Unleashing the Potential of Immuno-Oncology Therapies

November 7, 2024

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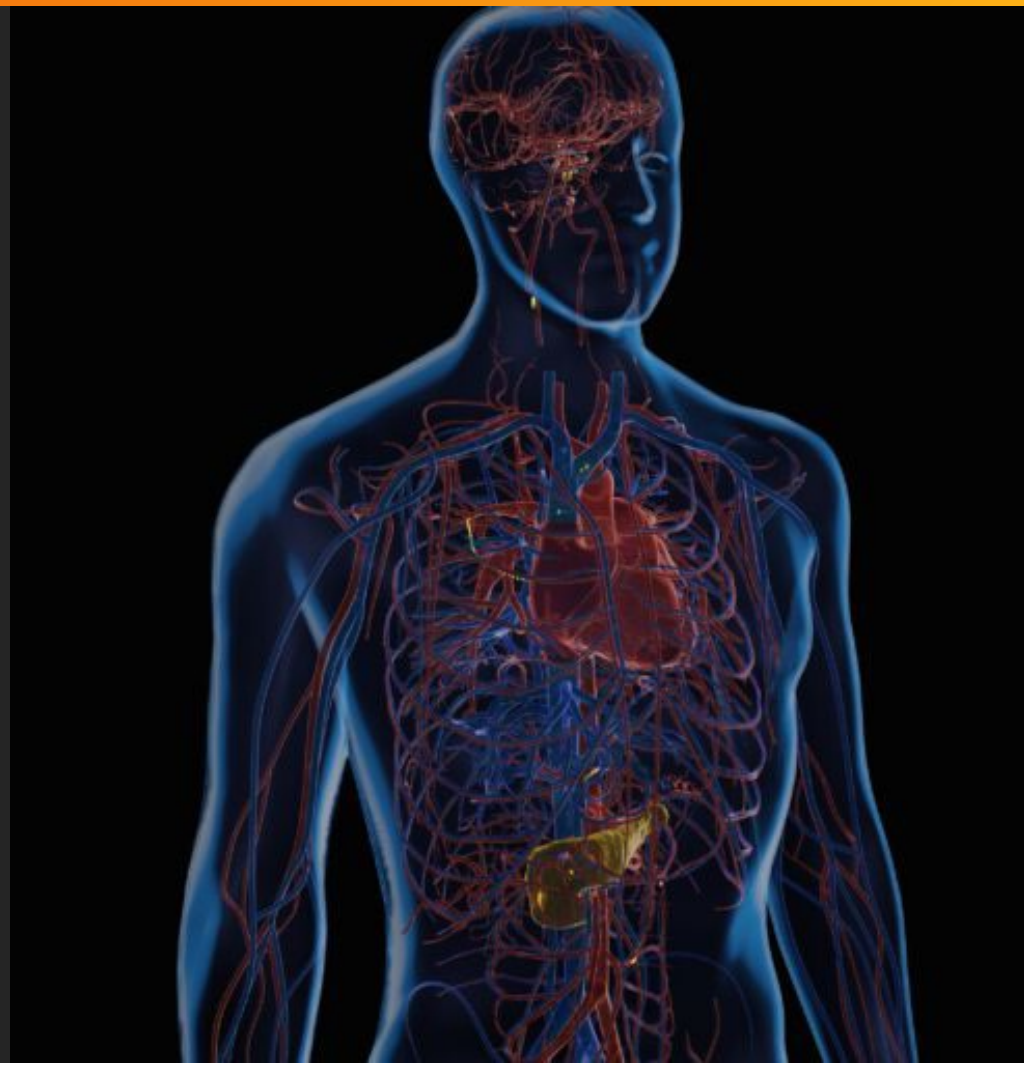
Immuno-Oncology Therapy is the Key to Curative Potential, But Continues to Be Limited by Systemic Toxicity

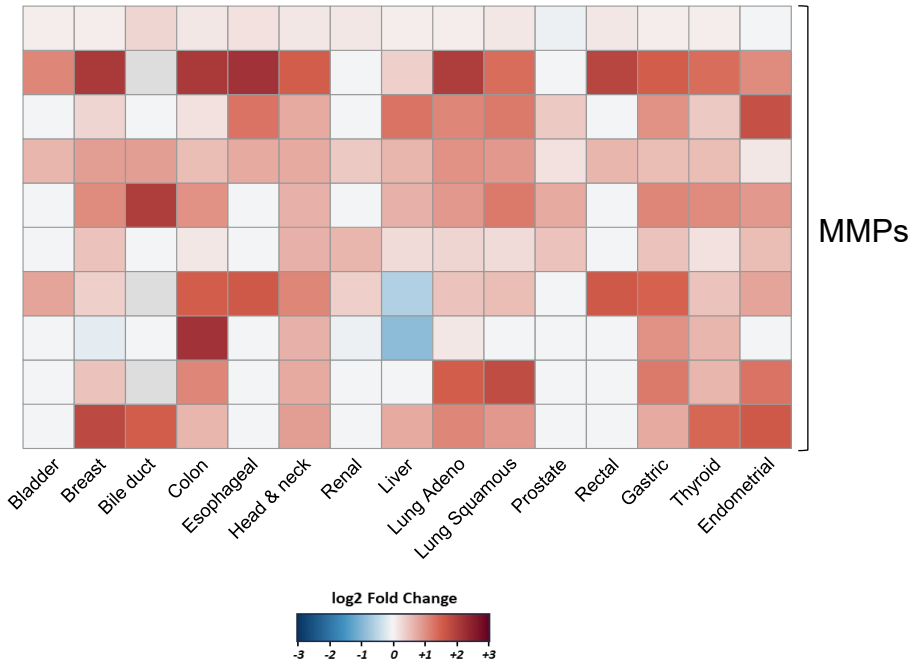
Xilio believes the next revolution in I-O therapy will **harness the power of the body's immune system** by **leveraging the dysregulated biology of the tumor against itself**



