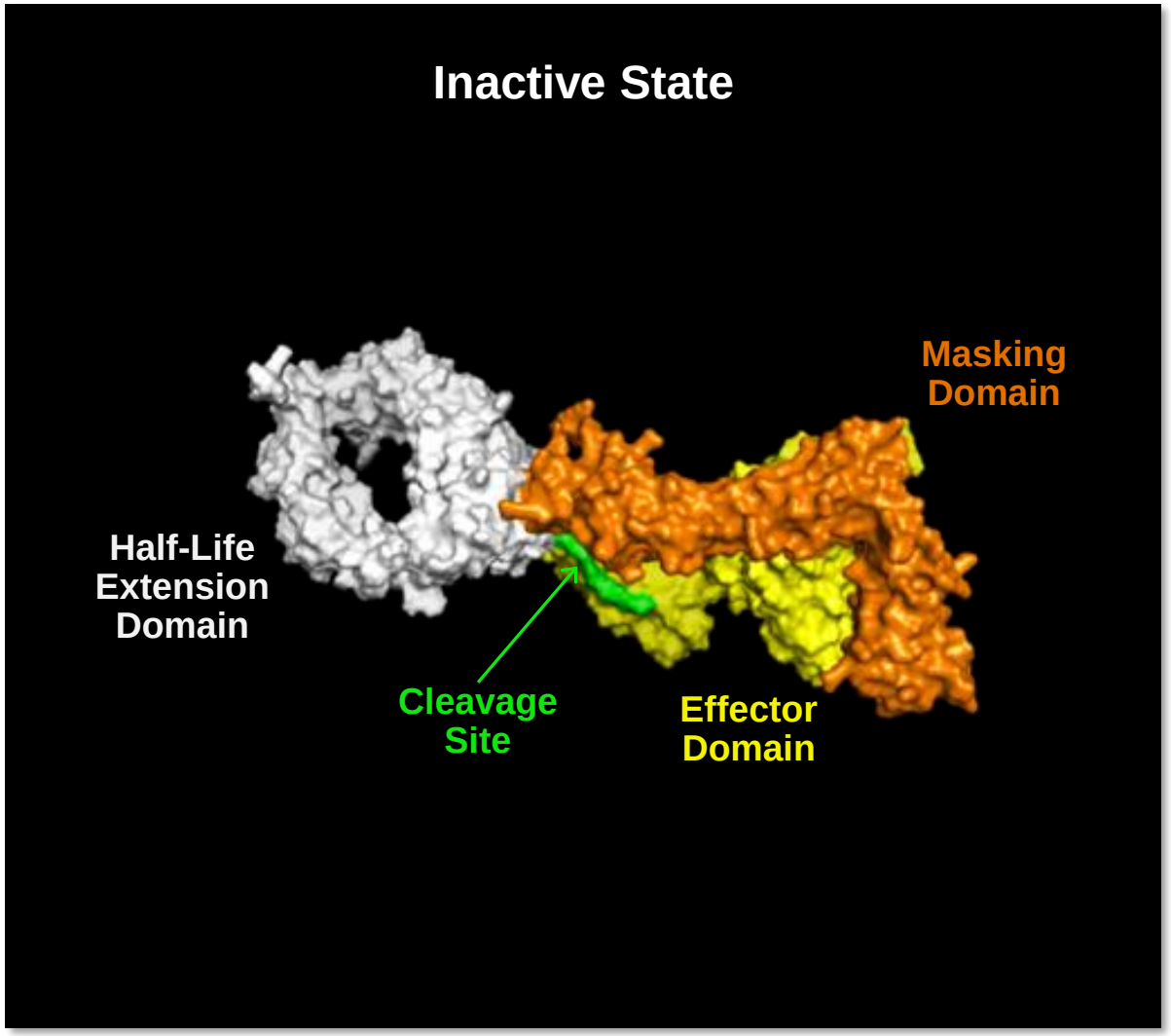
Capable of polarizing CD4 T-cells towards Th1 phenotype, thus driving cellular immunity against infection and cancer

Robust INFγ induction results in broad remodeling of the TME towards a more immune-permissive environment

Demonstrated single agent objective responses in patients, but poorly tolerated (MTD <500 ng/kg on repeat dosing)

INFγ is a pleiotropic molecule with associated antiproliferative, pro-apoptotic and antitumor mechanisms. Th1-type cytokines tend to produce the proinflammatory responses responsible for killing intracellular parasites and for perpetuating autoimmune responses.
INFγ: interferon gamma; g/kg: nanograms/kilogram; NK: natural killer.

XTX301: Tumor-Activated IL-12



XTX301 Designed to Overcome the Limitations of Systemic Recombinant Human IL-12

- Activated XTX301 designed to have optimized short half-life IL-12 (half-life extension domain not retained)
- Potential for broad therapeutic index supported by robust preclinical data
- Efficient activation by human tumors demonstrated *ex vivo*
- Robust anti-tumor activity and tumor-selective PD *in vivo*
- Preliminary Phase 1 data demonstrating promising clinical profile:(1)
  - Sustained IFNɣ signaling without evidence of tachyphylaxis throughout treatment cycles
  - Generally well-tolerated with no DLTs and no dose reductions observed to date
  - No Grade 4 or Grade 5 treatment-related AEs, with majority of treatment-related AEs Grade 1 or 2
- MTD not yet established and continuing to advance in Phase 1 dose escalation in partnership with Gilead

1. As of November 25, 2024. Treatment-related AEs most commonly consisted of flu-like symptoms, cytokine release syndrome, increased aspartate aminotransferase (AST) and alanine aminotransferase (ALT) and decreased blood cell counts.
IFNɣ: interferon gamma

XTX301 Advancing in Partnership with Gilead, Designed to Explore Broad Potential of IL-12 Across Solid Tumors with $75M Option Fee at Phase 1/2 Data Package

$55.0M
total received to date
($30M cash upfront payment +
$25M in total equity investments)

Up to $592.5M
additional contingent payments:

- **Up to $17.5M prior to transition fee for a development milestone**
- **$75M transition fee**
- **Up to $500M for additional development, regulatory and sales-based milestones after transition fee**

Tiered royalties:
high single-digits to mid-teens

Gilead received an exclusive global license to develop and commercialize Xilio's tumor-activated IL-12 program, including XTX301

- Xilio responsible for clinical development of XTX301 in ongoing Phase 1 trial through initial planned Phase 2 trial
- Following delivery by Xilio of specified clinical data package for XTX301, Gilead can elect to pay transition fee and transition development and commercialization to Gilead (1)

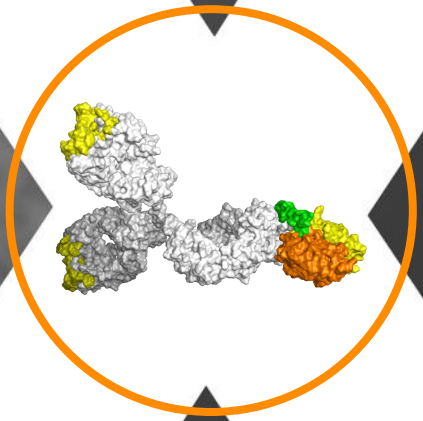
GILEAD
Creating Possible

xilio THERAPEUTICS

1. If Gilead elects not to transition responsibilities for development and commercialization, the agreement will automatically terminate.

