Unleashing the Potential of Immuno-Oncology Therapies

January 21, 2025

xilio THERAPEUTICS®

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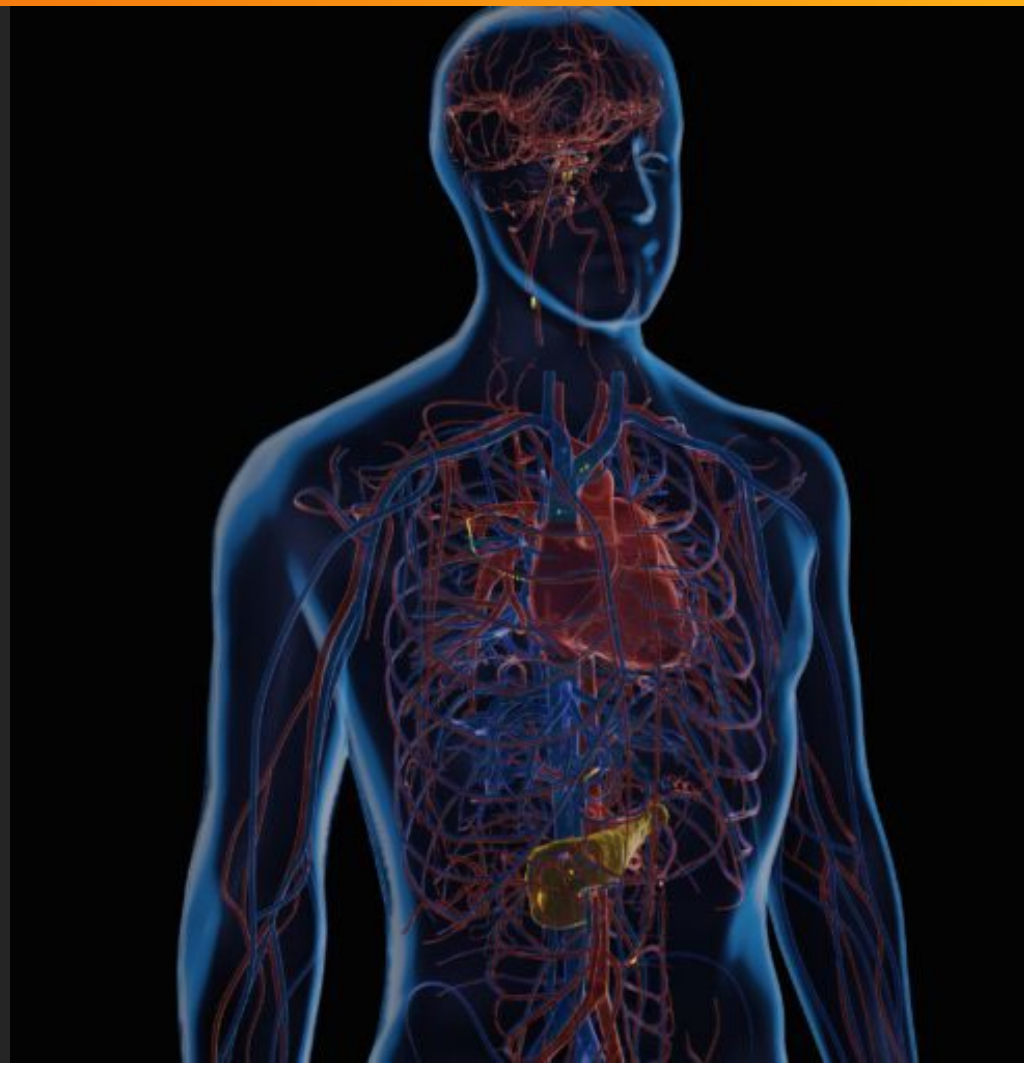
Immuno-Oncology Therapy is the Key to Curative Potential, But Continues to Be Limited by Systemic Toxicity

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**

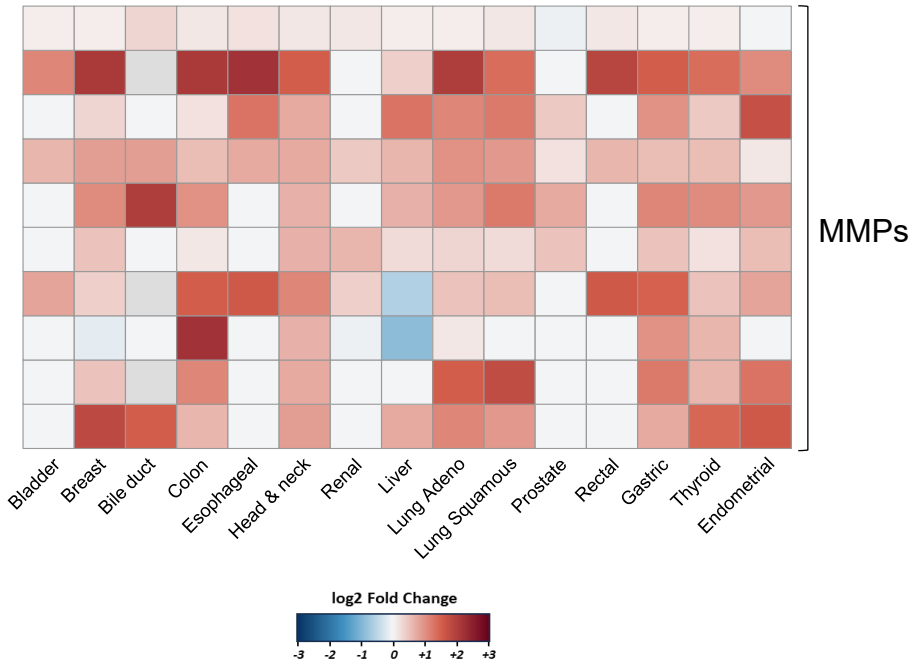


I-O: immuno-oncology

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

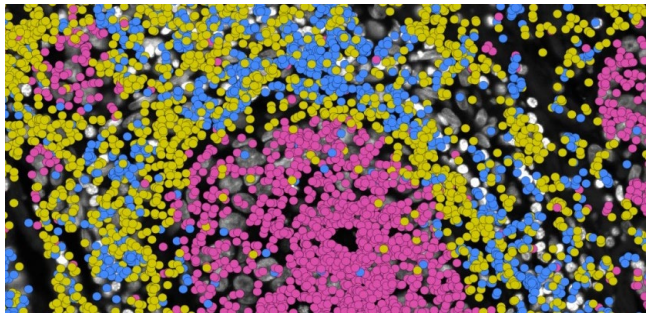
MMPs are dysregulated broadly across solid tumors

MMP mRNA expression in tumor vs. normal tissue

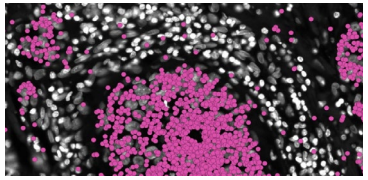


MMPs and immune cells co-localize at the invasive edge of tumors

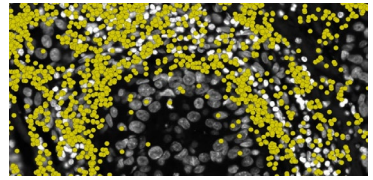
In situ mRNA expression in human breast cancer



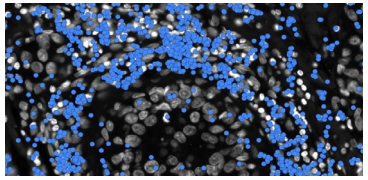
Tumor cells (TROP2)



MMP (MMP2)



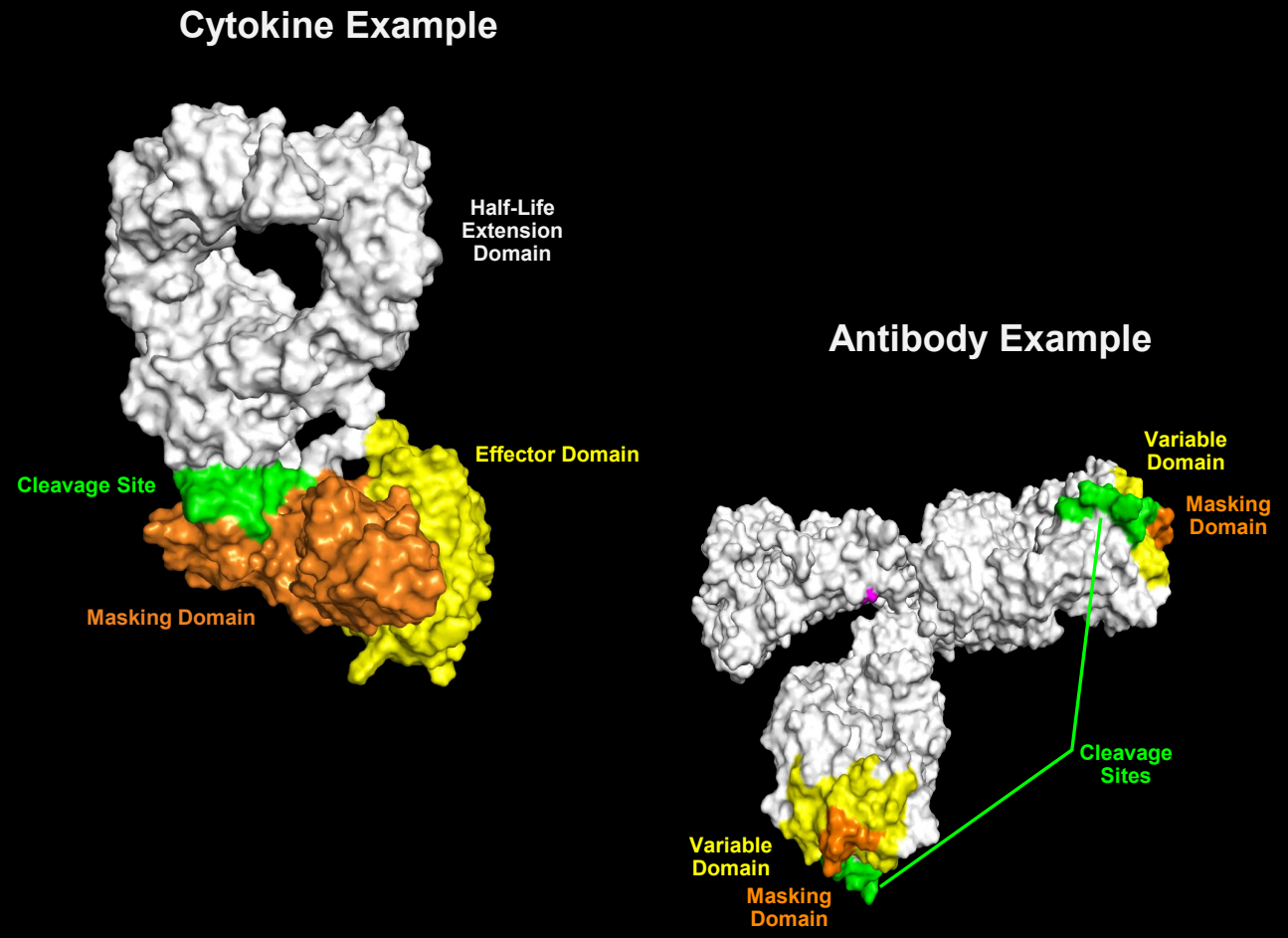
T cells (CD4, CD8A)



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

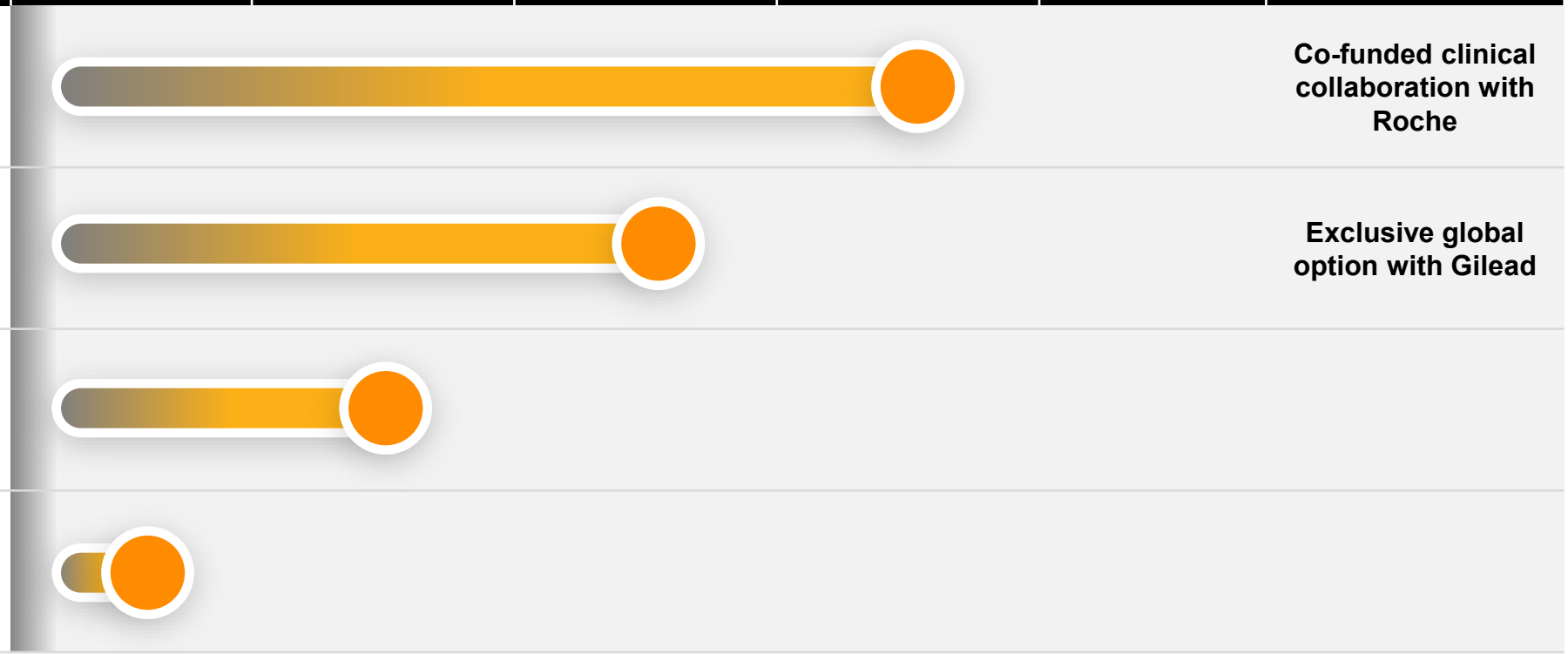
- Initial clinical validation, with >200 patients enrolled to date across clinical programs
- Molecules designed for tumor-selectivity with a masking domain to block interaction with healthy tissue and cells
- Dysregulated MMPs in the TME activate molecules via the protease cleavage site across a wide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



TME: tumor microenvironment

Advancing Pipeline of Tumor-Activated I-O Therapies

Program	Tumor Types	Mechanism of Action	Discovery	IND-Enabling	Phase 1	Phase 2	Phase 3	Partnerships
Vilastobart (XTX101) [1]	Metastatic MSS CRC	anti-CTLA-4 + PD-L1						**Co-funded clinical collaboration with Roche**
XTX301 [2]	Advanced Solid Tumors	IL-12						**Exclusive global option with Gilead**
XTX501 [3]	Advanced Solid Tumors	PD-1/IL2 bispecific						
Multiple research programs	Undisclosed	Tumor-activated cell engagers						

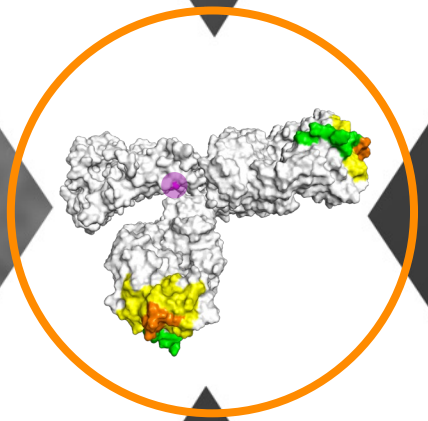


1. Evaluating vilastobart (XTX101) in combination with atezolizumab (Tecentriq®) in patients with metastatic MSS CRC under co-funded clinical collaboration with Roche.
2. Evaluating XTX301 in Phase 1 monotherapy dose escalation and dose expansion for the treatment of advanced solid tumors under exclusive global partnership with Gilead.
3. Conducting IND-enabling activities.