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

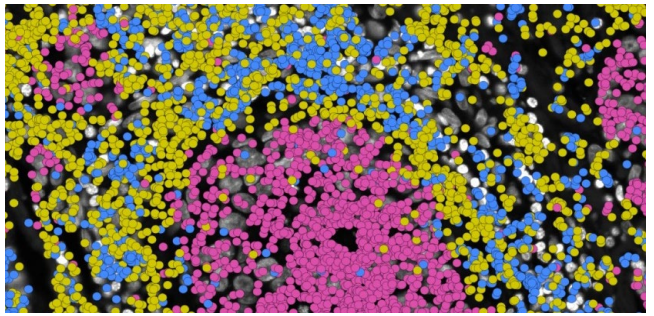
MMPs are dysregulated broadly across solid tumors

MMP mRNA expression in tumor vs. normal tissue

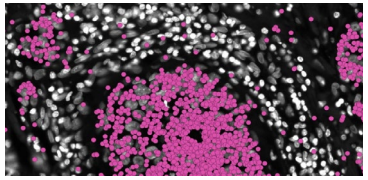


MMPs and immune cells co-localize at the invasive edge of tumors

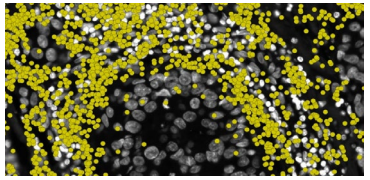
In situ mRNA expression in human breast cancer



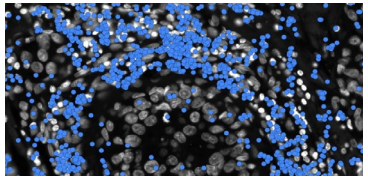
Tumor cells (TROP2)



MMP (MMP2)



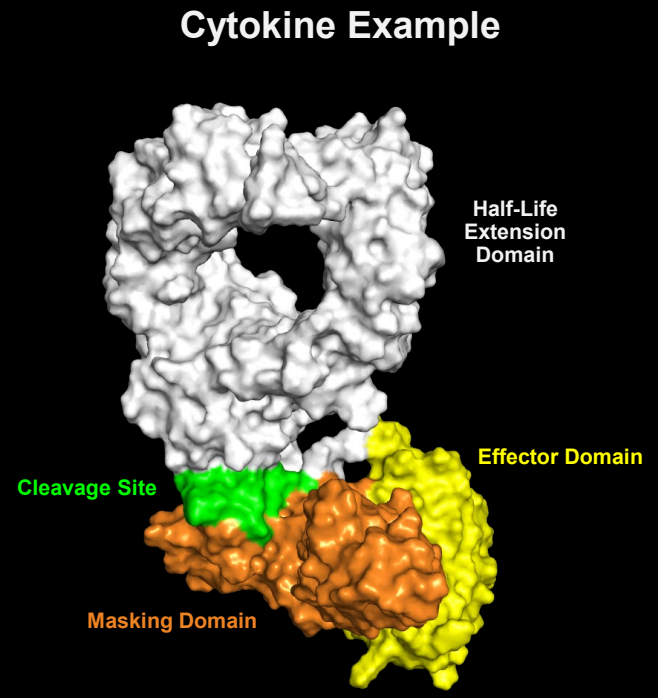
T cells (CD4, CD8A)

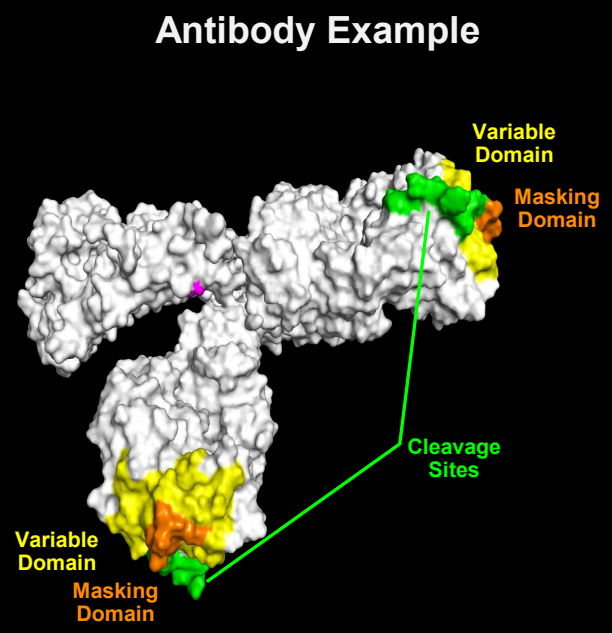


Left panel: Heatmap summarizing RNA expression changes of genes encoding for selected MMPs (bottom) in tumor vs. adjacent normal samples from multiple TCGA studies (x-axis). Color intensity tracks with log2-transformed fold changes (log2FC). Pre-processed TCGA data were obtained from UCSC Xena. **Right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