XTX501

PD1/IL2 bispecific



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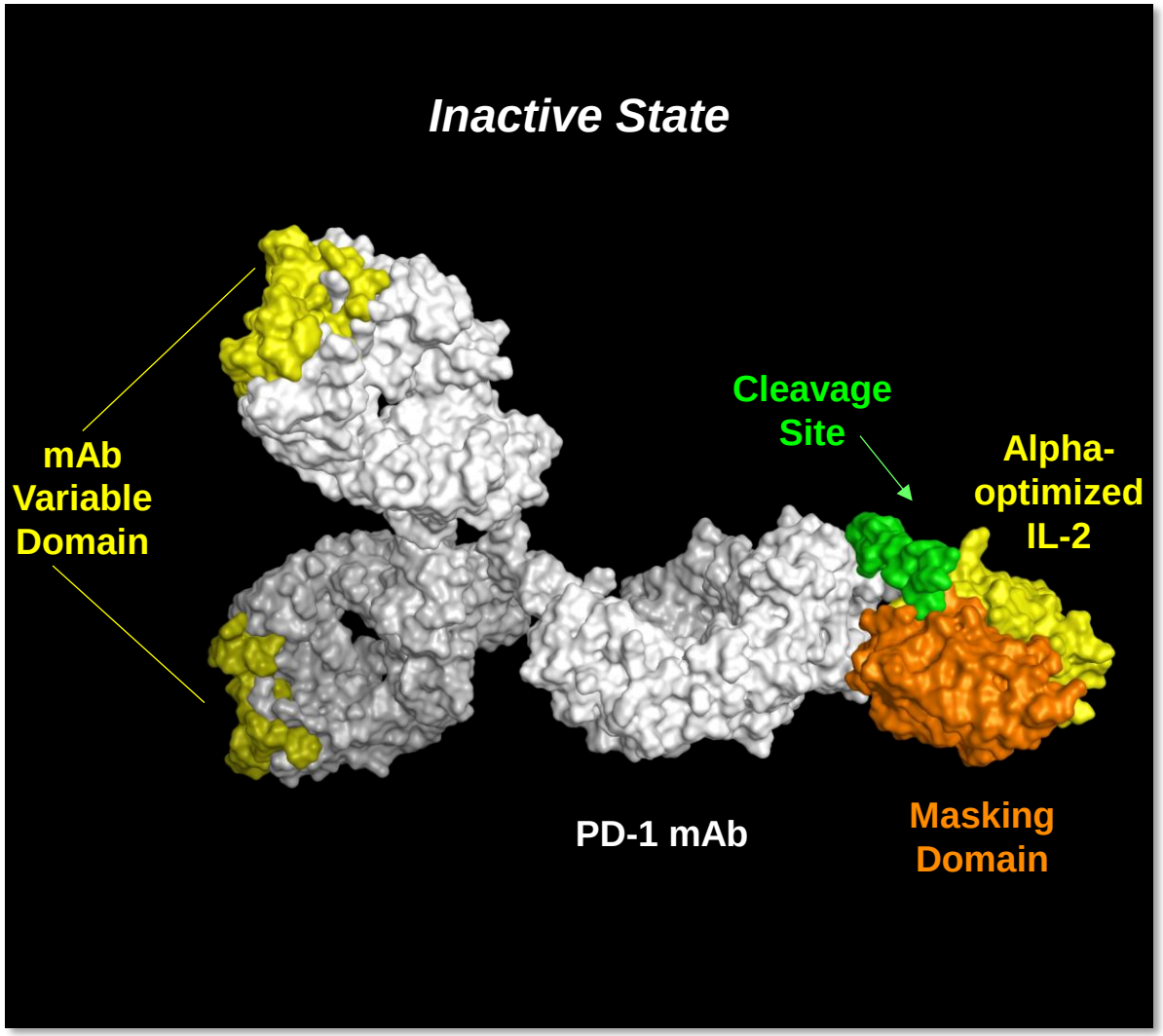
XTX501 Has Potential to be Best-in-Class PD1/IL2 Bispecific

XTX501 is designed to enable high potency, PD-1 antibody-like PK and tolerability

- Targeted delivery of IL-2 to PD1+ cells selectively enhances IL-2 signaling on tumor-reactive, stem-like T cells, endowing progeny T cells with enhanced effector function and fitness
- XTX501 designed to optimize each component of the molecule, including mask, antibody format, cleavage element and IL-2 variant
- XTX501 demonstrated robust monotherapy activity in preclinical models including settings insensitive to PD1, as well as tumor-selective pharmacodynamics consistent with its mechanism
- XTX501 currently advancing in initial IND-enabling activities

XTX501: Tumor-Activated PD1/IL2 Bispecific



Demonstrated Synergistic Anti-Tumor Activity, Antibody-Like PK and Favorable Tolerability in NHP

- Full potency alpha-optimized IL-2 with affinity-tuned, VHH-based mask
- Non-masked PD1 in Fc-silenced heterodimeric IgG1 backbone
- XTX501 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 PD-(L)1 + IL-2 combination
- Effective masking *in vitro,* potent *in vivo* pharmacology as monotherapy and antibody-like half-life and tolerability in NHP

NHP: non-human primate; VHH: variable heavy domain of heavy chain.

XTX501 is Designed to Overcome Limitations of Non-Masked PD1/IL2 Bispecifics

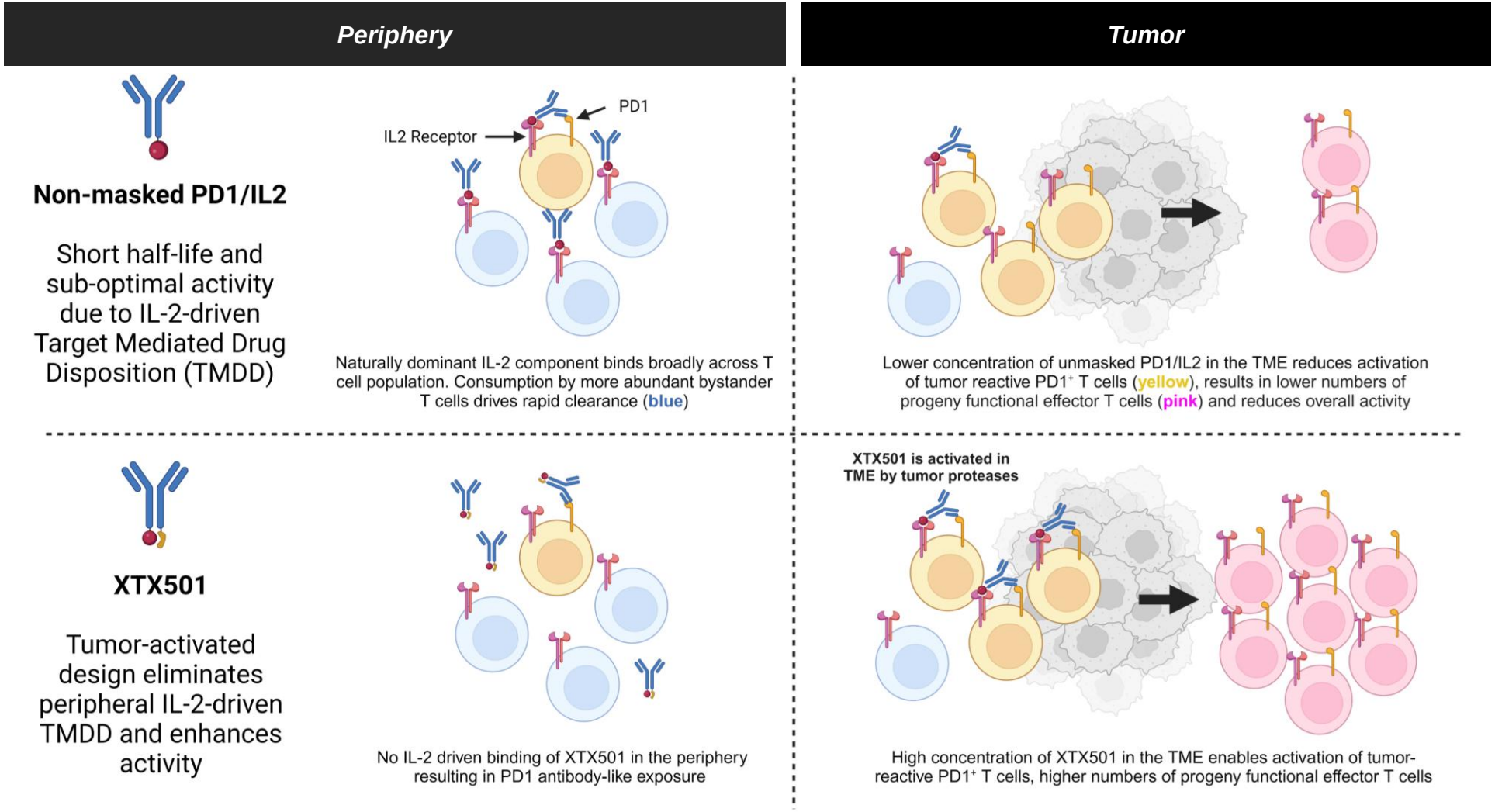
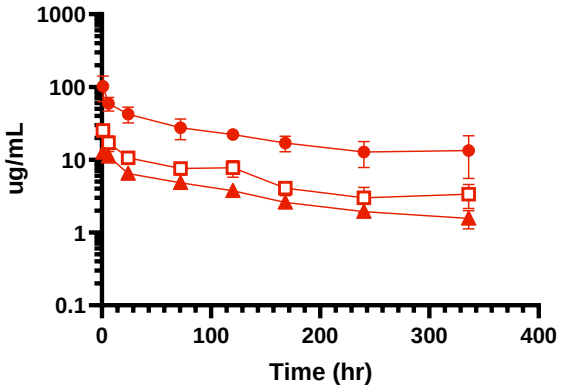