CRC: colorectal cancer; MSS: microsatellite stable

Vilastobart (XTX101)

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



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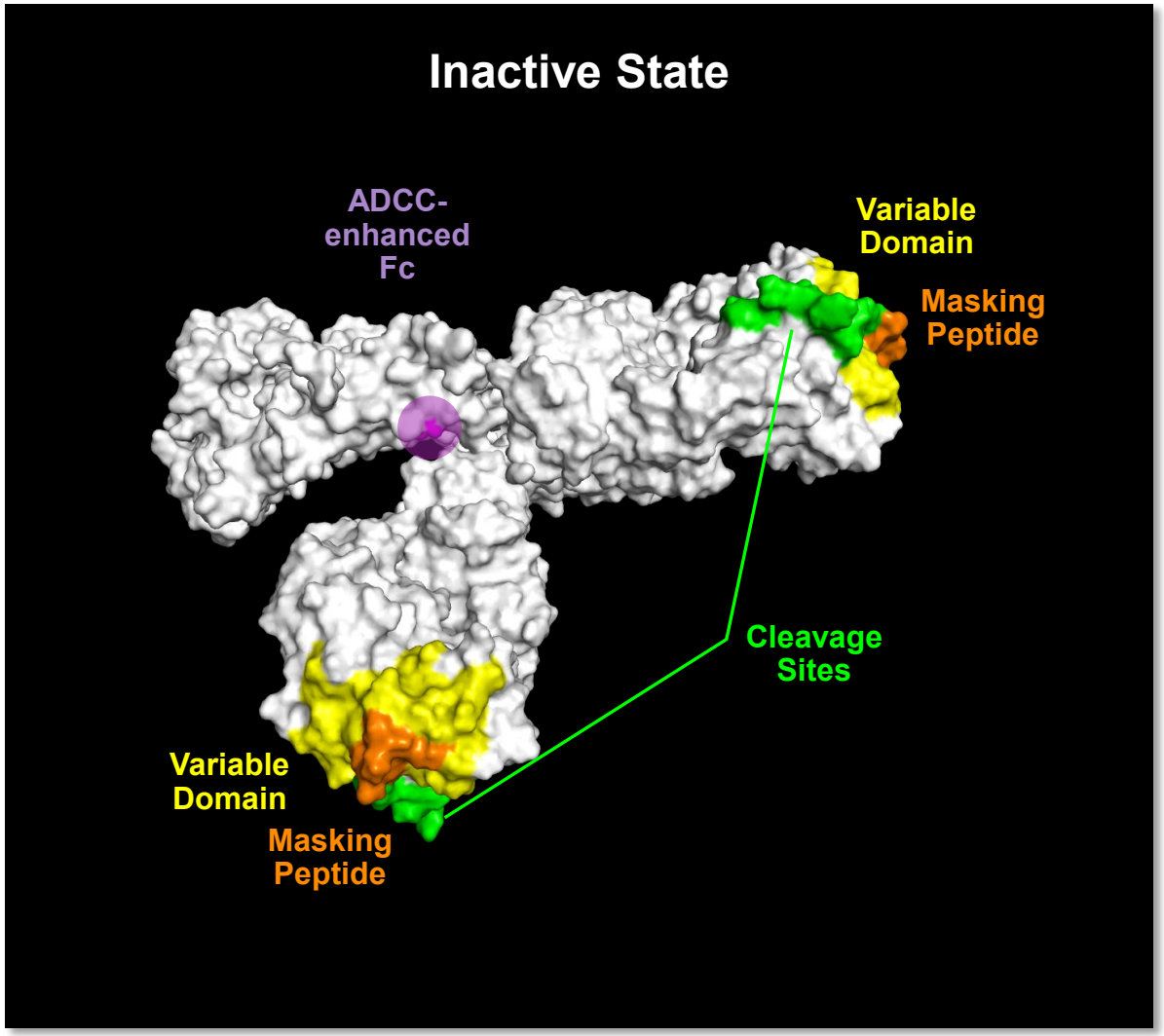
Vilastobart: Tumor-Activated, High Affinity Binding, Fc-Enhanced Anti-CTLA-4 in Phase 2 Development



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

Highlights from Previously Reported Data

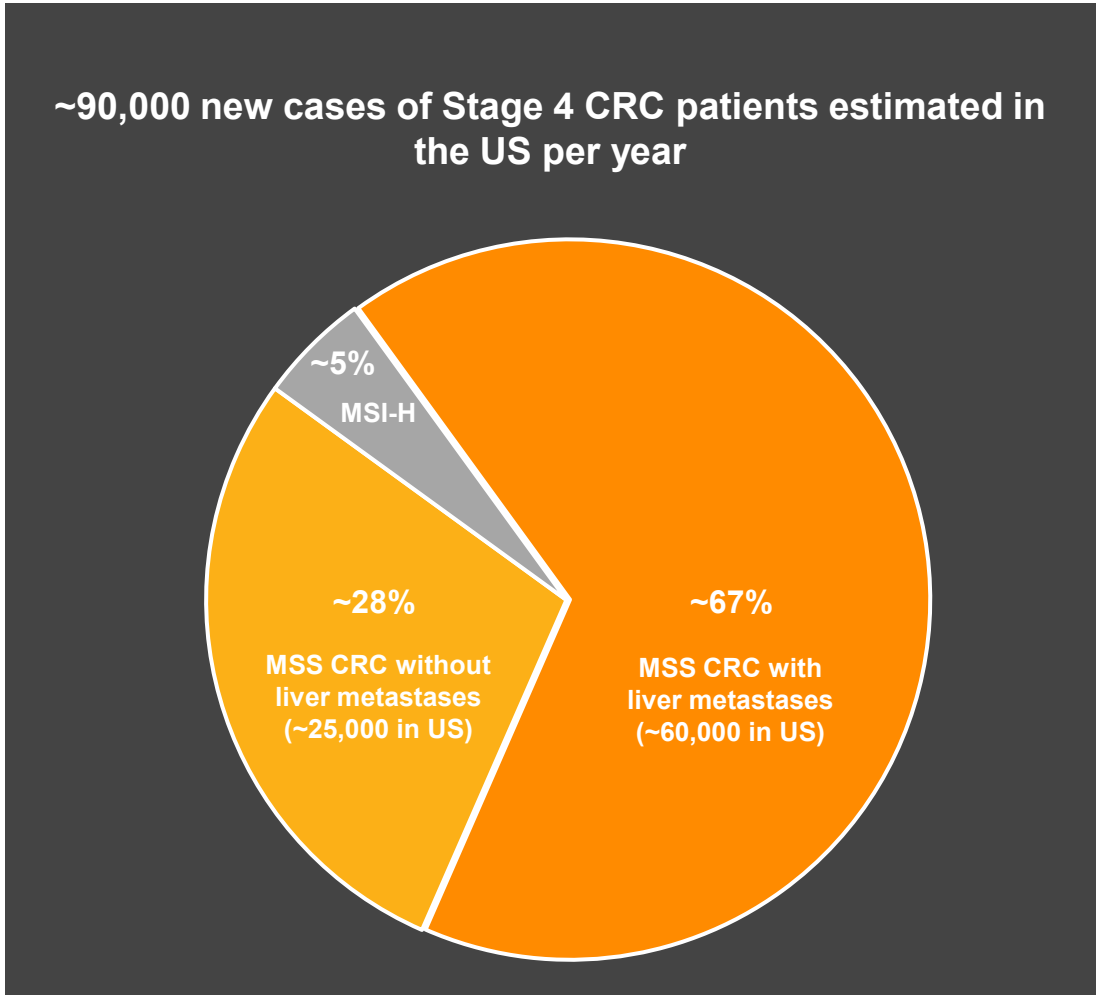
- High affinity binding, 10x potency of ipilimumab in preclinical studies (1)
- Fc mutations for enhanced effector function (ADCC), improved T cell priming and Treg depletion
- On-treatment biopsies in Phase 1 monotherapy demonstrated >70% activated molecule in tumor with <15% activated molecule in periphery
- 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
- PRs observed with combination in Phase 1, including MSS CRC patient with full resolution of liver metastasis (2)

1. Ipilimumab analog used for preclinical studies
2. PR (confirmed) in MSS CRC patient; PR (unconfirmed) in ampullary carcinoma patient.

ADCC: antibody-dependent cell-mediated cytotoxicity; NSCLC, non-small lung cancer; PR: partial response; Treg: regulatory T cells

CRC Incidence is Increasing, Particularly In Young Adults; New Cases Typically Identified at Later Stages and ~95% of Stage 4 Patients in the US are MSS CRC

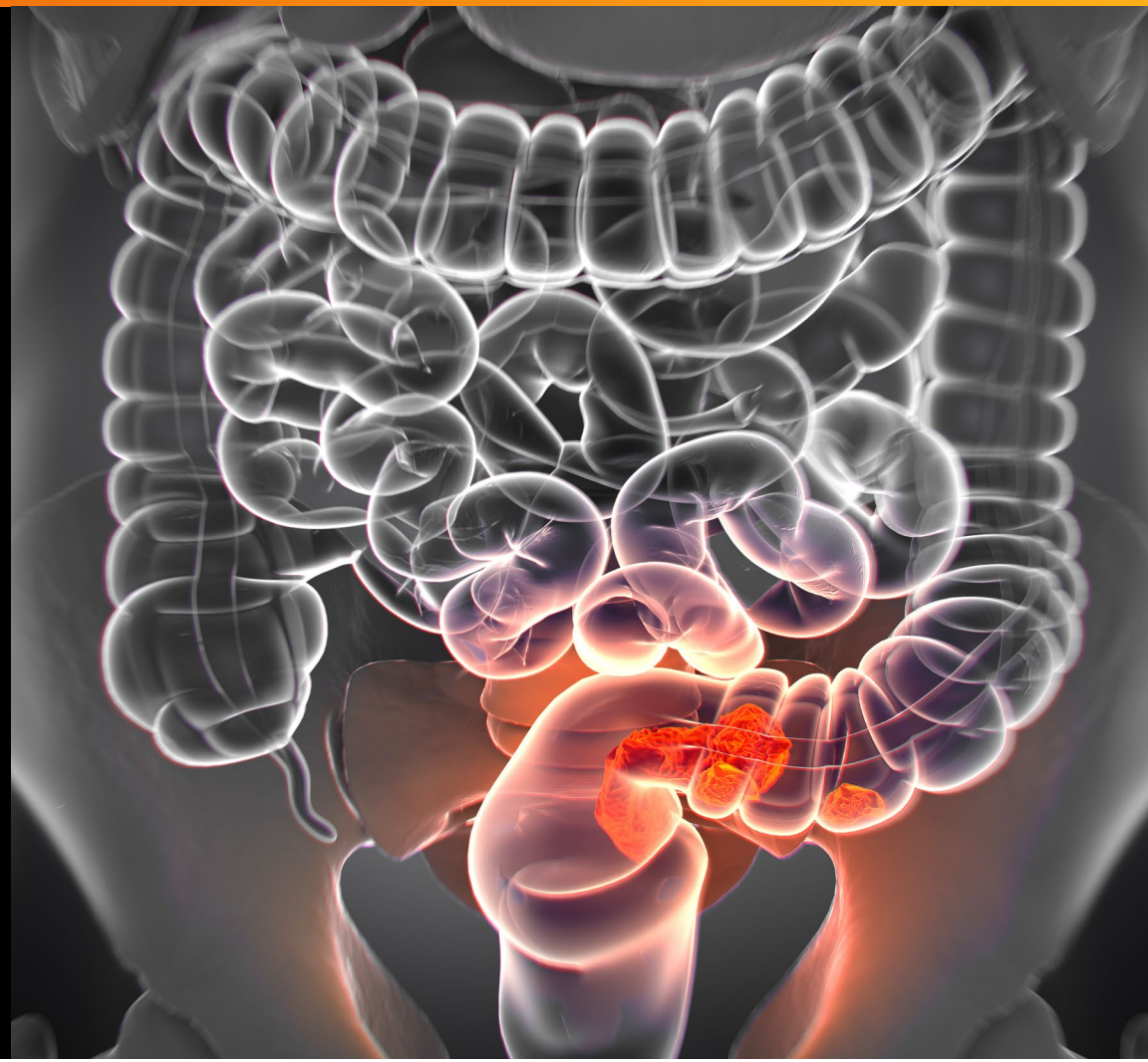
- CRC is 2nd in cancer-related deaths in the US and leading cause of cancer-related death in men younger than 50 in the US (1)
- CRC is 3rd in total annual new cases globally, with ~1.9M new cases and ~900,000 deaths related to CRC globally (2)
- >25% of Stage 4 CRC patients have MSS CRC without liver metastases (3)
- >65% of Stage 4 CRC patients have MSS CRC with liver metastases, which are typically 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 (XTX101)

Initial Phase 2 Data for Vilastobart (anti-CTLA-4) + Atezolizumab in Patients with Metastatic MSS CRC

Presented at ASCO GI in January 2025

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Phase 2 Enrolled Heavily Pre-Treated MSS CRC Patients With and Without Liver Metastases