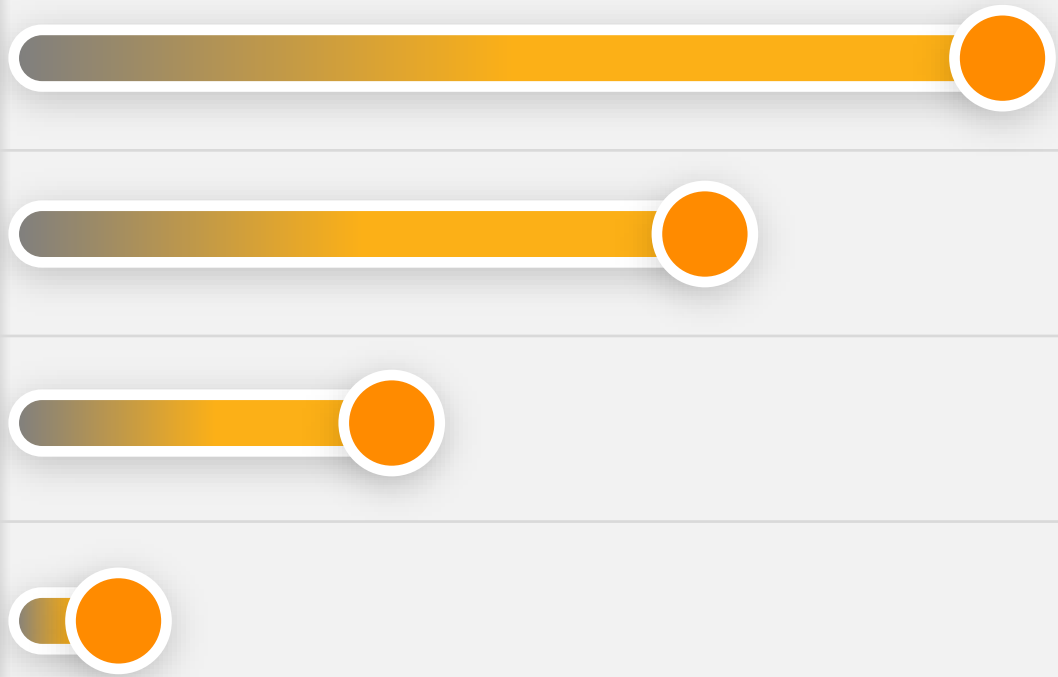




TME: tumor microenvironment

Advancing Pipeline of 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

Positioned for Multiple Anticipated Key Clinical Milestones in Q4 2024

Q1 2024

XTX301 (IL-12)
Announced Partnership with Gilead
Exclusive global license for IL-12 program

Q2 2024

XTX501 (PD-1/IL2 bispecific)
Preclinical Poster Presentation
Presented data at AACR demonstrating initial preclinical proof-of-concept

Q3 2024

Vilastobart (anti-CTLA-4) [1]
RP2D in Combination Dose Escalation
Selected RP2D for vilastobart + atezolizumab

Initiated Phase 2 Combination Trial
Initiated enrollment in Phase 2 trial for vilastobart + atezolizumab in MSS CRC

Q4 2024

Tumor-activated immune cell engagers
Preclinical Poster Presentation
Presented data at SITC demonstrating initial preclinical proof-of-concept for tumor-activated cell engagers in SEECR format

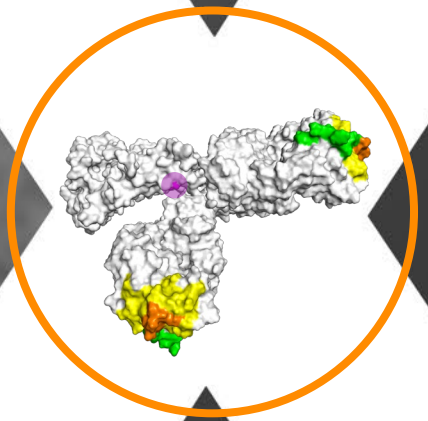
Vilastobart (anti-CTLA-4) [1]
Report Initial Phase 2 Combination Data
Plan to report initial Phase 2 data for vilastobart + atezolizumab in ~20 patients with MSS CRC

XTX301 (IL-12)
Report Phase 1 Data
Plan to report Phase 1 safety and PK/PD data for XTX301 in patients with advanced solid tumors

1. Evaluating vilastobart (XTX101) in combination with atezolizumab (Tecentriq®) under co-funded clinical collaboration with Roche in Phase 2 combination trial in metastatic MSS CRC.
PD: pharmacodynamic; PK: pharmacokinetic; SEECR: selective effector-enhanced cell engager

Vilastobart (XTX101)

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



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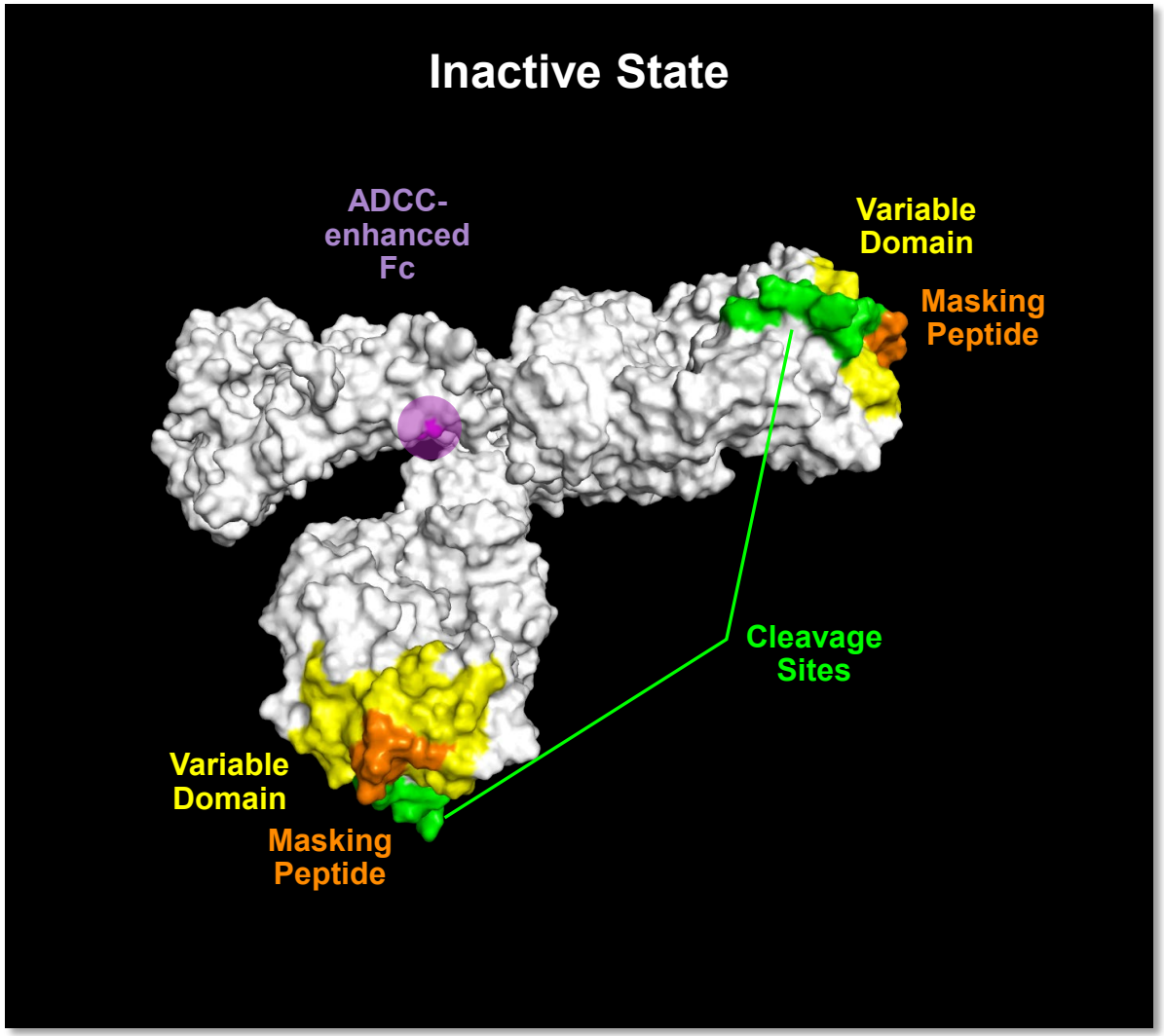
Vilastobart: Tumor-Activated, High Affinity Binding, Fc-Enhanced Anti-CTLA-4