Figure generated using BioRender.com.

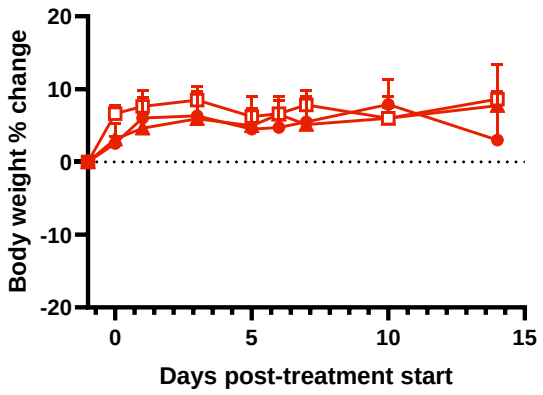
Tumor-Activated Design of XTX501 Enabled Optimal PK and Tolerability

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

XTX501
Concentration vs. Time



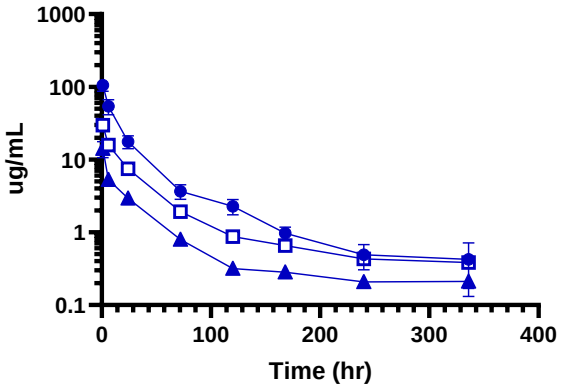
XTX501
Body weight change vs. Time



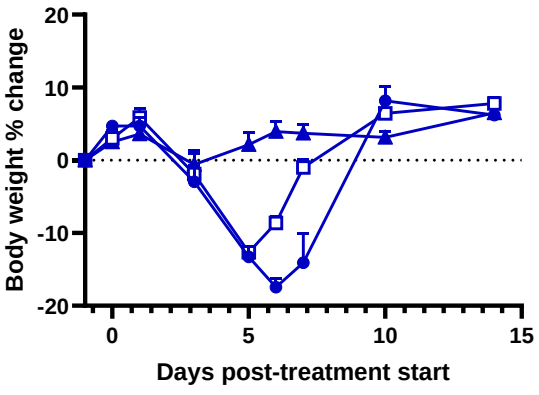
10 mg/kg (High)
3 mg/kg (Med)
1 mg/kg (Low)