Patient Characteristics	Total (N=40)
Demographics	
Age, median (range)	55 (25 - 82)
Female	20 (50%)
ECOG PS 0	17 (43%)
ECOG PS 1	23 (58%)
Prior Lines of Anti-Cancer Treatment	**Median 4 (range: 1-10)**
unknown	2 (5%)
1	5 (13%)
2	5 (13%)
3	7 (18%)
4	6 (15%)
5	7 (18%)
6 or more	8 (20%)

Tumor Types	Total (N=40)
MSS CRC	
Patients with liver metastases	16
Patients without liver metastases	24

Treatment Status	Total (N=40)
Continuing on Treatment	**23**
Discontinued Treatment	**17**
Disease Progression	6
Clinical Progression	8
Adverse Events	3

70% of patients had 3 or more prior lines of treatment

Data cutoff date: January 13, 2025

ECOG PS: Eastern Cooperative Oncology Group Performance Status

27% Preliminary ORR for Combination of Vilastobart (anti-CTLA-4) and Atezolizumab in MSS CRC Patients Without Liver Metastases

- 40 patients with MSS CRC enrolled in ongoing Phase 2 trial
- Patients were heavily pre-treated, with 70% of patients having previously received ≥3 prior lines of treatment
- 18 patients had at least 1 imaging scan reported and were evaluable for response assessment
- 23 patients are ongoing on treatment, including 13 patients who have not yet had a first response assessment

Best Response	Without Liver Metastases *(n = 11 response-evaluable)*	With Liver Metastases *(n = 7 response-evaluable)*
PR	3(1)	—
SD	3	1
ORR	27%(1)	—
DCR (2)	55%	14%

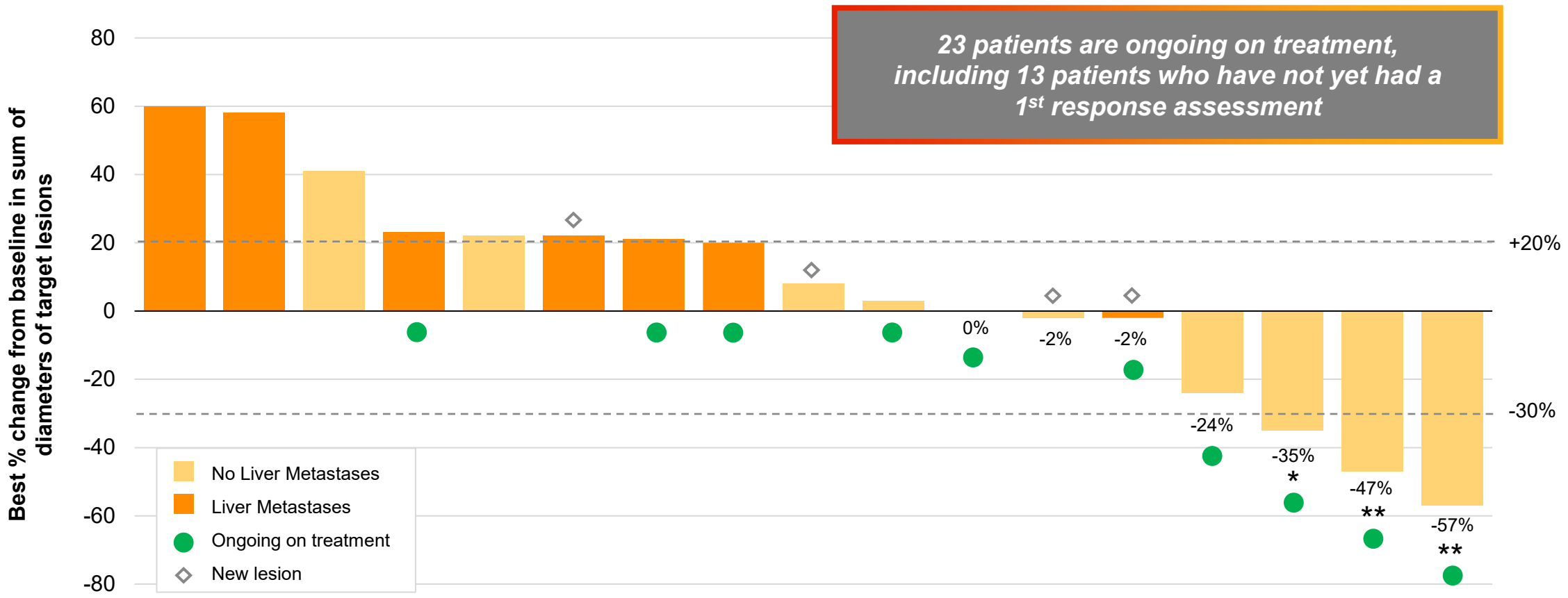
One additional patient (with peritoneal metastasis) had significant reduction in tumor burden (24% reduction) and is currently ongoing on treatment

Data cutoff date: January 13, 2025. Patients were administered combination of vilastobart (100 mg Q6W) and atezolizumab (1200 mg Q3W).

1. Includes 2 confirmed PRs (Patient A and Patient B vignettes) and 1 unconfirmed PR (Patient C vignette, based on initial assessment by investigator at 9 weeks with radiology assessment pending).
2. DCR is defined as PR or SD through the first on treatment imaging scan as defined by the protocol (~9 weeks).

DCR: disease control rate; PR: partial response; ORR: objective response rate; SD: stable disease

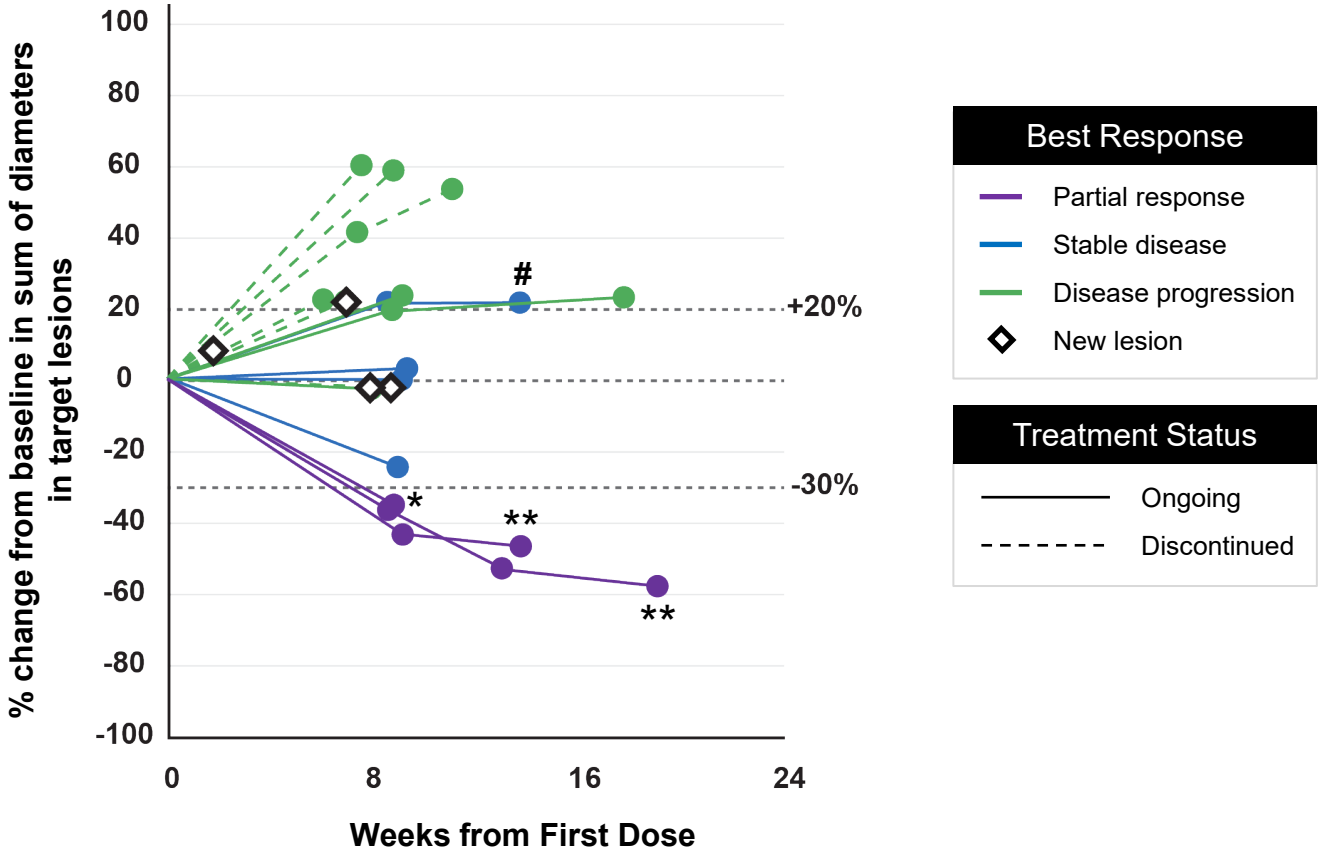
Anti-Tumor Activity in MSS CRC Patients, Including 3 PRs (2 Confirmed), Demonstrated for Combination of Vilastobart (anti-CTLA-4) and Atezolizumab



Data cutoff date: January 13, 2025. One patient was found to have new brain metastases (progressive disease per RECIST) but did not yet undergo imaging of target lesions. This patient is evaluable for response but not included in the waterfall above.

* Initial assessment of unconfirmed PR (35%) by investigator at 9 weeks (radiology assessment pending) (see Patient C vignette). ** Confirmed PR (Patient A and B vignettes).

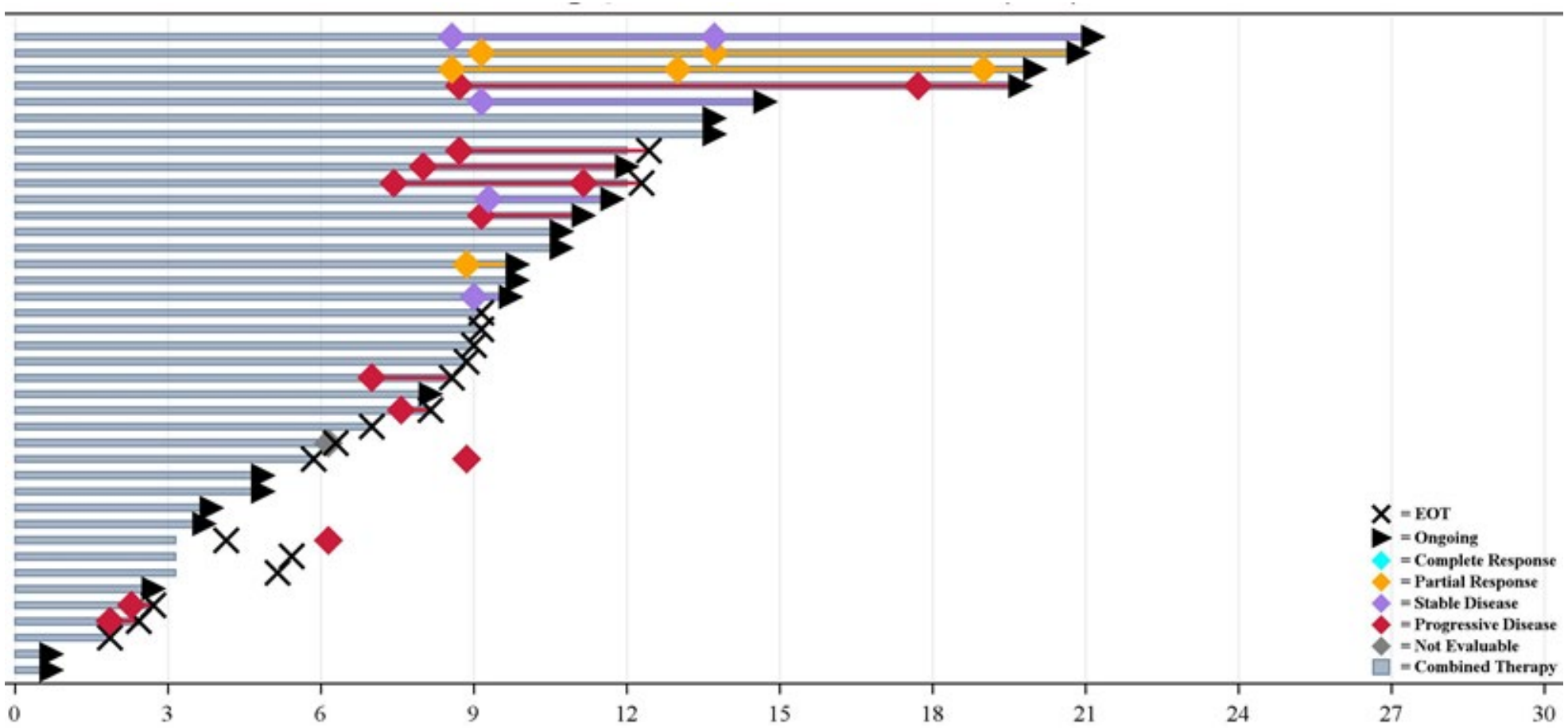
Confirmed PRs in MSS CRC Patients Without Liver Metastases Deepening Through Up to 18 Weeks To Date



Data cutoff date: January 13, 2025. One patient was found to have new brain metastases (progressive disease per RECIST) but did not yet undergo imaging of target lesions. This patient is evaluable for response but not included in the spider plot above.

Patient with <5 mm tumor size increase, which is considered stable disease per RECIST.
* Initial assessment of unconfirmed PR (35%) by investigator at 9 weeks (radiology assessment pending) (Patient C vignette). ** Confirmed PR (Patient A and B vignettes).