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

* 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

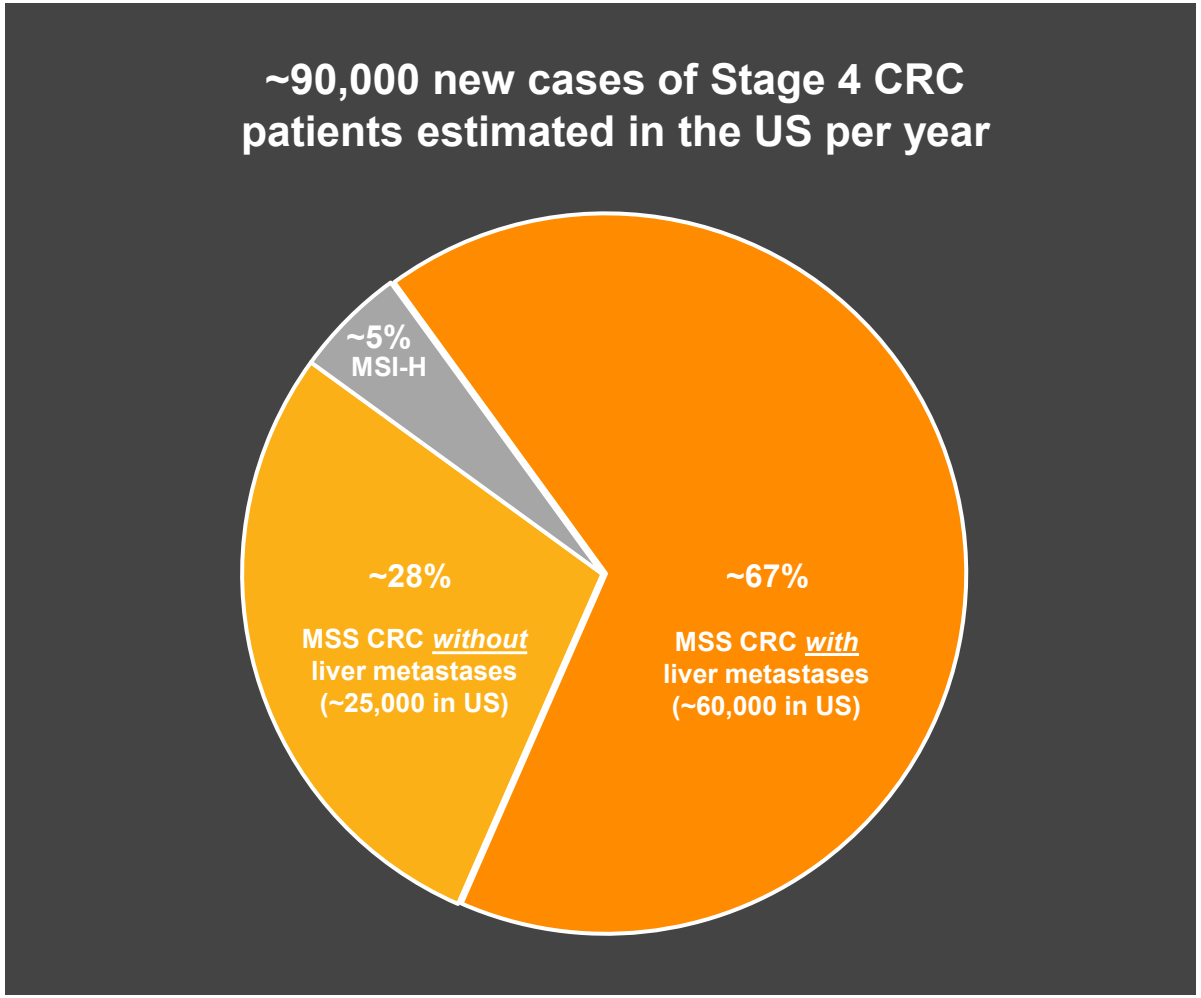
Anticipated Near-Term Phase 2 Data Milestones

- ❑ Initial data (n = ~20 total) in MSS CRC in Q4 2024
- ❑ Additional data (n = ~40 total) in MSS CRC in Q1 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