Non-Masked PD1/IL2 Bispecific Was Rapidly Cleared and Poorly Tolerated

Non-masked PD1/IL2 Bispecific
Concentration vs. Time



Non-masked PD1/IL2 Bispecific
Body weight change vs. Time



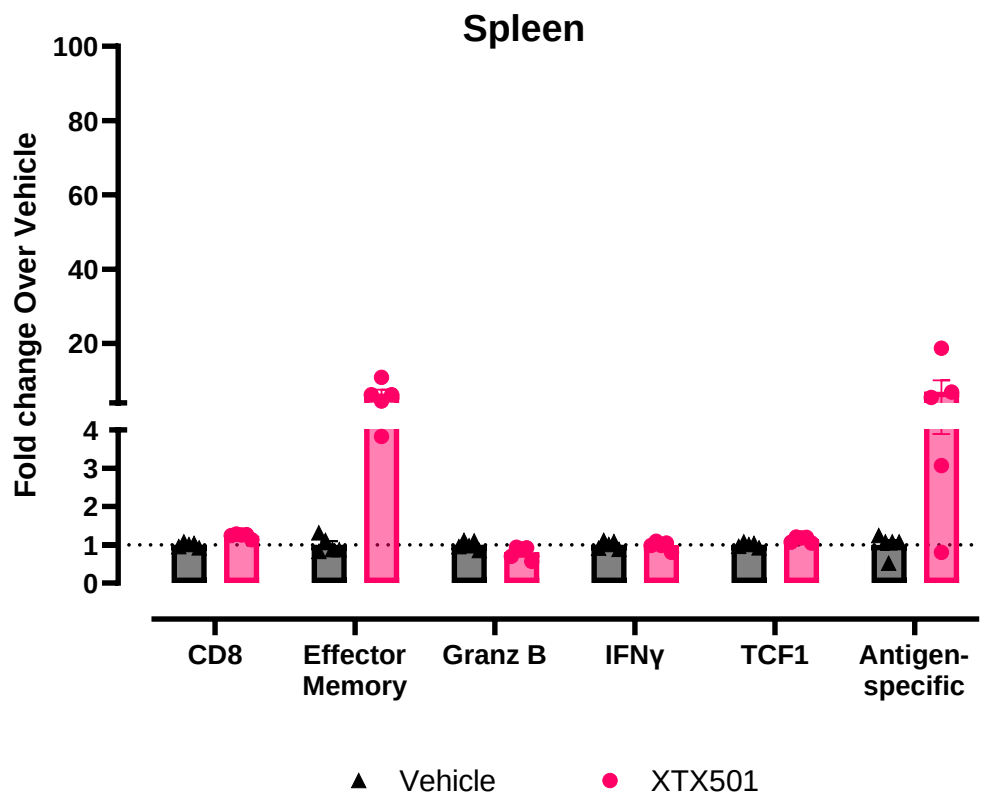
High
Med
Low

Equimolar dosing
aligned with XTX501

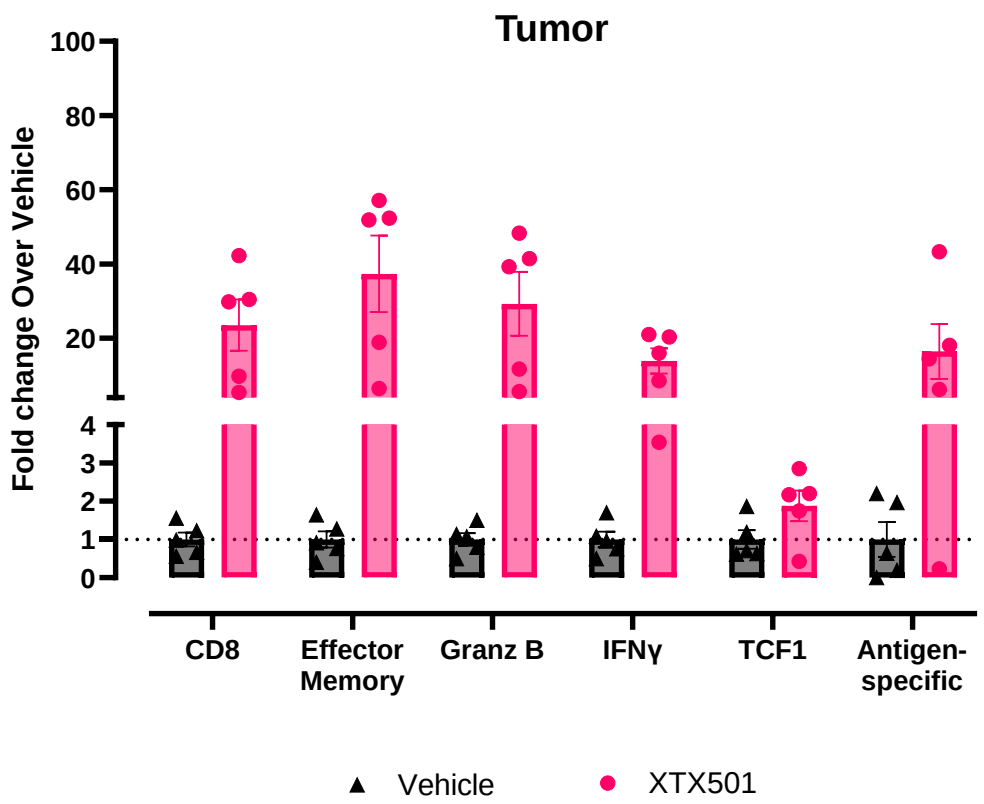
XTX501 exposure after a single 10, 3 or 1 mg/kg intravenous (i.v) injection in non-tumor bearing C57BL/6-hFcRn mice. Non-masked PD1/IL2 exposure after a single equal molar dose of 9.25, 2.75 or 0.92 mg/kg intravenous (i.v) injection in non-tumor bearing C57BL/6-hFcRn mice. Body weight data are displayed until day 14 the last time point measured.

XTX501 Demonstrated Tumor-Specific Pharmacology with Peripheral Effects Limited to Increases in Antigen-Specific/Memory Cells

Peripheral Expansion of T Cells in Response to XTX501 Was Limited to Antigen-specific/Memory Cells



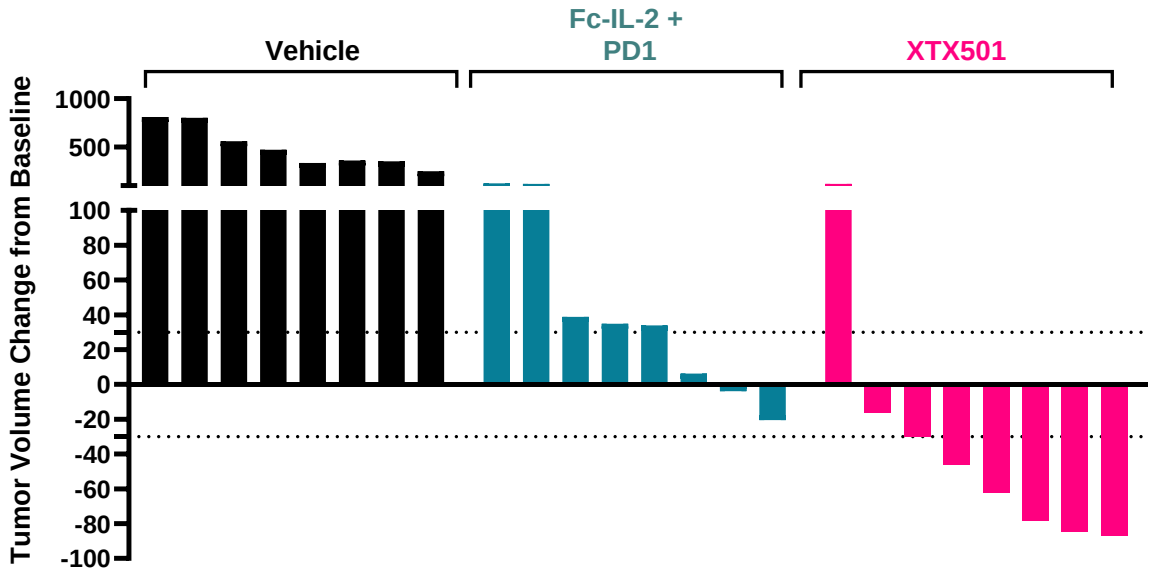
XTX501 Treatment Induced Robust Increases in Activated T Cell Populations in Tumor



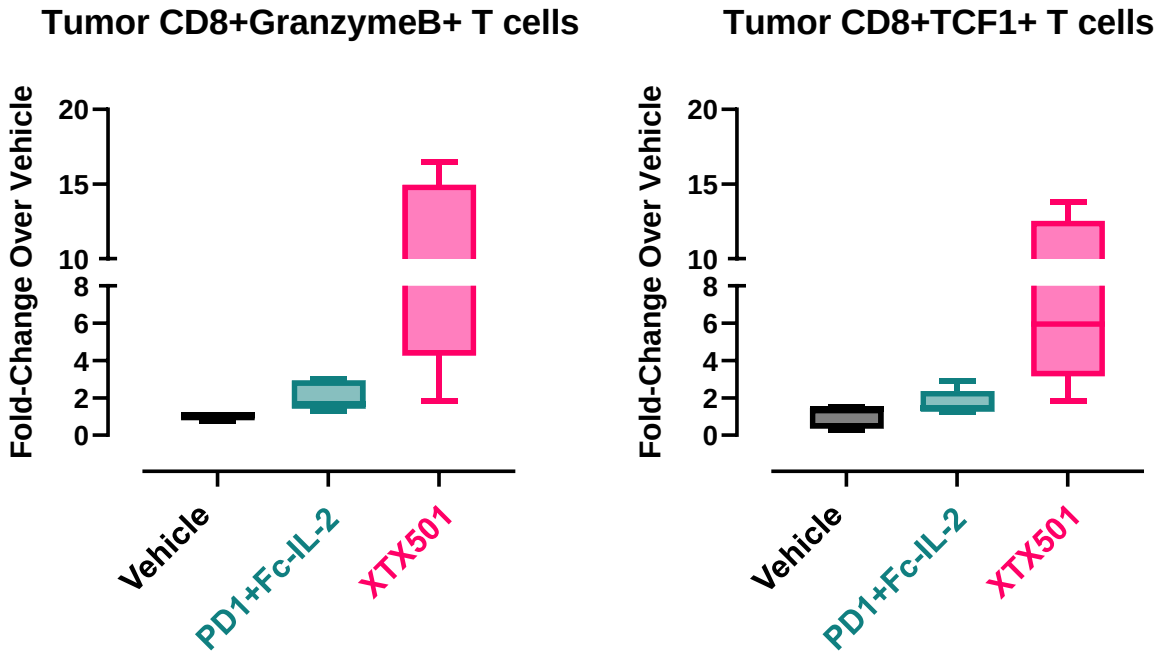
Female C57BL/6 hPD-1 mice (n=5 in each treatment group) were inoculated with 0.5x106 MC38 tumor cells subcutaneously in the right flank. On day 0, 3 mice received XTX501 bispecific or vehicle. The percentage of cells for each immune phenotype was calculated as percentage of live CD45+ cells and the ratio of percent cells after XTX501 treatment to vehicle treatment is presented as mean ± SEM. Effector memory (CD44+CD62L-), Antigen-Specific (p15E-Pentamer).
Data generated with analogue of XTX501 with minimal variance in amino acid sequence.