23 Patients Ongoing on Treatment with Combination of Vilastobart (anti-CTLA-4) and Atezolizumab, Including 13 Patients Who Have Not Yet Had a First Response Assessment

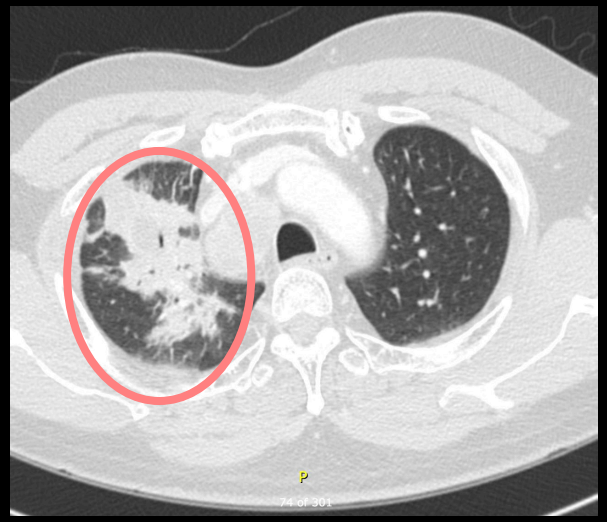


Data cutoff date: January 13, 2025
EOT: end of treatment

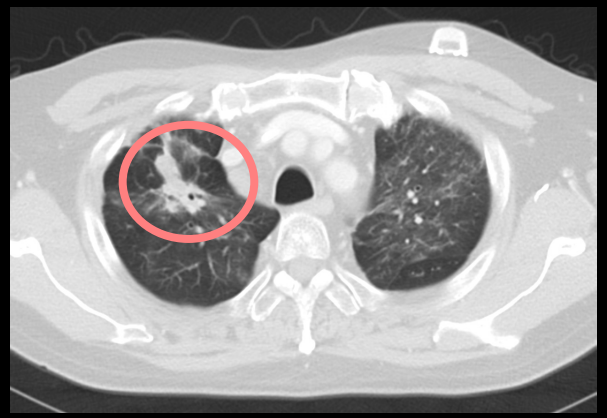
Patient A: Confirmed PR in Patient with MSS CRC Without Liver Metastases (47% Reduction), With Decreased CEA and ctDNA and Improvement in Clinical Symptoms

- 50 year-old male
- 4 prior lines of therapy:
  - FOLFOXIRI + bevacizumab
  - FOLFIRI + panitumumab
  - FOLFOX + bevacizumab
  - Regorafenib
- PR (confirmed) with 47% reduction through 13 weeks
- Accompanied by:
  - Decrease in serum tumor marker CEA from 17.7 (C1D1) to 10.7 (C3D1)
  - Multi-log fold decrease in ctDNA
  - Improvement of clinical symptoms, such as cough

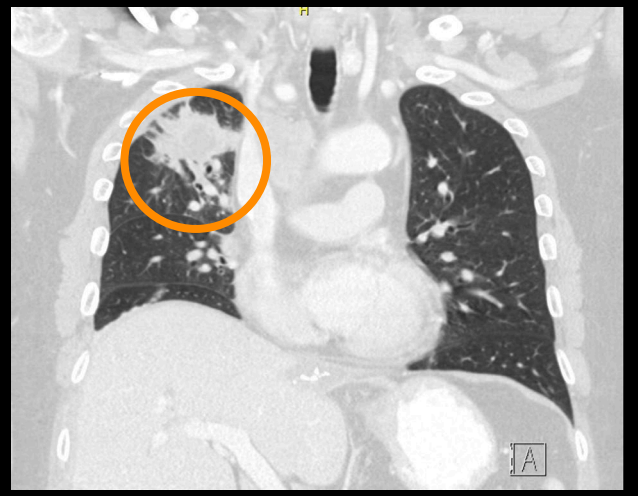
Baseline



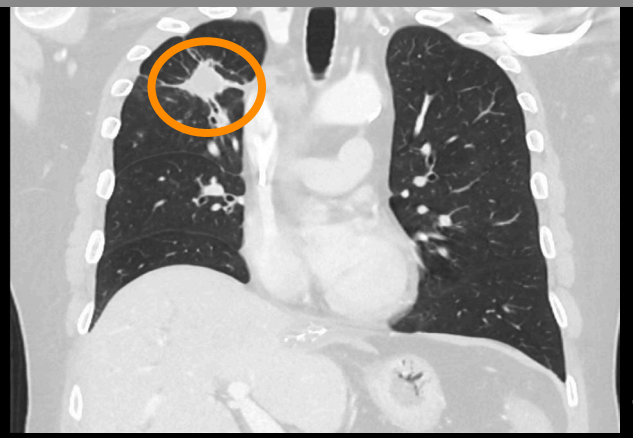
13 Week Follow-Up (2nd Scan)



Baseline



13 Week Follow-Up (2nd Scan)



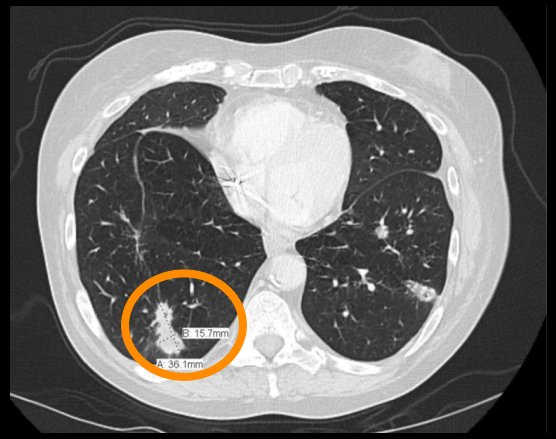
CEA: carcinoembryonic antigen;
ctDNA: circulating tumor DNA

Patient B: Confirmed PR in Patient with MSS CRC Without Liver Metastases (57% Reduction), With Undetectable ctDNA and CEA Normalized

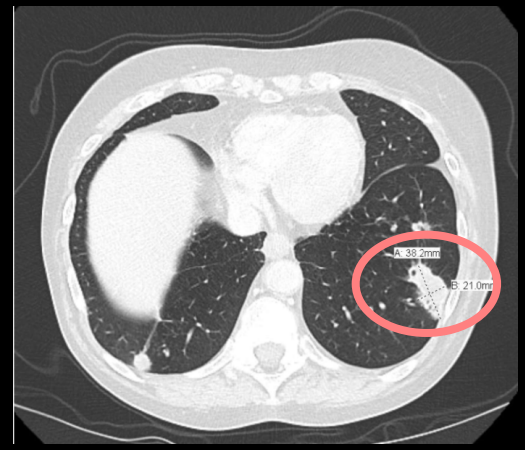
- 63 year-old female
- 2 prior lines of therapy:
  - FOLFOX
  - 5FU and irinotecan
- PR (confirmed) and continues to deepen:
  - 37% reduction (1st scan, 9 weeks)
  - 53% reduction (2nd scan, 13 weeks)
  - 57% reduction (3rd scan, 18 weeks)
- Accompanied by:
  - 100% decrease in ctDNA while on treatment (multi-log fold change to non-detectable)
  - Significant decrease in serum tumor marker CEA:

	Screening	C3	C4	C5	C7
CEA value (ng/ml)	192.9	23.6		3.5 (normal)	1.9 (normal)
Target lesions	74 mm		47 mm	35 mm	32 mm

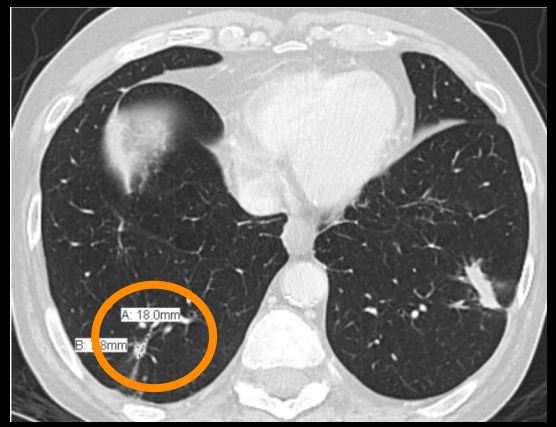
Lung Lesion #1 – Baseline



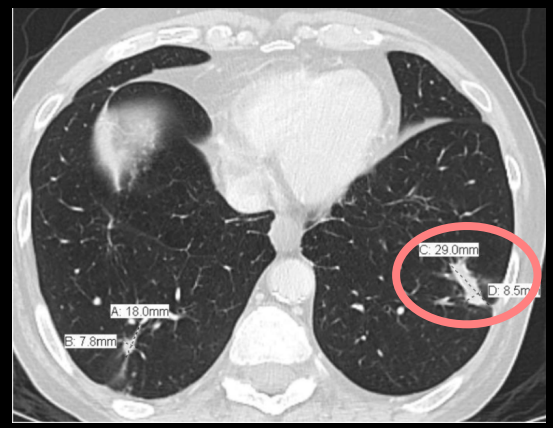
Lung Lesion #2 – Baseline



Lung Lesion #1 – 9 Week Follow-Up (1st Scan)



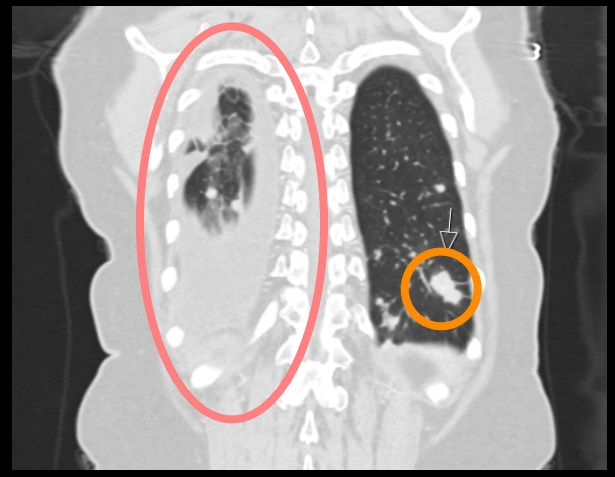
Lung Lesion #2 – 9 Week Follow-Up (1st Scan)



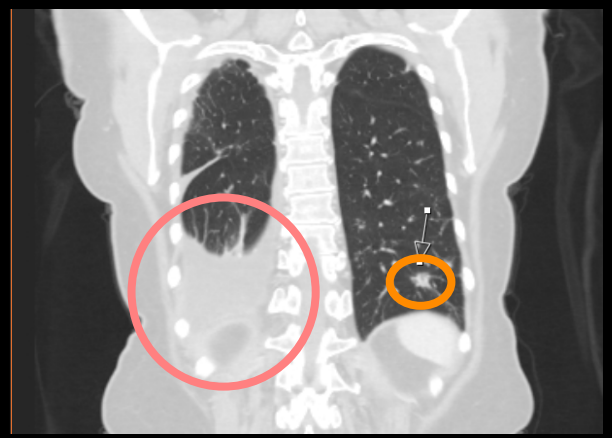
Patient C: PR (Unconfirmed) in Patient with MSS CRC Without Liver Metastases (35% Reduction), With Decreased CEA and ctDNA and Improvement in Clinical Symptoms

- 67 year-old female
- 6 prior lines of therapy:
  - FOLFOX
  - Capecitabine + bevacizumab
  - 5FU + bevacizumab
  - 5FU + panitumumab
  - FOLFIRI + panitumumab
  - 5FU + panitumumab
- PR (pending confirmation)* with 35% reduction at 9 weeks
- Accompanied by:
  - Substantial decrease in ctDNA
  - Decrease in serum tumor marker CEA from 7.95 (C1D1) to a normal value 2.8 (C3D1)
  - Improvement of symptoms, such as cough

Lung Lesions – Baseline

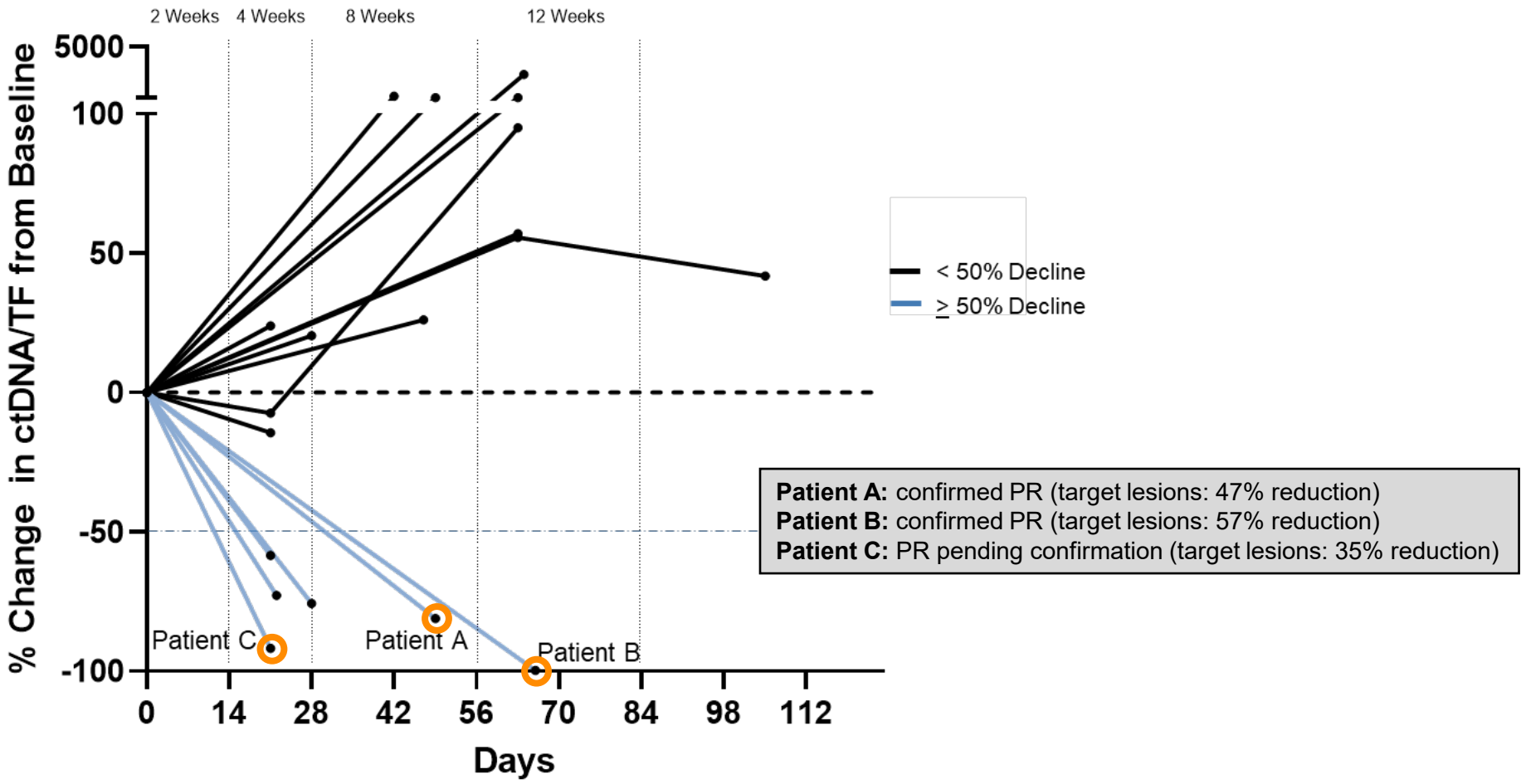


Lung Lesions – 9 Week Follow-Up (1st Scan)



* Initial assessment of unconfirmed PR by investigator at 9 weeks (radiology assessment pending)

Significant Decreases in ctDNA Observed in Multiple Phase 2 MSS CRC Patients Treated With Combination of Vilastobart (XTX101) and Atezolizumab



Patient A: confirmed PR (target lesions: 47% reduction)
Patient B: confirmed PR (target lesions: 57% reduction)
Patient C: PR pending confirmation (target lesions: 35% reduction)

Available blood plasma samples (baseline and on-treatment) were analyzed with an analytically validated next generation sequencing ctDNA assay (Guardant Infinity, a multi-omic assay), that identifies somatic alterations across >750 cancer-related genes and measuring thousands of differentially methylated regions to produce a Tumor Fraction score at each timepoint. A negative 100% indicates ctDNA negative status.