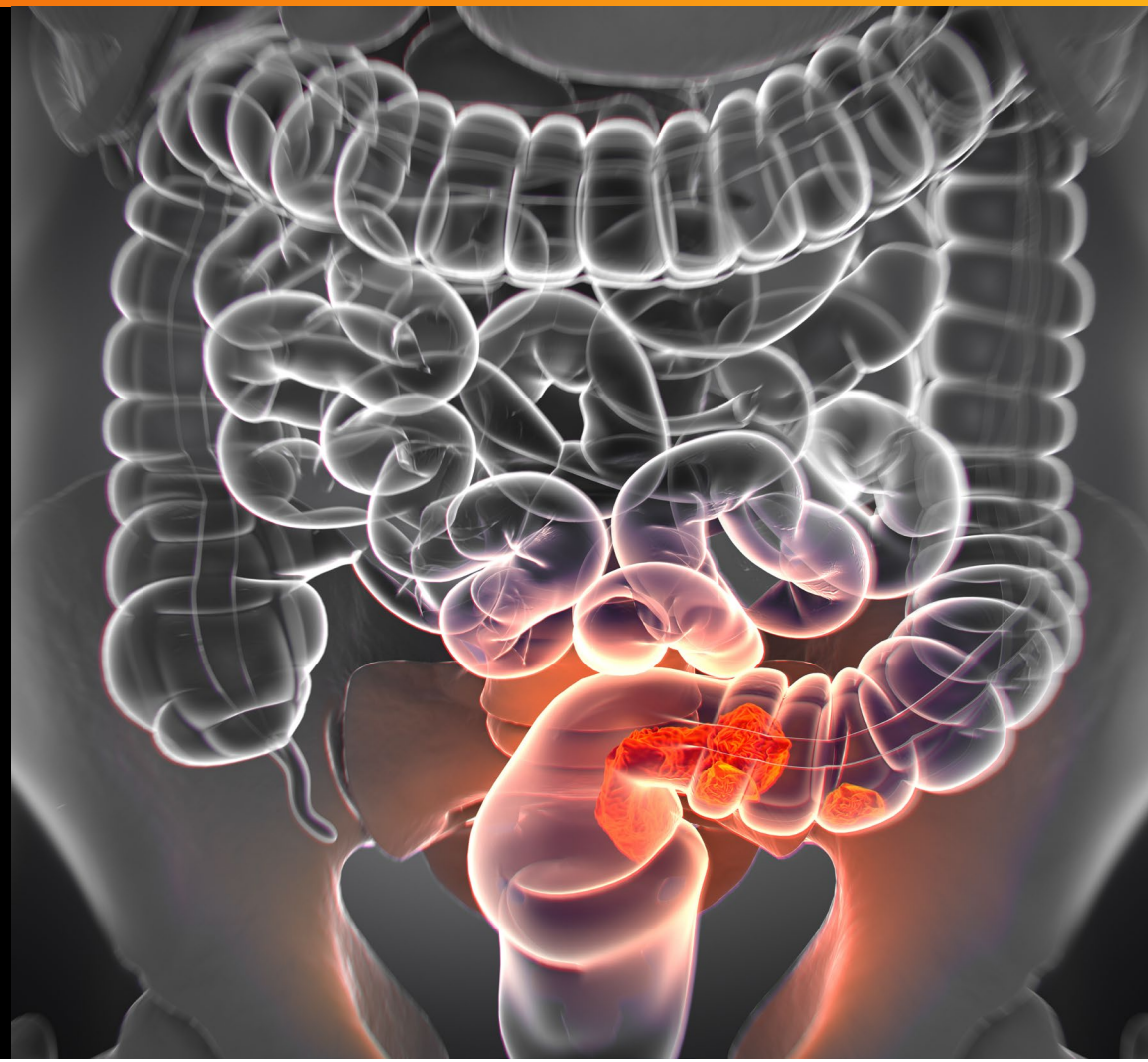
- CRC is 2nd in cancer-related deaths in the US and leading cause of cancer-related death in men younger than 50 in the US (1)
- CRC is 3rd in total annual new cases globally, with ~1.9M new cases and ~900,000 deaths related to CRC globally (2)
- >65% of Stage 4 CRC patients present with liver metastases,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

Phase 1C Combination Dose Escalation for Vilastobart (anti-CTLA-4) and Atezolizumab Enrolled Heavily Pre-Treated Patients with Cold Tumors

Vilastobart Phase 1 Trial Design

Phase 1A
Monotherapy Dose-Escalation
Advanced Solid Tumors

Phase 1B
Monotherapy Expansion

Phase 1C Combination Dose Escalation (vilastobart + atezolizumab)

Advanced Solid Tumors
(n=17)

Enrollment ongoing at vilastobart 150 mg Q6W dose level

Patient Characteristics	Total (n=17)
Demographics	
Age, median (range)	69 (39, 77)
Female	6 (35%)
ECOG PS 0	7 (41%)
ECOG PS 1	10 (59%)
Prior Lines of Anti-Cancer Treatment	**Median 3 (1-12)**
1	2 (12%)
2	1 (6%)
3	6 (35%)
4	1 (6%)
5	3 (18%)
6 and more	4 (24%)
Progressed on Prior Treatment with I-O	
≥1	4 (24%)

Tumor Types	Total (n=17)
Colorectal cancer (MSS)	12
Colorectal cancer (MSI-H)	1
Ampullary carcinoma	1
NSCLC	1
Esophageal cancer	1
Abdomen	1

Treatment Status	Total (n=17)
Continuing on Treatment	**7**
Discontinued Treatment	**10**
Progressive Disease	1
Adverse Events	2
Consent Withdrawal	4
Death	0
Investigator Decision	3