XTX501 Demonstrated Differentiated Pharmacology vs PD1 and PD1+Fc-IL-2 Combination in MB49 Mouse Tumor Model, Indicating Enhanced Anti-Tumor Immunity

Robust Preclinical Monotherapy Activity Beyond Fc-IL-2 + PD1 Combination was Observed



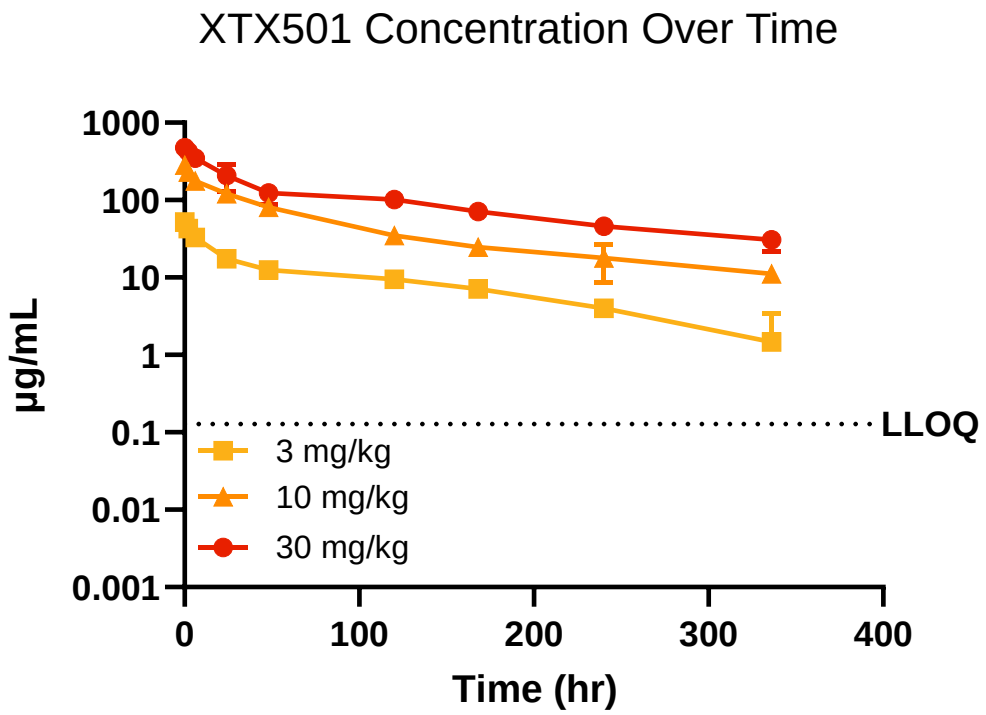
XTX501 Increased Intra-Tumoral Cytotoxic and TCF1+ Stem-Like T Cells



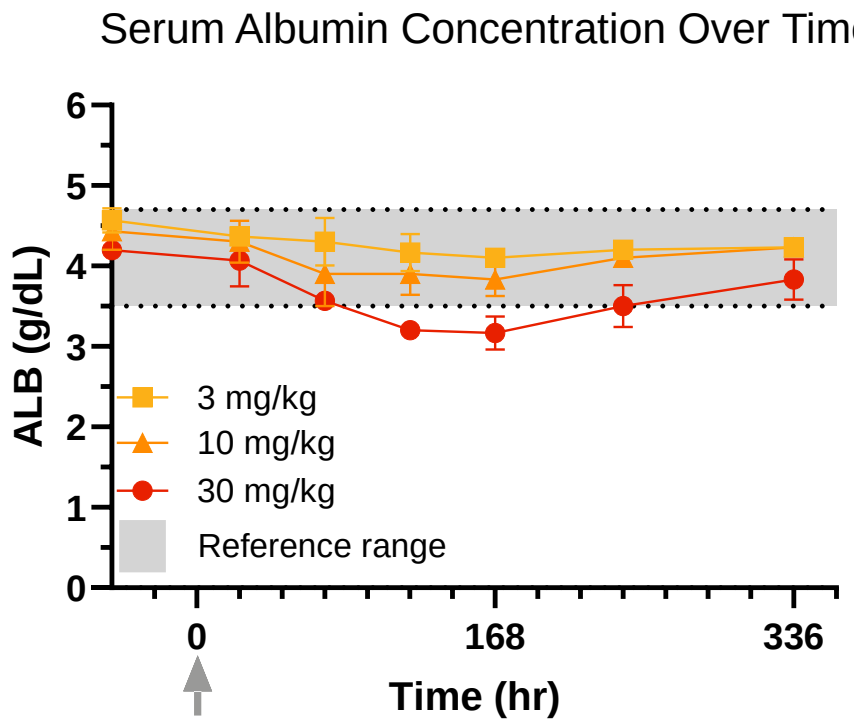
Left panel: Female C57BL/6 hPD-1 mice (n=8 in each treatment group) were inoculated with MB49 tumor cells. On day 0, 5 mice received vehicle or equimolar doses of anti-PD1 antibody (pembrolizumab) plus XTX202 (Masked βγIL-2), or XTX501. Tumor volume change on day 12 post treatment relative to baseline 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 XTX202 (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 Demonstrated Favorable Tolerability in NHP

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

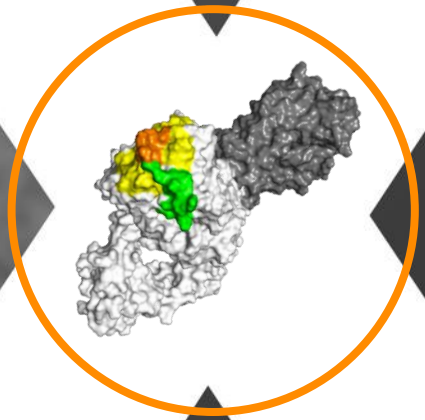


Minimal Effects of XTX501 on Serum Albumin
(i.e., No Signs of Vascular Leak Syndrome)



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. (A) PK analysis demonstrated dose-proportional exposure and linear elimination across all doses tested. (B) Albumin remained within normal ranges in animals receiving 3 and 10 mg/kg PD1/IL2 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.

Tumor-Activated Cell Engager Programs



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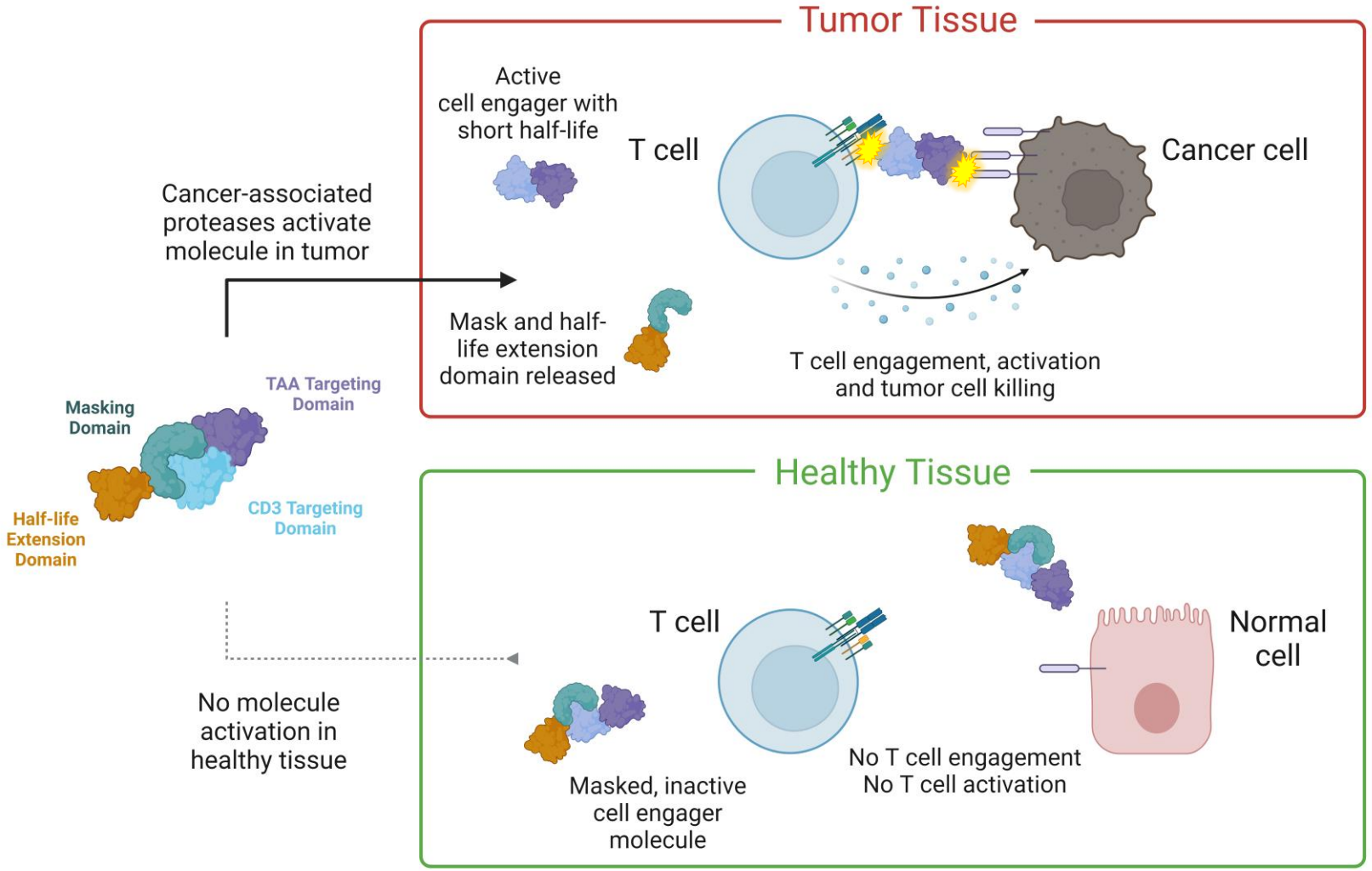
ATACR Format Designed to Optimize Therapeutic Index of T Cell Engagers by Maximizing Tumor Exposure and Minimizing Healthy Tissue Binding