Combination of Vilastobart (XTX101) and Atezolizumab Continued to be Well-Tolerated With Highly Differentiated Safety Profile

- Only 6 patients experienced Grade 3 or 4 TRAEs (related to vilastobart or atezolizumab)
- Only 2 Grade 4 TRAEs (laboratory abnormalities) and no Grade 5 TRAEs
- Minimal endocrine irAEs and limited skin irAEs
- No patients experienced a dose reduction for vilastobart due to an AE (1)
- Only 3 patients discontinued treatment for the combination of vilastobart and atezolizumab due to a TRAE (2)

AE Category / Term *All TRAEs with ≥10% incidence or Grade 3/4 TRAE with ≥ 5%*	All Phase 2 Patients (n = 40)	
	Any	Grade 3 (3)
Fatigue	12 (30%)	0
Diarrhea	8 (20%)	0
Infusion related reactions	5 (13%)	0
Related to vilastobart	3 (8%)	0
Related to atezolizumab	2 (5%)	0
Pyrexia	4 (10%)	0
ALT increased	4 (10%)	0
AST increased	4 (10%)	1 (3%)
Colitis	2 (5%)	2 (5%)

Data cutoff date: January 13, 2025. Patients were administered combination of vilastobart (100 mg Q6W) and atezolizumab (1200 mg Q3W).

1. Dose reduction of atezolizumab is not permitted per protocol.
2. Reflects discontinuation of both vilastobart and atezolizumab.
3. Non-laboratory Grade 3 TRAEs not included in the table above consisted of: maculopapular rash and febrile neutropenia in 1 patient; lower gastrointestinal hemorrhage in 1 patient with thrombocytopenia; and 1 patient with Triple M overlap syndrome (myocarditis, myositis and myasthenia gravis).

Q3W: once every three weeks; Q6W: once every six weeks; ALT: alanine aminotransferase; AST: aspartate aminotransferase TRAE: treatment-related adverse event

Initial Data Highlight Potential for Vilastobart (anti-CTLA-4) in Combination in MSS CRC and a Range of Tumor Types, Including "Cold" Tumors Historically Resistant To Immunotherapy

Clinical Experience for Vilastobart (anti-CTLA-4)

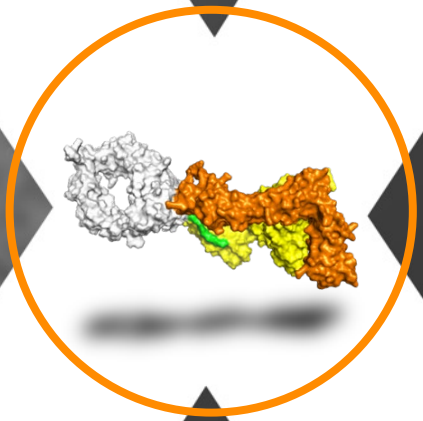
- ✓ Differentiated safety profile, well-tolerated at high doses and in combination
- ✓ Confirmed activation in patient tumors and T reg depletion
- ✓ Monotherapy activity in Phase 1 in "cold" tumors, including confirmed PR in NSCLC with complete resolution of liver metastases
- ✓ Early evidence of combination activity in Phase 1C (combination dose escalation), including confirmed PR in MSS CRC with liver metastasis
- ✓ Initial evidence of combination activity in Phase 2 (proof-of-concept), with preliminary 27% ORR (3 PRs) in MSS CRC without liver metastasis [1]

- *Plan to report additional Phase 2 data for vilastobart (anti-CTLA-4) in combination with atezolizumab in MSS CRC patients (n=40 total enrolled) in mid 2025*
- *Plan to seek opportunities for partnering to prioritize further clinical development beyond initial Phase 2 proof-of-concept trial (including additional tumor types and combinations)*

1. Includes 2 confirmed PRs (see Patient A and Patient B vignettes) and 1 unconfirmed PR (pending confirmation, see Patient C vignette).

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

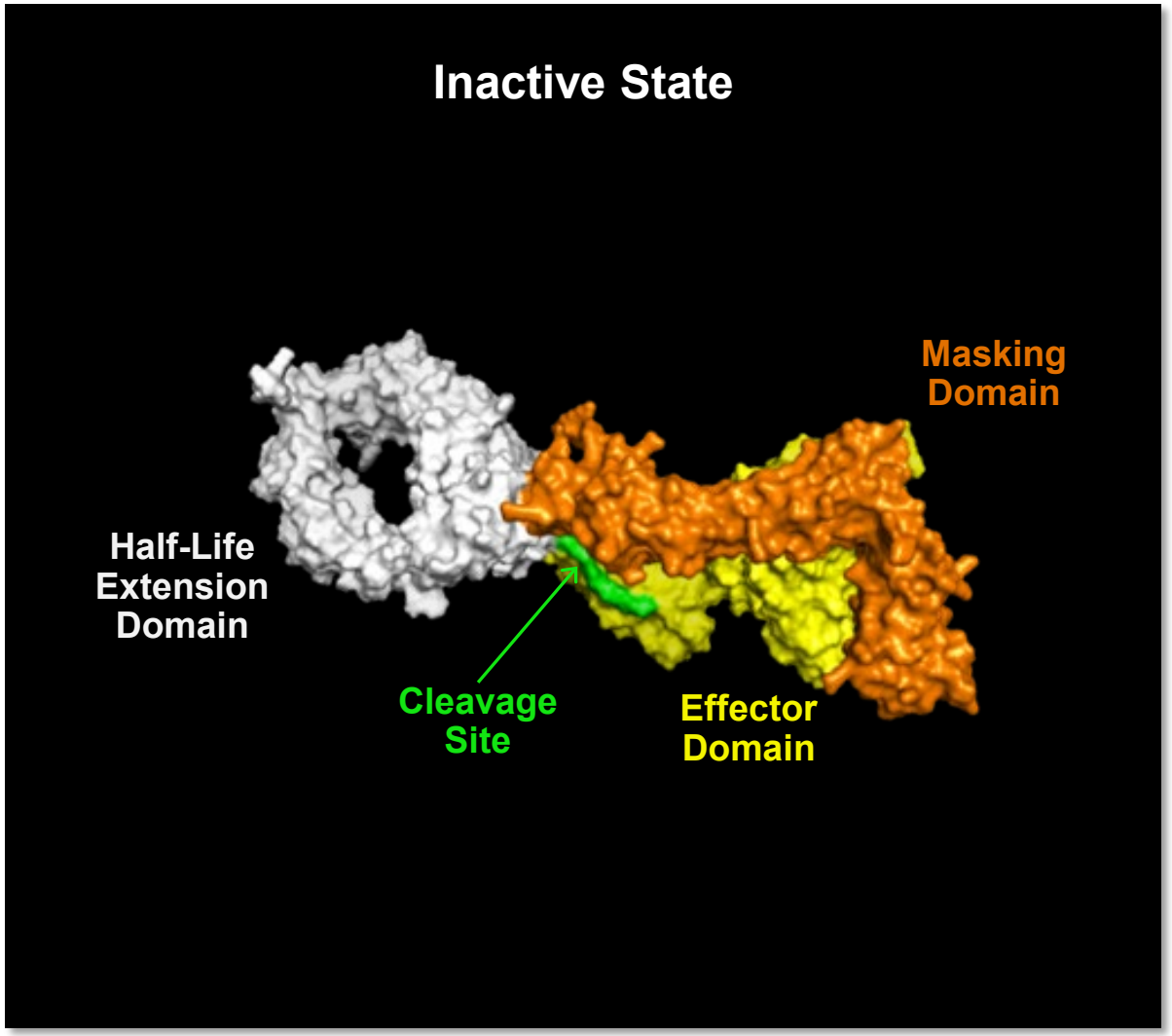
Capable of polarizing CD4 T-cells towards Th1 phenotype, thus driving cellular immunity against infection and cancer

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
  - 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.

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

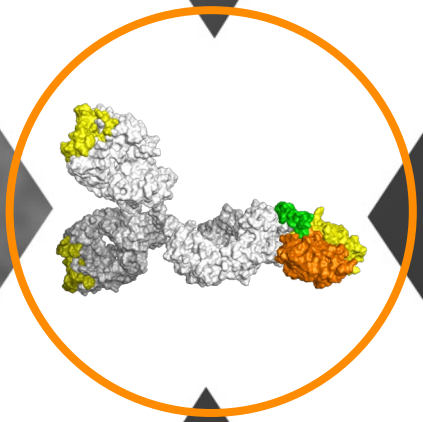
- Xilio responsible for clinical development of XTX301 in ongoing Phase 1 trial through initial planned Phase 2 trial
- Following delivery by Xilio of specified clinical data package for XTX301, Gilead can elect to pay option fee and becomes responsible for all further development and commercialization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

GILEAD
Creating Possible

1. If Gilead elects not to opt-in, the agreement will automatically terminate.

XTX501

PD1/IL2 bispecific



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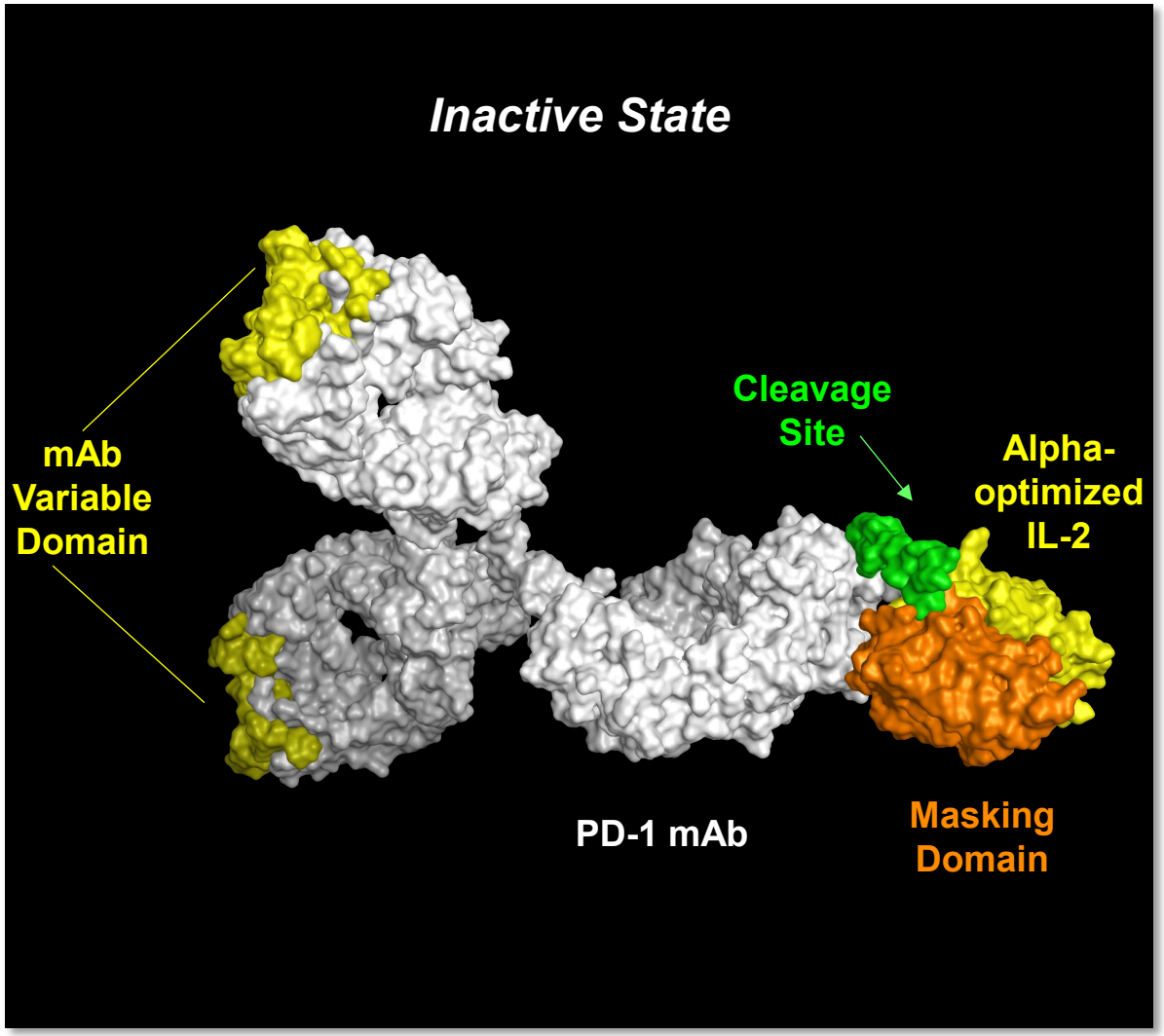
XTX501 Has Potential to be Best-in-Class PD1/IL2 Bispecific

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) and tumor-selective PD 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

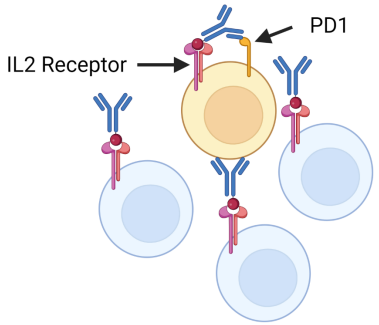
NHP: non-human primate; VHH: variable heavy domain of heavy chain.