83% of patients had ≥3 prior lines of treatment

Data cutoff date: October 7, 2024
ECOG PS: ECOG performance status

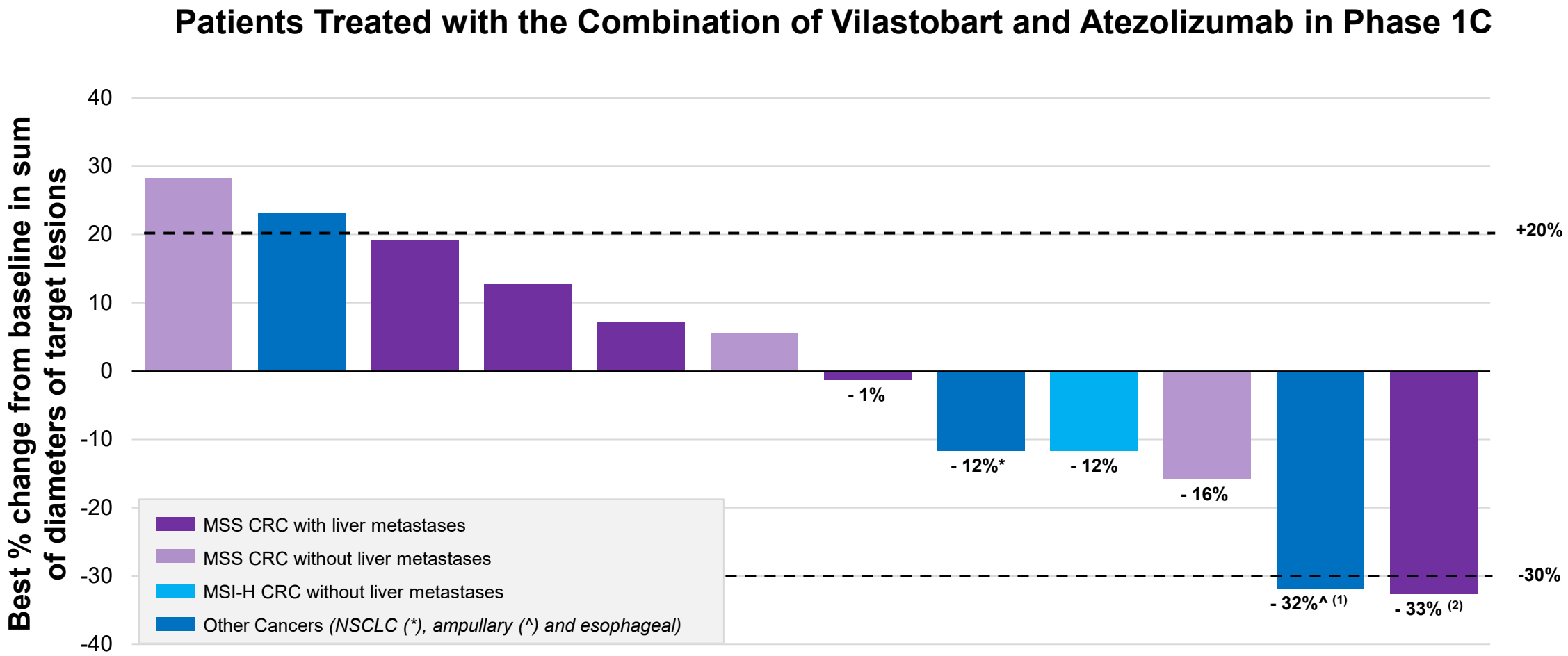
Combination of Vilastobart (anti-CTLA-4) and Atezolizumab Was Generally Well-Tolerated with Minimal irAEs

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

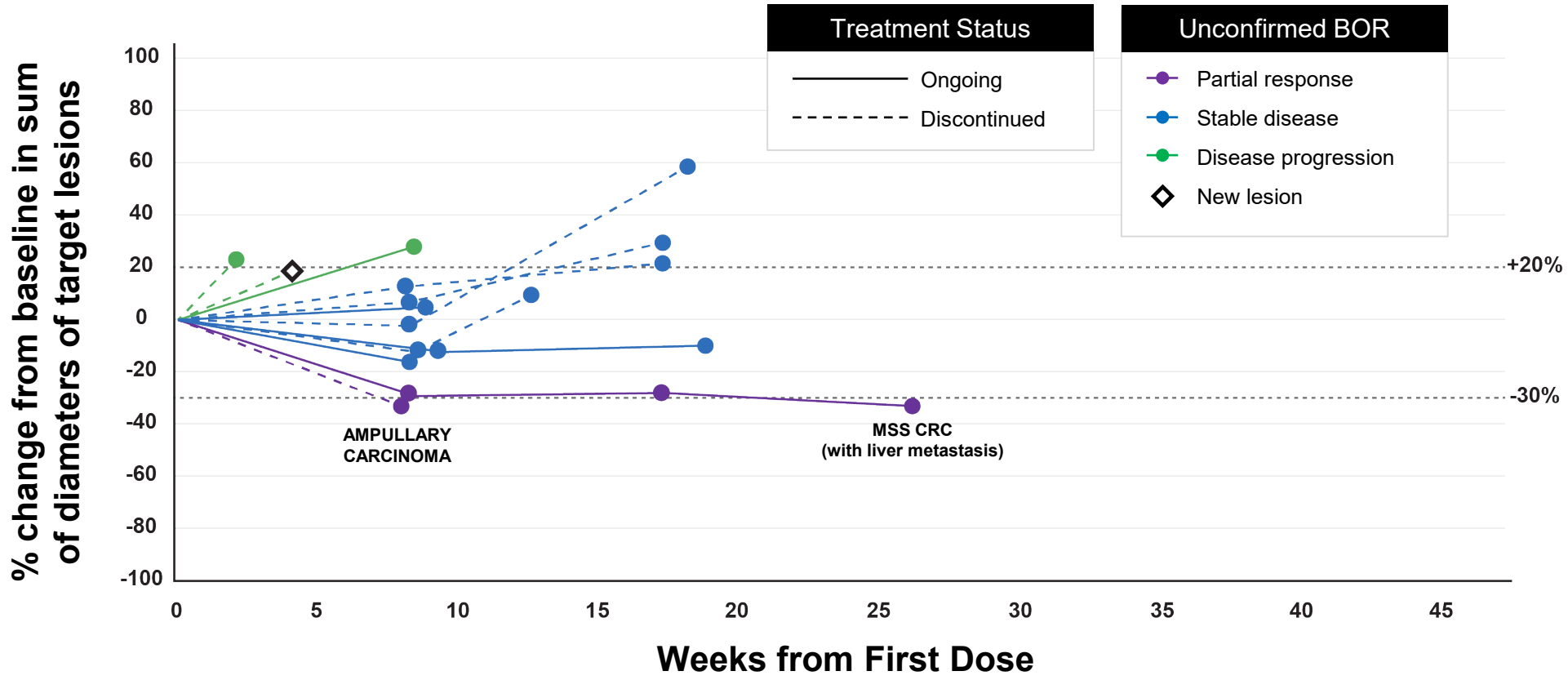
Combination of Vilastobart (anti-CTLA-4) and Atezolizumab Demonstrated Anti-Tumor Activity in Cold Tumors, Including a Sustained Tumor Reduction in a MSS CRC Patient with Metastatic Liver Disease