"ATACR":
Advanced Tumor-Activated Cell EngageR

Design Goals:

- Potent tumor-selective T cell engagement with conditional half-life modulation
- Minimal peripheral activity and off-tumor cytotoxicity



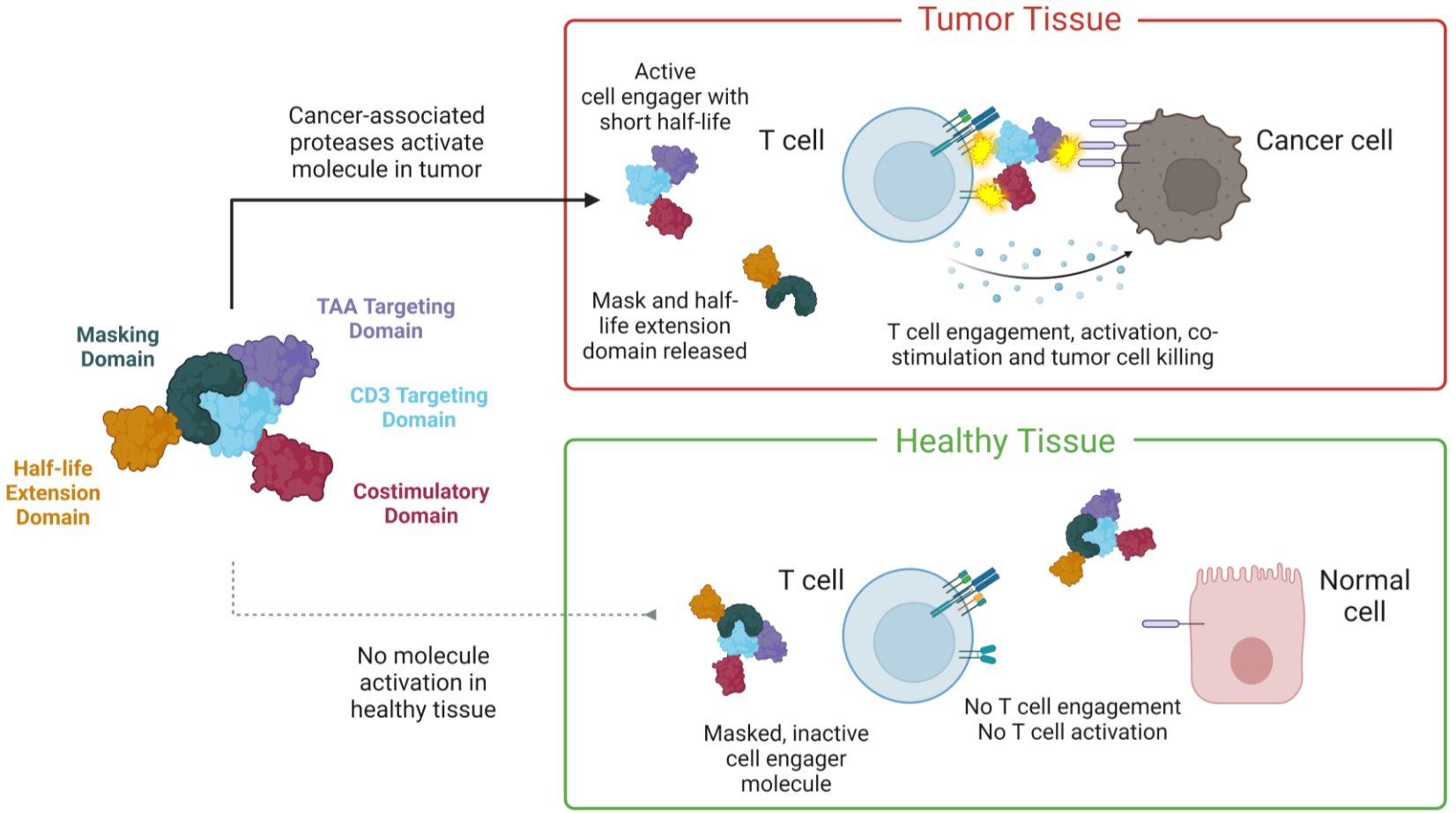
Illustrations generated using Biorender.com

Xilio's Tumor-Activated SEECR Molecules are Designed to Deliver Potent T Cell Activation ***and*** Co-Stimulation Specifically to Tumors

"SEECR":
Selective Effector-Enhanced Cell EngageR

Design Goals:

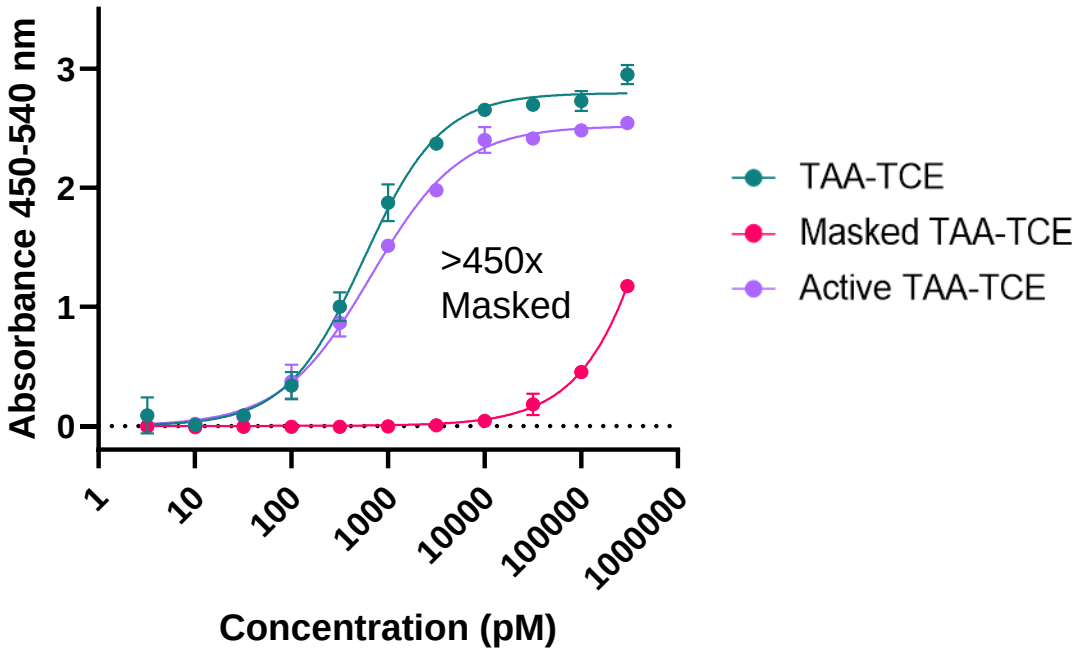
- Potent tumor-selective T cell engagement and co-stimulation
- Minimal peripheral activity and off-tumor cytotoxicity