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

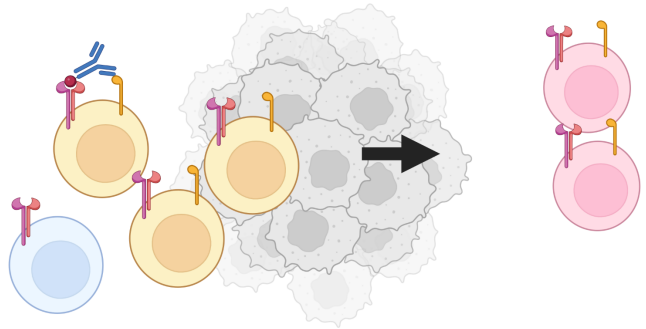
Periphery	*Tumor*

Non-masked PD1/IL2

Short half-life and sub-optimal activity due to IL-2-driven Target Mediated Drug Disposition (TMDD)



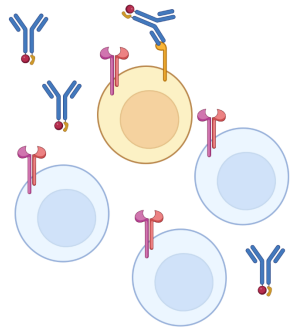
Naturally dominant IL-2 component binds broadly across T cell population. Consumption by more abundant bystander T cells drives rapid clearance (**blue**)



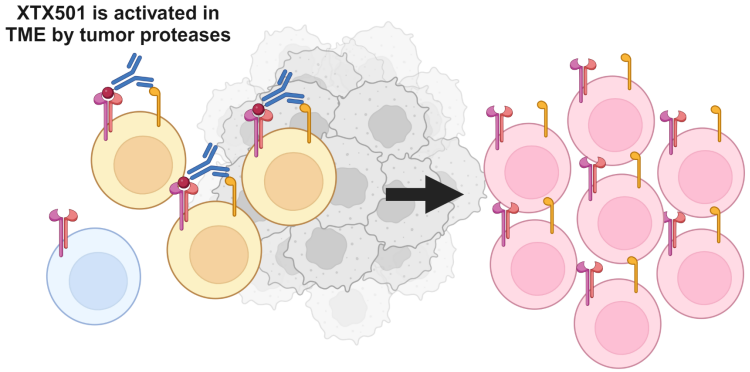
Lower concentration of unmasked PD1/IL2 in the TME reduces activation of tumor reactive PD1⁺ T cells (**yellow**), results in lower numbers of progeny functional effector T cells (**pink**) and reduces overall activity

XTX501

Tumor-activated design eliminates peripheral IL-2-driven TMDD and enhances activity



No IL-2 driven binding of XTX501 in the periphery resulting in PD1 antibody-like exposure



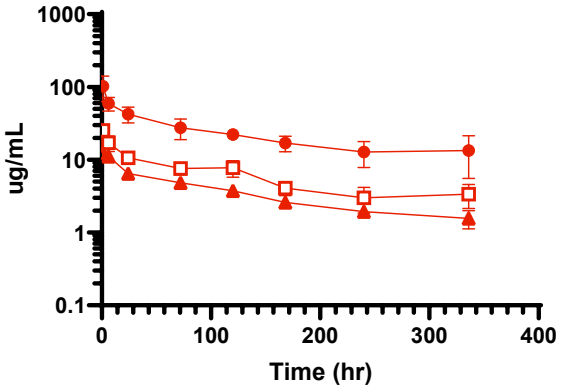
High concentration of XTX501 in the TME enables activation of tumor-reactive PD1⁺ T cells, higher numbers of progeny functional effector T cells

Figure generated using BioRender.com.

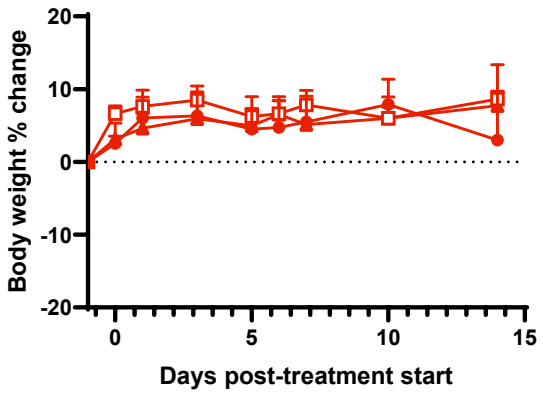
Tumor-Activated Design of XTX501 Demonstrated Optimal PK and Tolerability Preclinically

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

XTX501
Concentration vs. Time



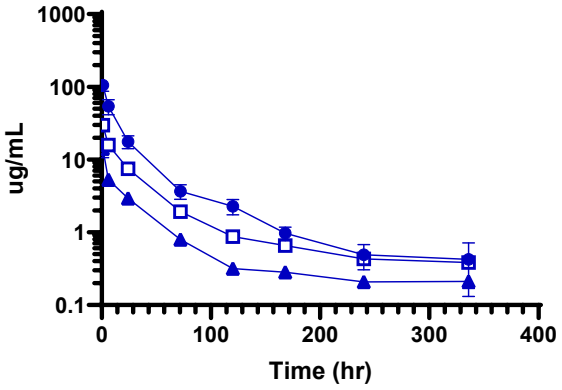
XTX501
Body weight change vs. Time



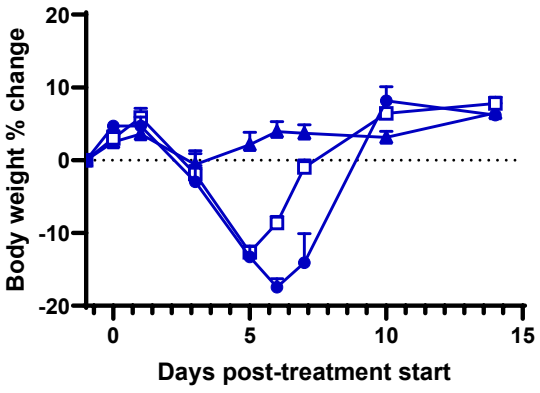
10 mg/kg (High)
3 mg/kg (Med)
1 mg/kg (Low)

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



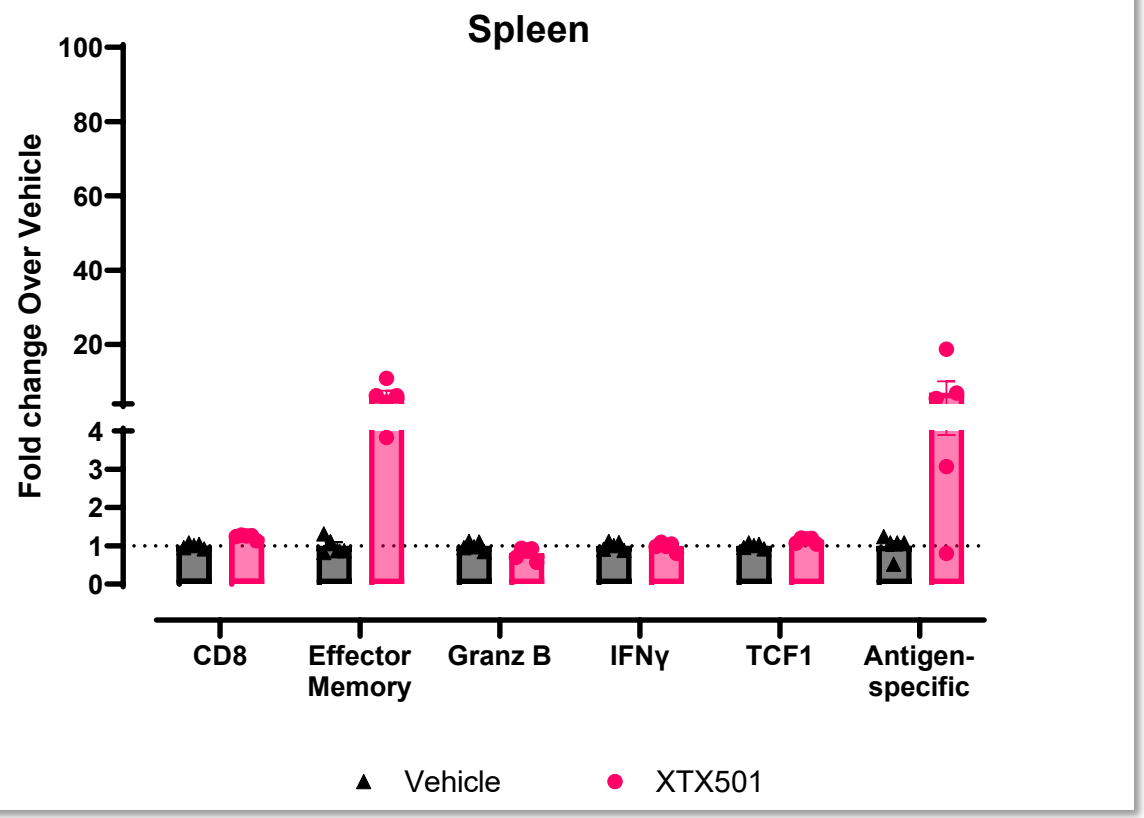
High
Med
Low

Equimolar dosing aligned with XTX501

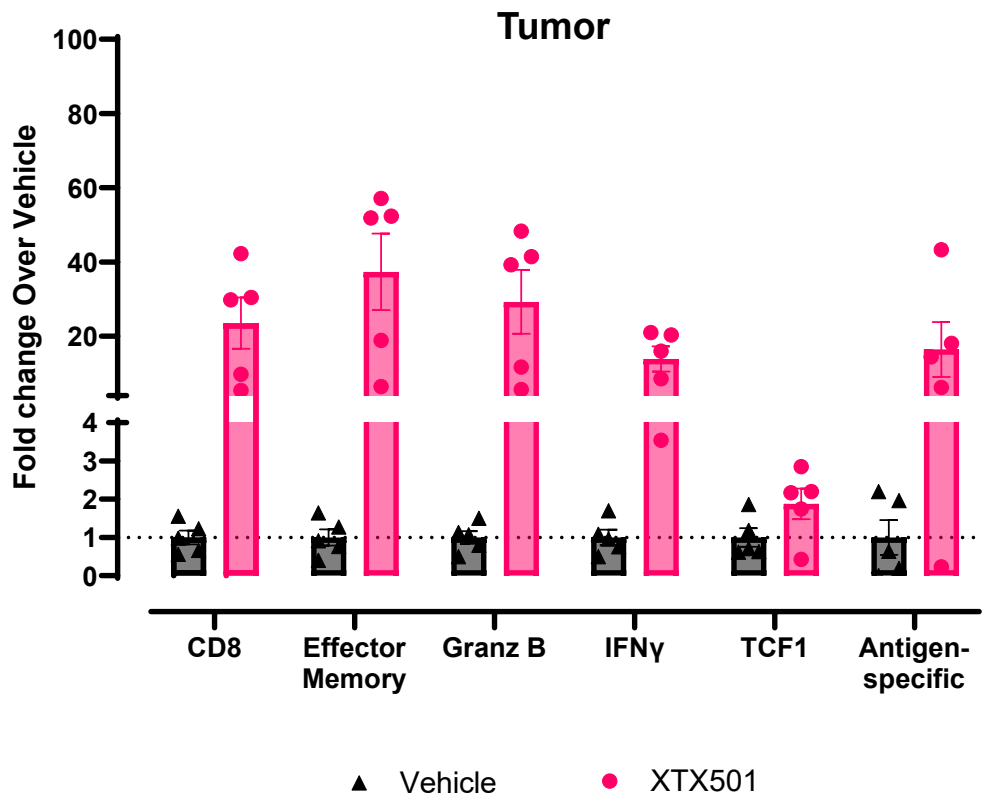
XTX501 exposure after a single 10, 3 or 1 mg/kg intravenous injection in non-tumor bearing C57BL/6-hFcRn mice. Non-masked PD1/IL2 exposure after a single equal molar dose of 9.25, 2.75 or 0.92 mg/kg intravenous injection in non-tumor bearing C57BL/6-hFcRn mice. Body weight data are displayed until day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



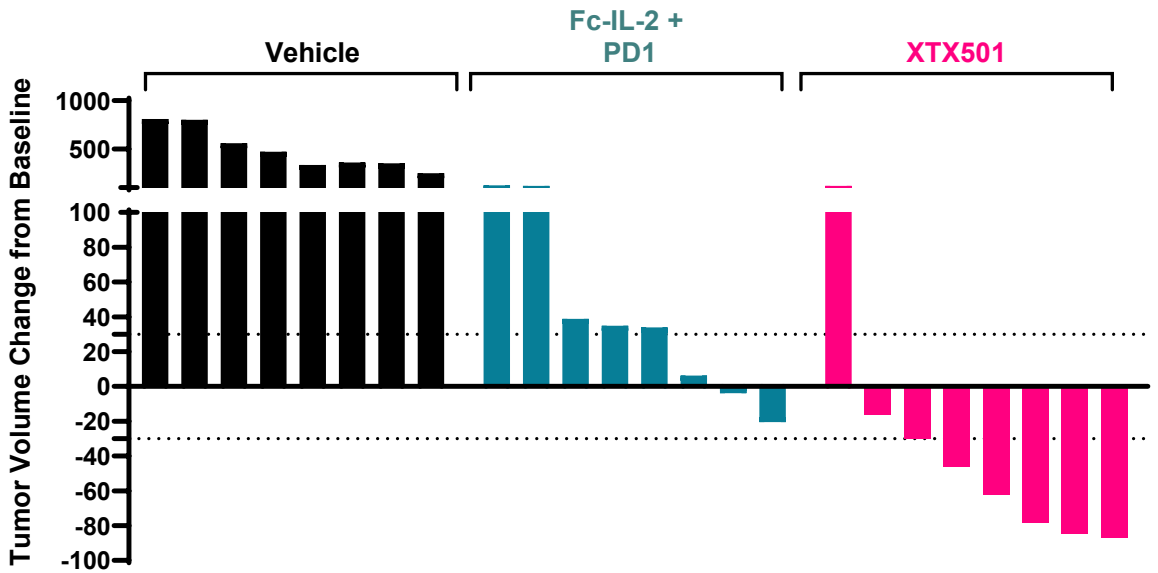
XTX501 Treatment Demonstrated Robust Increases in Activated T Cell Populations in Tumor



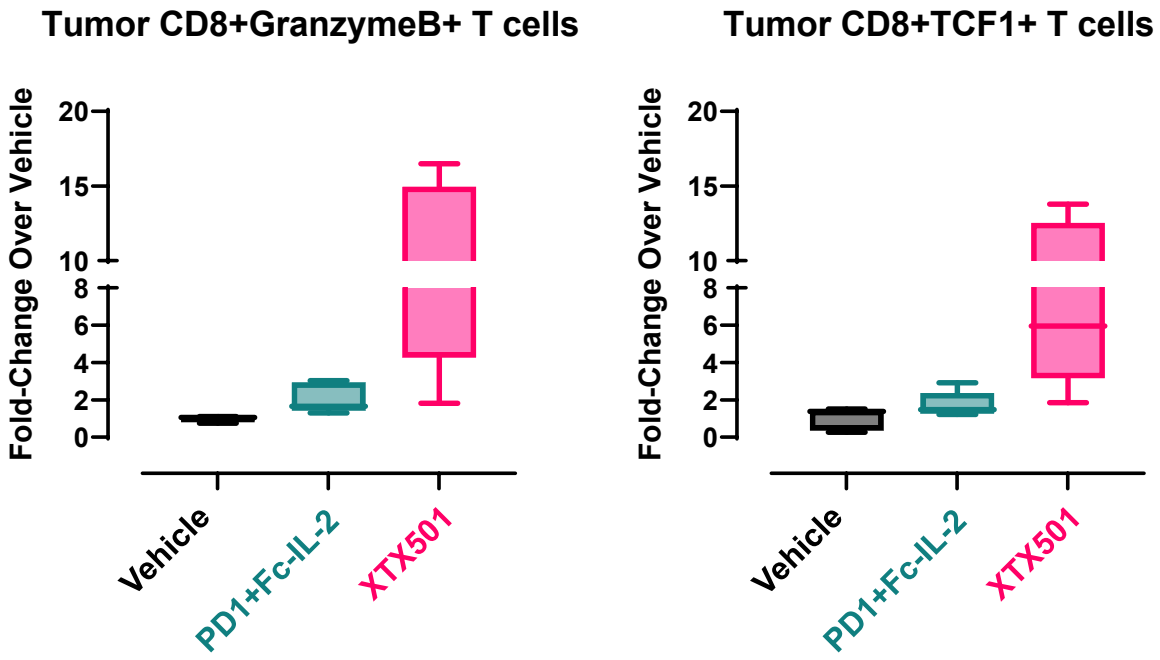
Female C57BL/6 hPD-1 mice (n=5 in each treatment group) were inoculated with 0.5x106 MC38 tumor cells subcutaneously in the right flank. On day 0, 3 mice received XTX501 bispecific or vehicle. The percentage of cells for each immune phenotype was calculated as percentage of live CD45+ cells and the ratio 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 Combination of PD1+IL-2 in Tumor Model, Suggesting Enhanced Anti-Tumor Immunity Preclinically