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

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

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

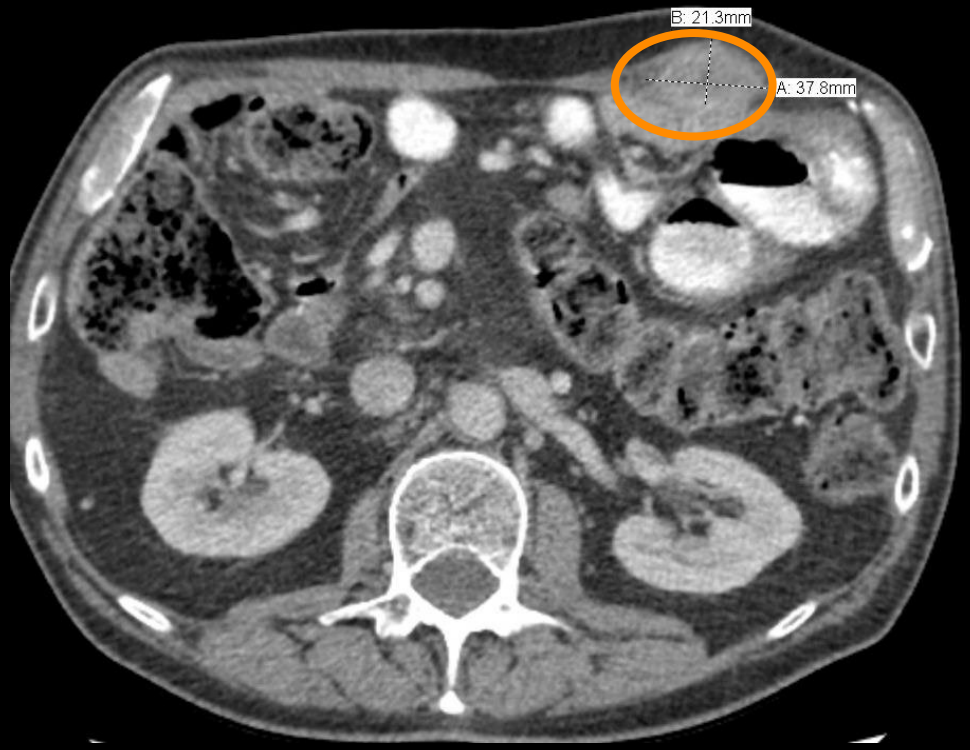
- 76 year-old male
- 2 prior lines of therapy:
  - Gemcitabine + nab-Paclitaxel
  - 5-fluorouracil + Irinotecan Liposome + Leucovorin
- Administered vilastobart (150 mg Q6W) + atezolizumab (1200 mg Q3W)
- Significant CA 19-9 decrease after a single cycle of the combination

	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**

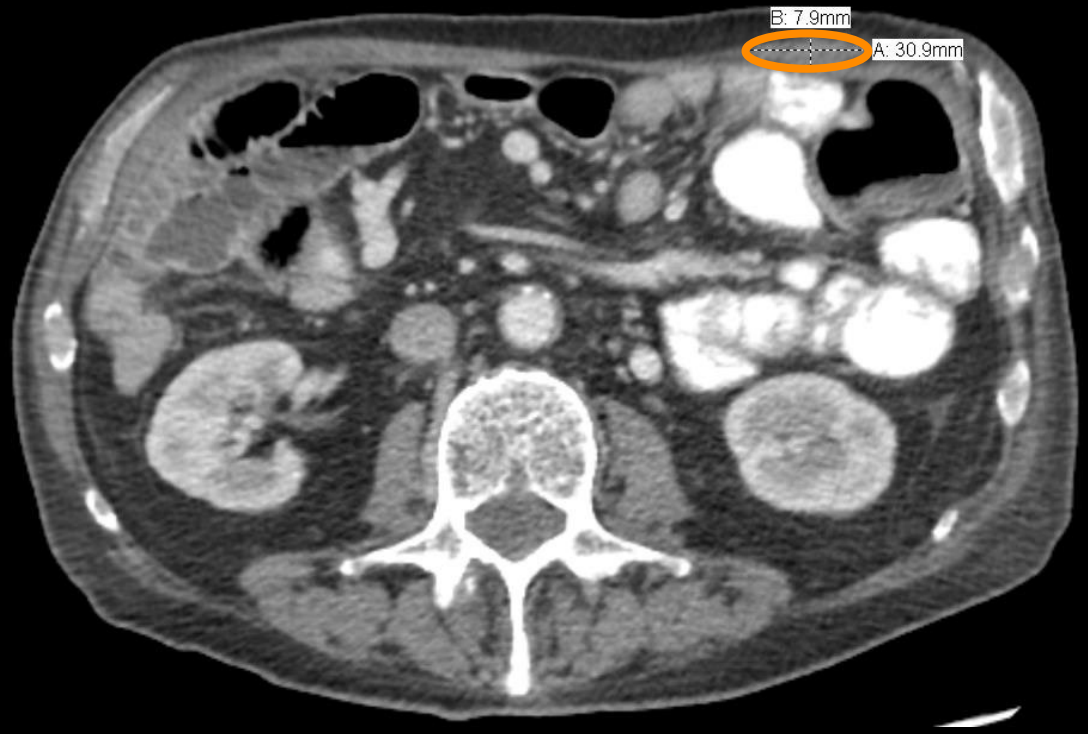
Data cutoff date: October 7, 2024
* Patient withdrew consent prior to confirmatory scan.
C1D1: cycle 1, day 1

PR (Unconfirmed)* in Ampullary Carcinoma After Single Cycle of Combination of Vilastobart (anti-CTLA-4) and Atezolizumab (*32% Reduction in Sum of Diameters*)

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).
* Patient withdrew consent prior to confirmatory scan.