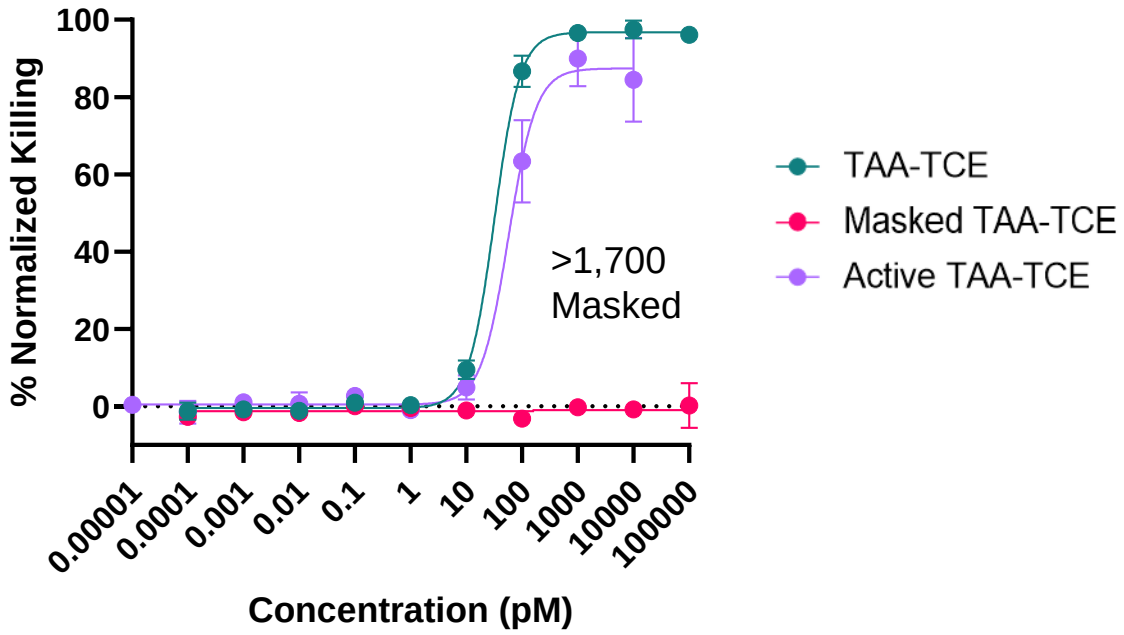
Illustrations generated using Biorender.com

Xilio's Masking Technology Enabled Efficient Masking of the CD3 Binding Domain of Cell Engagers

Demonstrated Protease-Dependent Binding to CD3 by ELISA



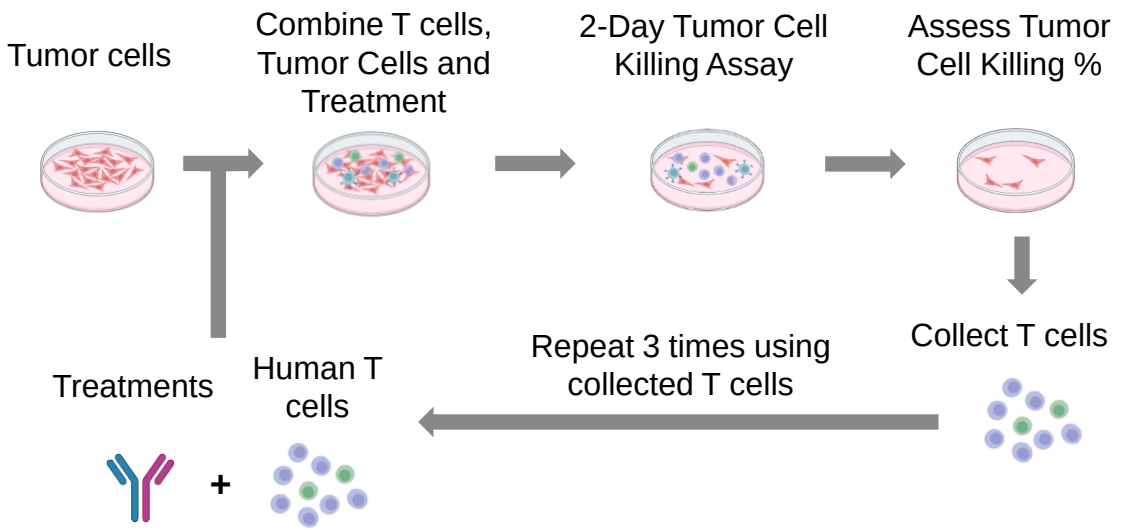
Confirmed Protease-Dependent Activity in Primary T Cell Assay



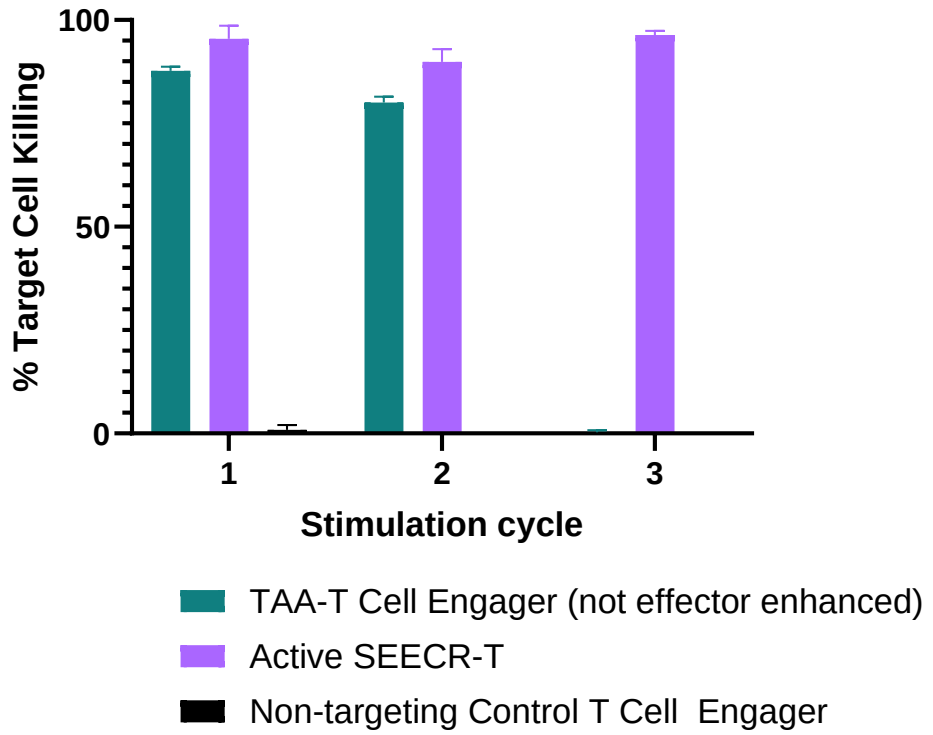
Left panel: Protease dependent CD3-binding demonstrated via TAA-TCEs bound to immobilized CD3 in an ELISA. **Right panel:** Protease-dependent tumor cell killing. Active TAA-TCEs led to killing in co-culture assay. A375 tumor cells were cultured overnight before addition of expanded T cells at a 5:1 E:T. Test articles were titrated into the wells and then plates were incubated for 2 days at 37°C. Effector cells were washed away and then remaining viable tumor cells were measured.
TAA: Tumor-associated antigen; TCE: T cell engager