Robust Preclinical Monotherapy Activity Beyond Fc-IL-2 + PD1 Combination was Observed with XTX501



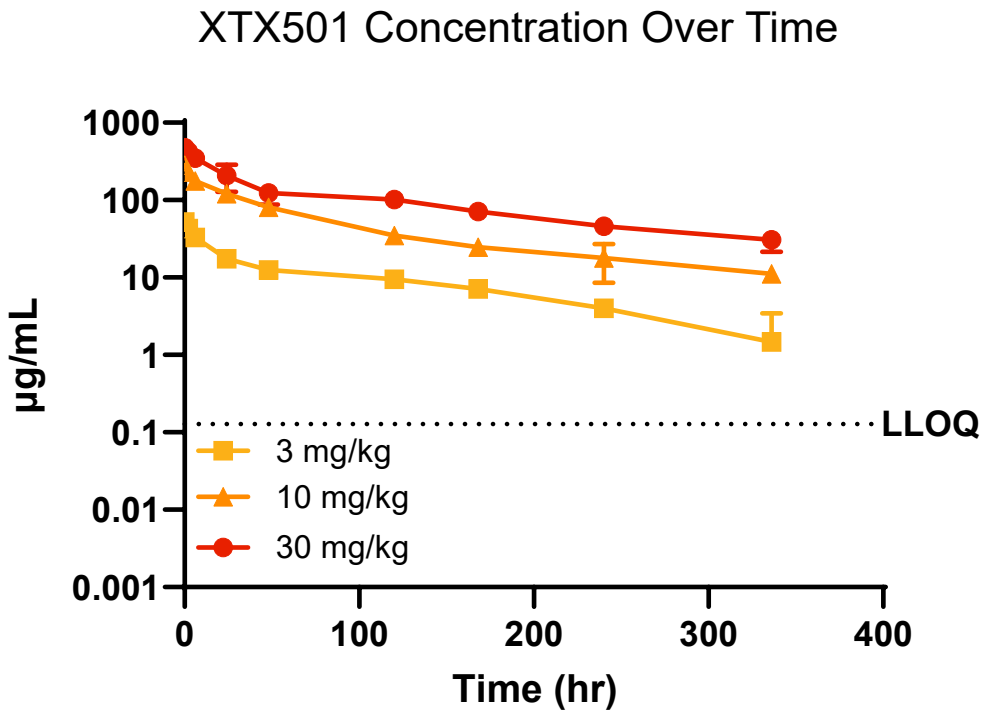
XTX501 Increased Intra-Tumoral Cytotoxic and TCF1+ Stem-Like T Cells



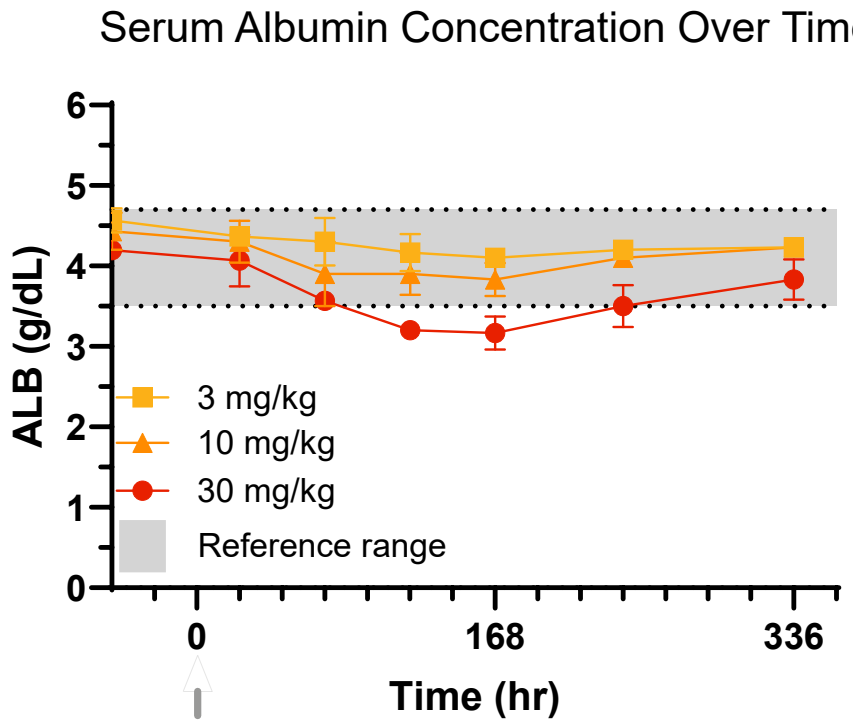
Left panel: Female C57BL/6 hPD-1 mice (n=8 in each treatment group) were inoculated with MB49 tumor cells. On day 0, 5 mice received vehicle or equimolar doses of anti-PD1 antibody (pembrolizumab) plus XTX202 (Masked βγIL-2), or XTX501. Tumor volume change on day 12 post treatment relative to baseline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

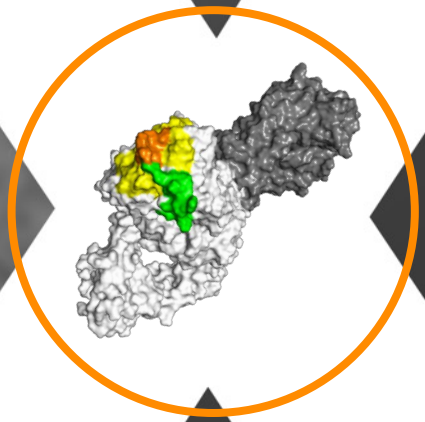


Minimal Effects of XTX501 on Serum Albumin
(i.e., No Signs of Vascular Leak Syndrome)



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

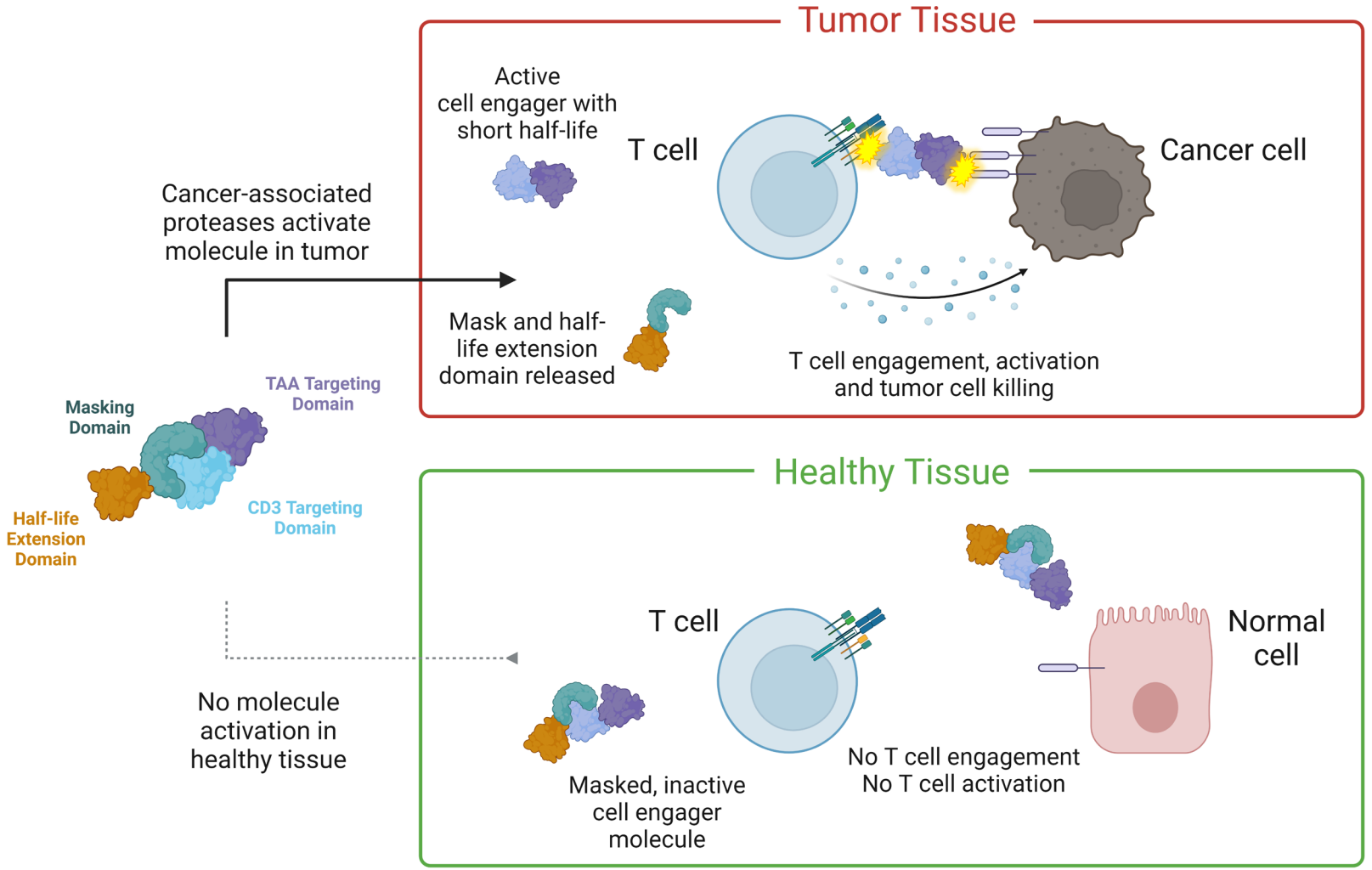


Figure generated using BioRender.com.

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

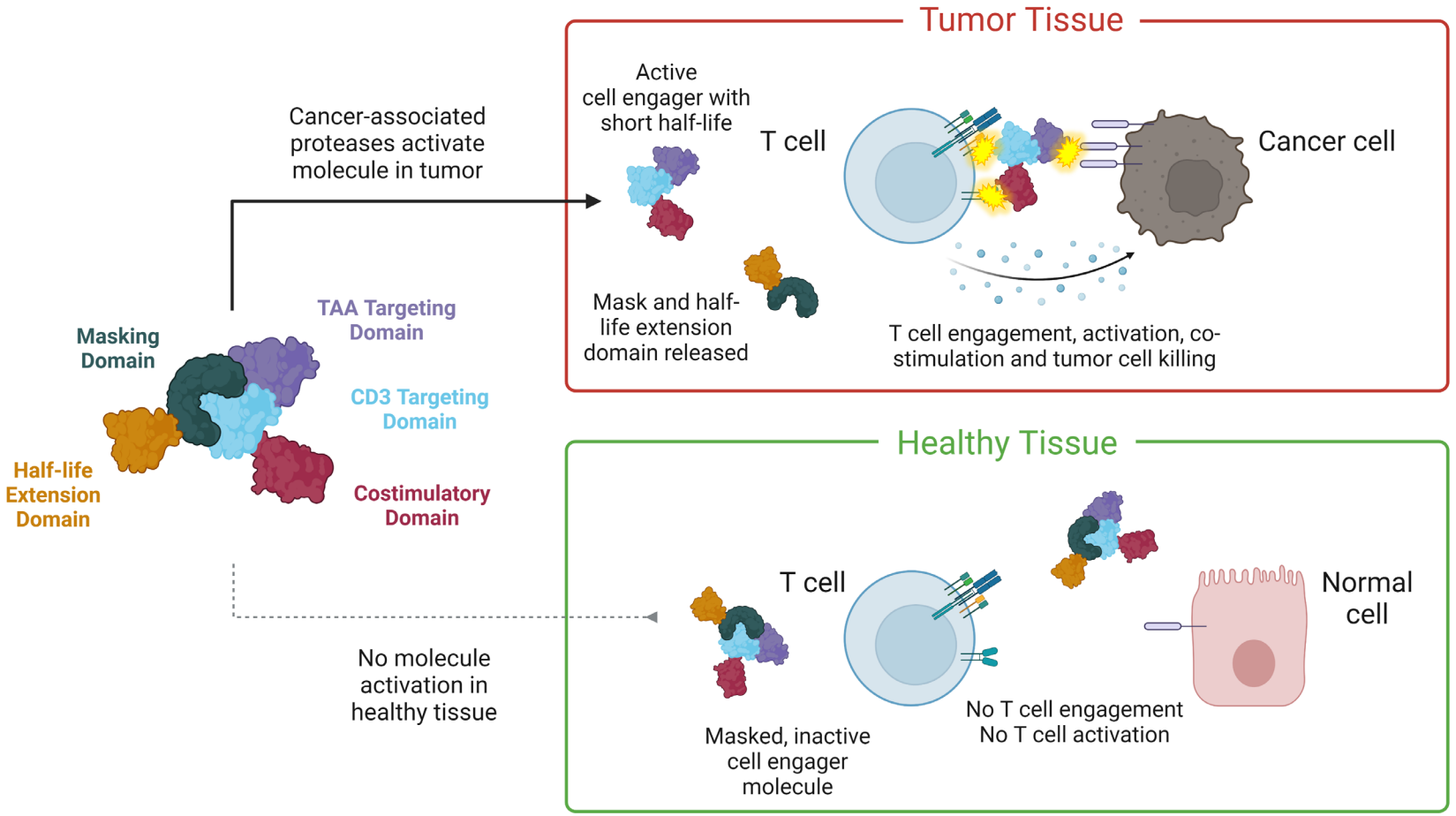
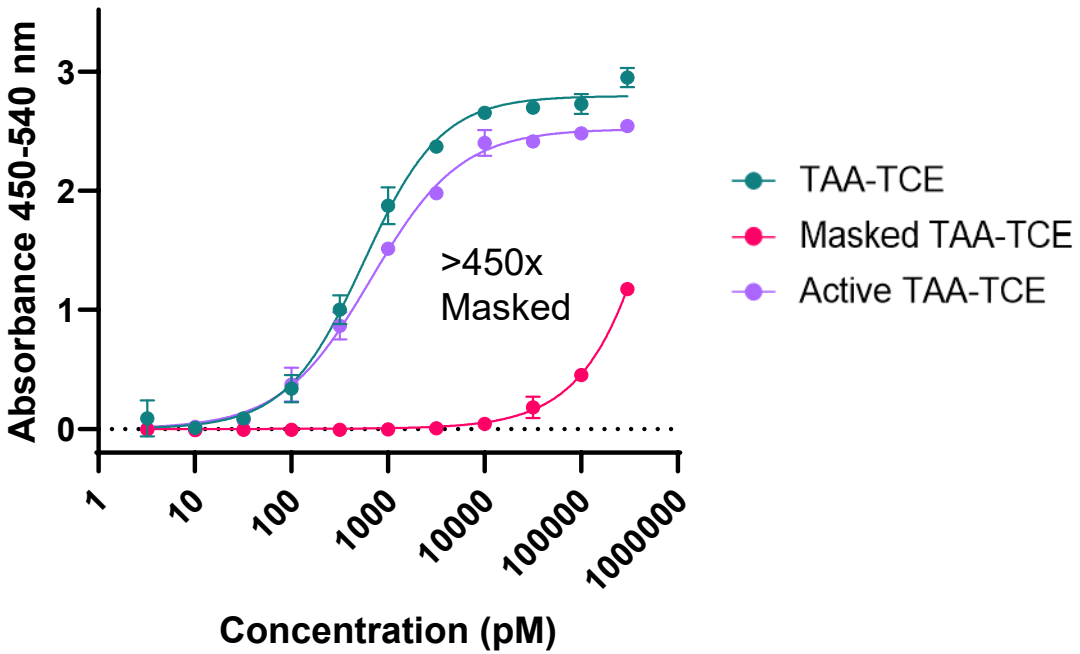