SEECR Molecule Demonstrated Unique Ability to Drive Sustained, Serial Tumor Cell Killing Over Multiple Rounds of Stimulation in Preclinical Model

Preclinical Repeat Stimulation Assay to Evaluate Ability of Molecules to Elicit Serial Tumor Cell Killing



Only SEECR Format Enabled Sustained Tumor Cell Killing

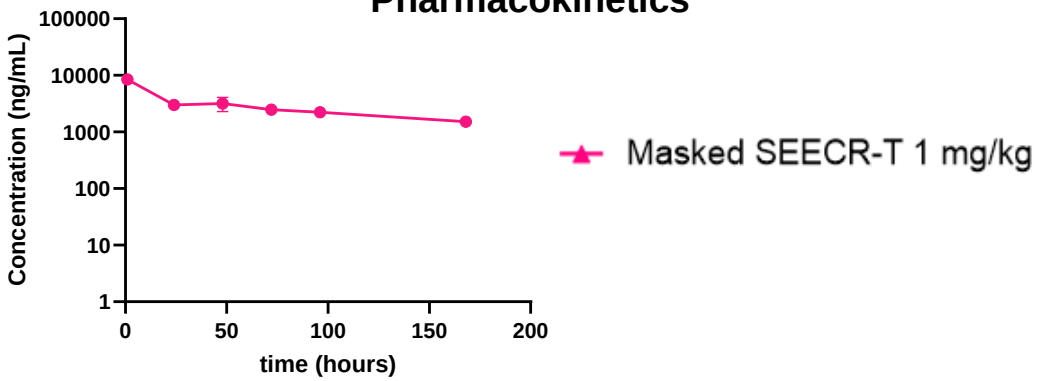


Human T cells were incubated over three consecutive rounds with indicated test articles and A431 cancer cells and percent tumor cell killing was assessed using a luminescence readout.

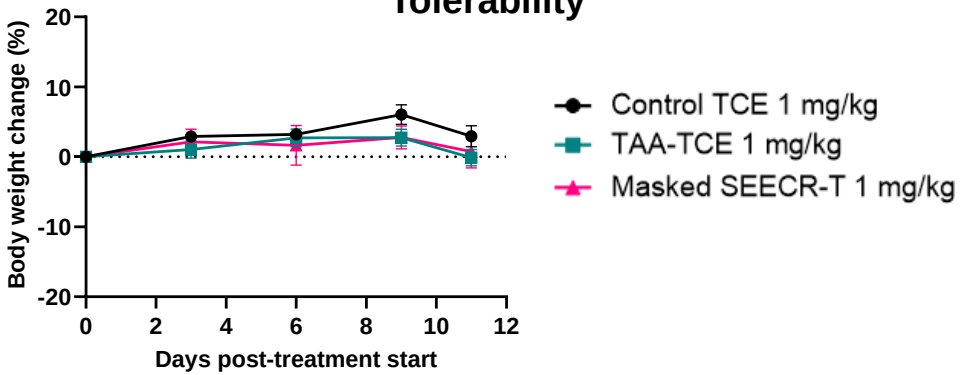
SEECR Molecule Demonstrated Potent Anti-Tumor Activity, Antibody-Like PK and was Well-Tolerated in Murine Models

SEECR Featured Antibody-Like PK and Tolerability Comparable to Control

Pharmacokinetics

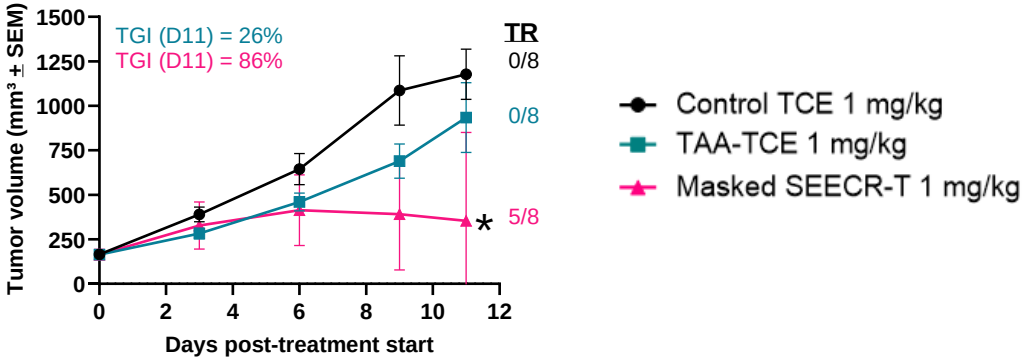


Tolerability

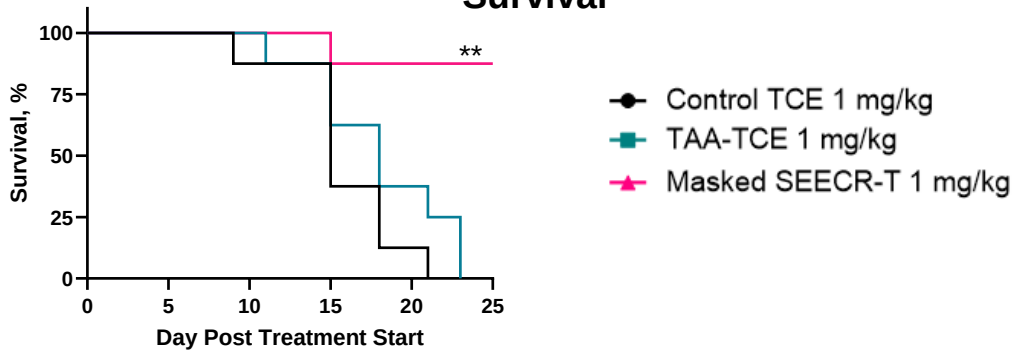


SEECR Showed Significantly Enhanced Activity and Survival Compared to Standard TCE

Anti-Tumor Activity



Survival



PK, tolerability, and anti-tumor activity of SEECR-T molecules were evaluated in the human A375 melanoma model in NSG mice engrafted with human T cells. In the efficacy study, animals received IV doses of TAA-TCE (1 mg/kg, Q3Dx8), masked SEECR-T (1 mg/kg, Q3Dx8), or control TCE molecules (1 mg/kg, Q3Dx8). **Left panel top:** TAA-TCE and masked SEECR-T demonstrated similar PK profiles. **Left panel bottom:** All treatments were well tolerated, and no body weight loss was observed. **Right panel top:** Masked SEECR-T molecule (IV, 8 doses) significantly inhibited tumor growth, achieving 86% TGI on Day 11 (Data presented as mean ±SEM, two-way ANOVA followed by post hoc Dunnett's test on Day 11, *P < 0.05). **Right panel bottom:** The treatment with masked SEECR-T molecule improved median animal survival from 17 days to more then 27 days (Gehan-Breslow-Wilcoxon test, **P < 0.005).
TR: tumor regression

Management Overview and Recent Financial Results

xilio THERAPEUTICS®

Deep Expertise to Build a Transformational Immuno-Oncology Company

ULI BIALUCHA, PH.D.
Chief Scientific Officer

SCOTT COLEMAN, PH.D.
Chief Development Officer

CHRIS FRANKENFIELD
Chief Financial and Operating Officer

CAROLINE HENSLEY
Chief Legal Officer

KATARINA LUPTAKOVA, M.D.
Chief Medical Officer

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

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

Q3 2024 Financial Results
*Anticipate Cash Runway Into Q3 2025**

Balance Sheet

	September 30, 2024 (1)	December 31, 2023
Cash and Cash Equivalents	$61.3M	$44.7M

Statement of Operations

	Three Months Ended September 30	
	2024 (1)	2023 (1)
License Revenue	$2.3M	$—
Research & Development Expenses	$10.8M	$11.1M
General & Administrative Expenses	$6.3M	$6.3M
Net Loss	$(14.0M)	$(16.7M)

1. Unaudited
* After giving effect to remaining $8.2M equity investment by Gilead on December 18, 2024.