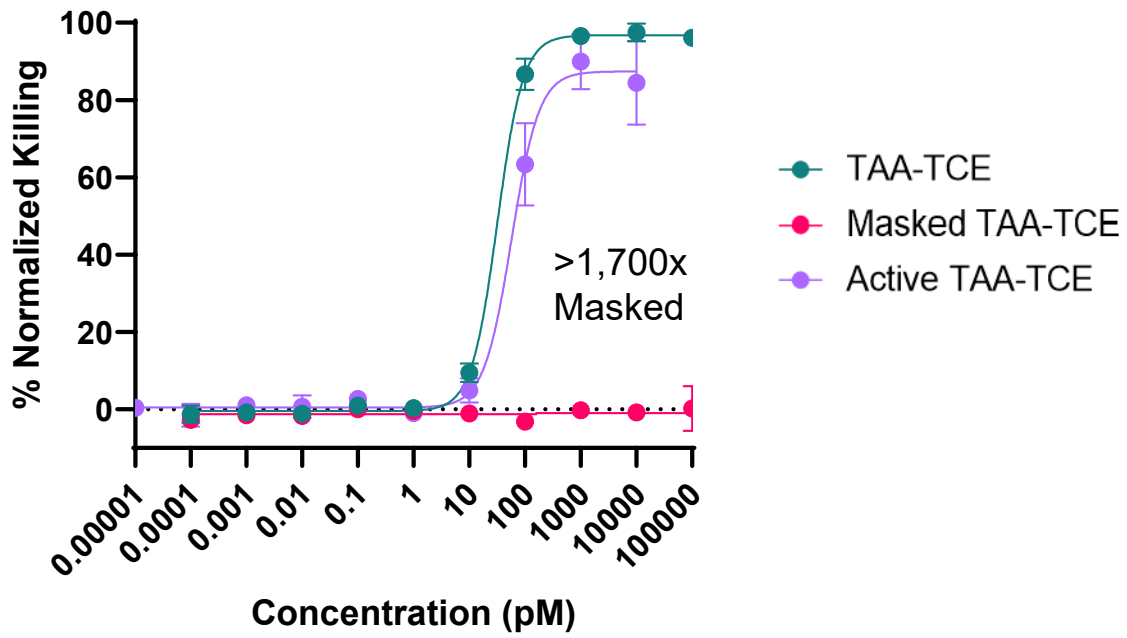
Figure generated using BioRender.com.

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

Demonstrated Protease-Dependent Binding to CD3 by ELISA



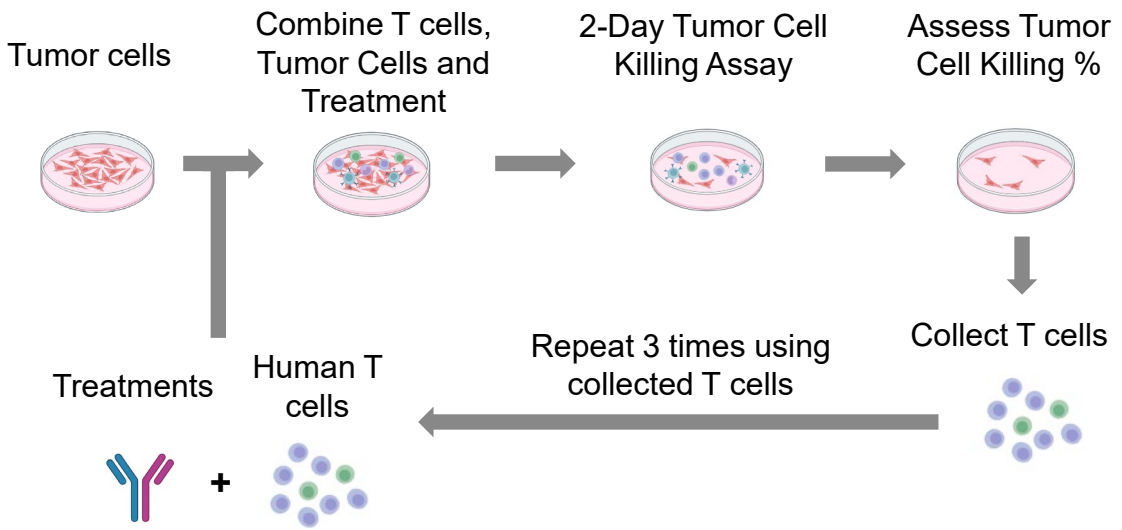
Confirmed Protease-Dependent Activity in Primary T Cell Assay



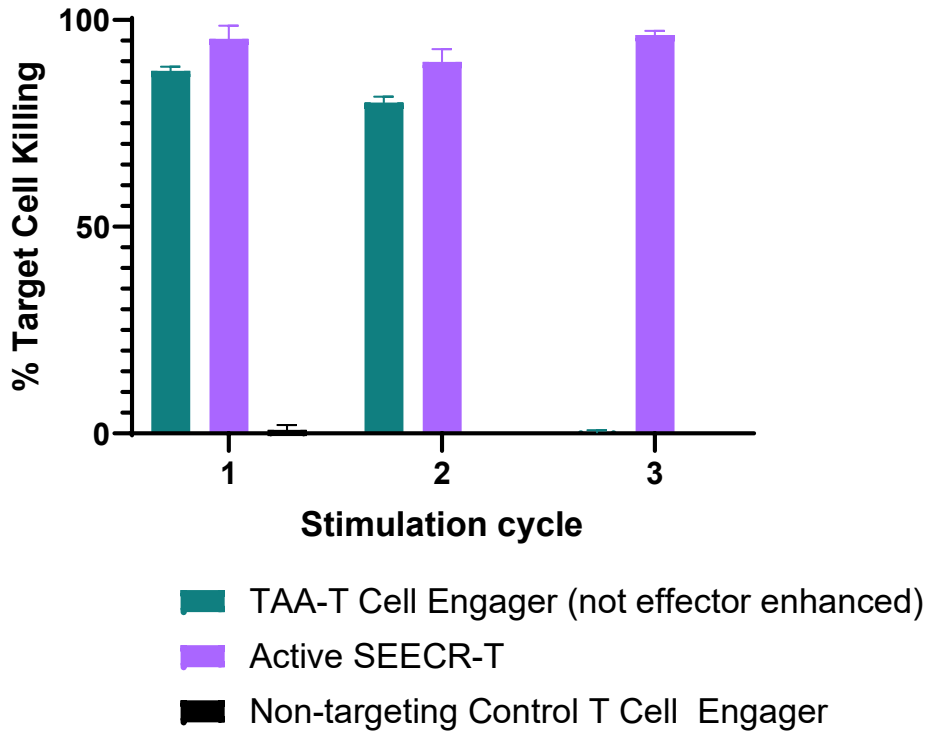
Left panel: Protease dependent CD3-binding demonstrated via TAA-TCEs bound to immobilized CD3 in an ELISA. **Right panel:** Protease-dependent tumor cell killing. Active TAA-TCEs led to killing in co-culture assay. A375 tumor cells were cultured overnight before addition of expanded T cells at a 5:1 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 Format Demonstrated Unique Ability to Drive Sustained, Serial Tumor Cell Killing Over Multiple Rounds of Stimulation in Preclinical Model

Developed Custom Primary Cell Assay to Evaluate Ability of Treatments to Elicit Serial Tumor Cell Killing



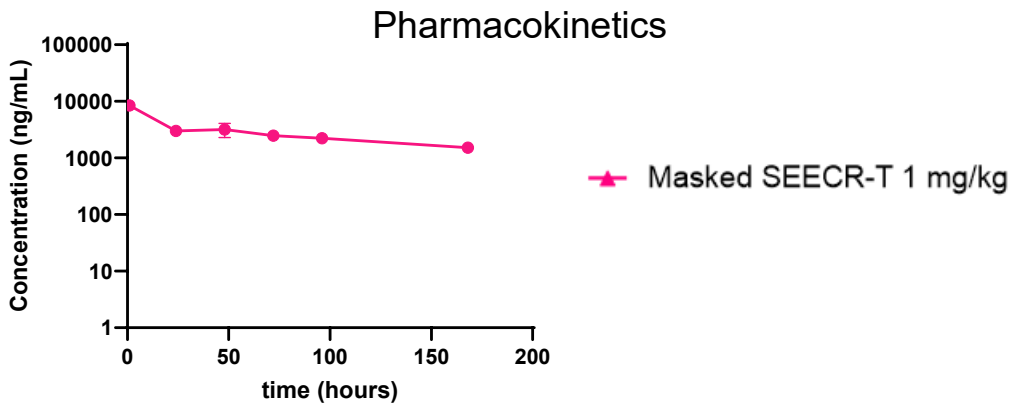
SEECR Format Enabled Sustained Tumor Cell Killing Over Multiple Rounds

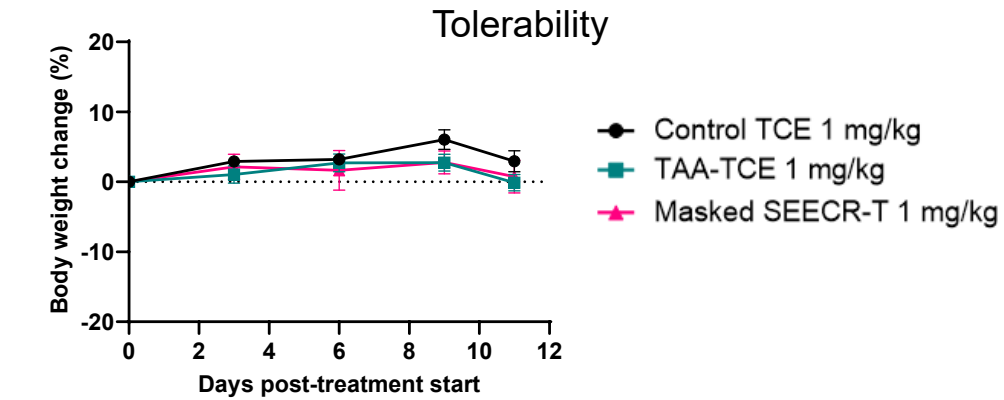


Human T cells were incubated over three consecutive rounds with indicated test articles and A431 cancer cells and percent tumor cell killing was assessed using a luminescence readout.

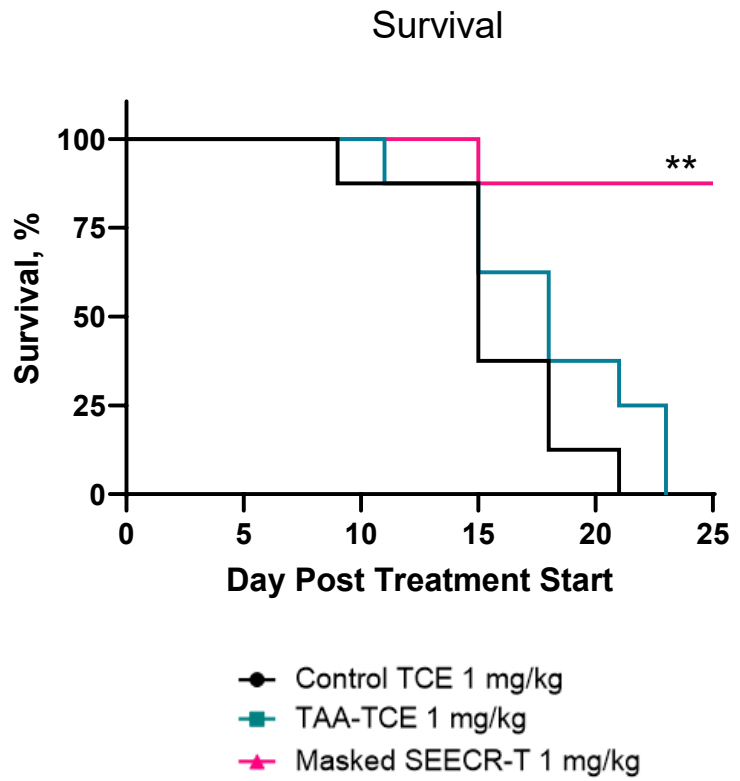
Prototype SEECR Molecules Exhibited Antibody-Like PK, Were Well-Tolerated and Increased Survival in Murine Models

SEECR Featured Antibody-Like PK and Tolerability Comparable to Control





SEECR Showed Significantly Enhanced Survival Compared to Standard TCE



Pharmacokinetics (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:** The treatment with masked SEECR-T molecule improved median animal survival. TR: Tumor regression

Management Overview and Recent Financial Results

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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.