PR (Unconfirmed)* in Patient With MSS CRC, Including Full Resolution of Target Lesion in Liver

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)

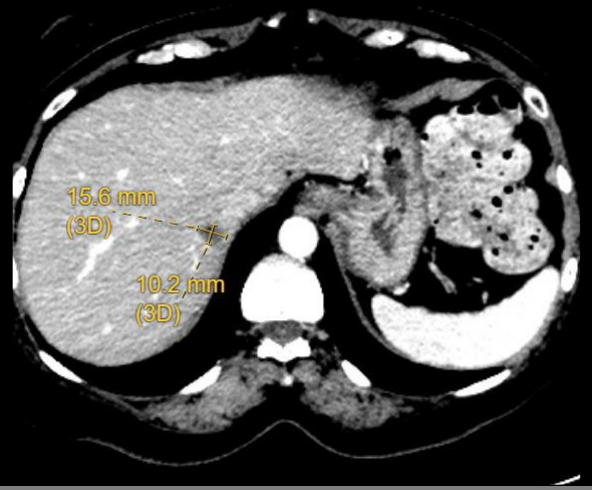
	Screening	1st follow-up (9 weeks)	2nd follow-up (18 weeks)	3rd follow-up (27 weeks)
Sum of diameters	98.4 mm	70.5 mm	71.0 mm	66.3 mm
Change		**- 28%**	**- 28%**	**- 33%**

Including full resolution of target lesion in the liver

Data cutoff date: October 7, 2024
* PR pending confirmation

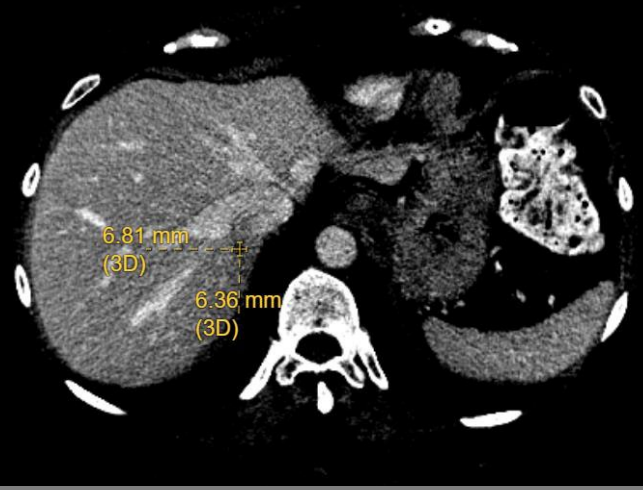
PR (Unconfirmed)* Including Resolution of Liver Metastatic Lesion in Patient With MSS CRC (33% Reduction in Sum of Diameters)

Target Liver Lesion – Baseline



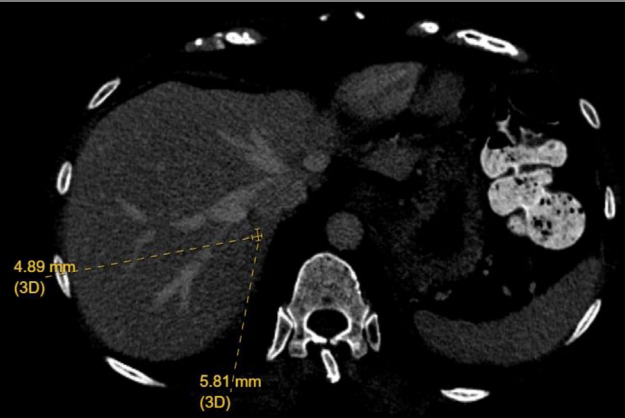
15.6 mm

Target Liver Lesion – After 9 weeks



6.8 mm

Target Liver Lesion – After 18 weeks



5.8 mm

Target Liver Lesion – After 27 weeks

No visible lesion

Data cutoff date: October 7, 2024. Patient administered vilastobart (150 mg Q6W) and atezolizumab (1200 mg Q3W)
* PR pending confirmation

Encouraging Initial Evidence of Combination Activity Observed in Phase 1C; Anticipate Initial Phase 2 Combination Proof-of-Concept Data in Q4 2024

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 PR (unconfirmed) in a patient with MSS CRC with complete resolution of liver metastasis

Anticipated Near-Term Phase 2 Data Milestones

- ❑ Initial data (n = ~20 total) in MSS CRC in Q4 2024
- ❑ Additional data (n = ~40 total) in MSS CRC in Q1 2025

Data cutoff date: October 7, 2024

Vilastobart (XTX101)

Phase 1 Monotherapy Clinical Data

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Phase 1 Monotherapy Trial for Vilastobart (anti-CTLA-4) Included Patients With a Wide Range of Advanced/Refractory Solid Tumors

Vilastobart Monotherapy Phase 1 Trial Design

Phase 1A
Monotherapy Dose-Escalation
Advanced Solid Tumors
(n=20)

Phase 1B
Monotherapy Expansion
(n=19)

Enrollment Completed

n=21 patients treated at the monotherapy RP2D (150 mg Q6W)

Patient Characteristics	Total (n=39)
Demographics	
Age, median (range)	62 (43, 80)
Female	19 (49%)
ECOG PS 0	12 (31%)
ECOG PS 1	27 (69%)
Prior Lines of Anti-Cancer Treatment	**Median 4 (1-12)**
1	4 (10%)
2	4 (10%)
3	9 (23%)
4	8 (21%)
5	5 (13%)
6 and more	9 (23%)
Progressed on Prior Treatment with I-O	
≥1	21 (54%)

Tumor Types	Total (n=39)
Colorectal cancer	12
NSCLC	5
Pancreatic cancer	3
Breast cancer	3
Melanoma	3
Merkel cell carcinoma	2
Squamous cell skin	2
Esophageal cancer	1
Cervical cancer	1
Prostate cancer	1
Gastric cancer	1
Fallopian tube cancer	1
Leiomyosarcoma	1
Renal cell carcinoma	1
Uterine cancer	1
Endometrial cancer	1

Treatment Status	Total (n=39)
Continuing on Treatment	**2**
Discontinued Treatment	**37**
Progressive Disease	16
Adverse Events	5
Consent Withdrawal (Hospice)	5
Death	3
Investigator Decision	3
Unacceptable Toxicity	2
Other	3

- 80% of patients had 3 or more prior lines of treatment
- 54% of patients progressed on prior I-O treatment

Data cutoff date: October 7, 2024

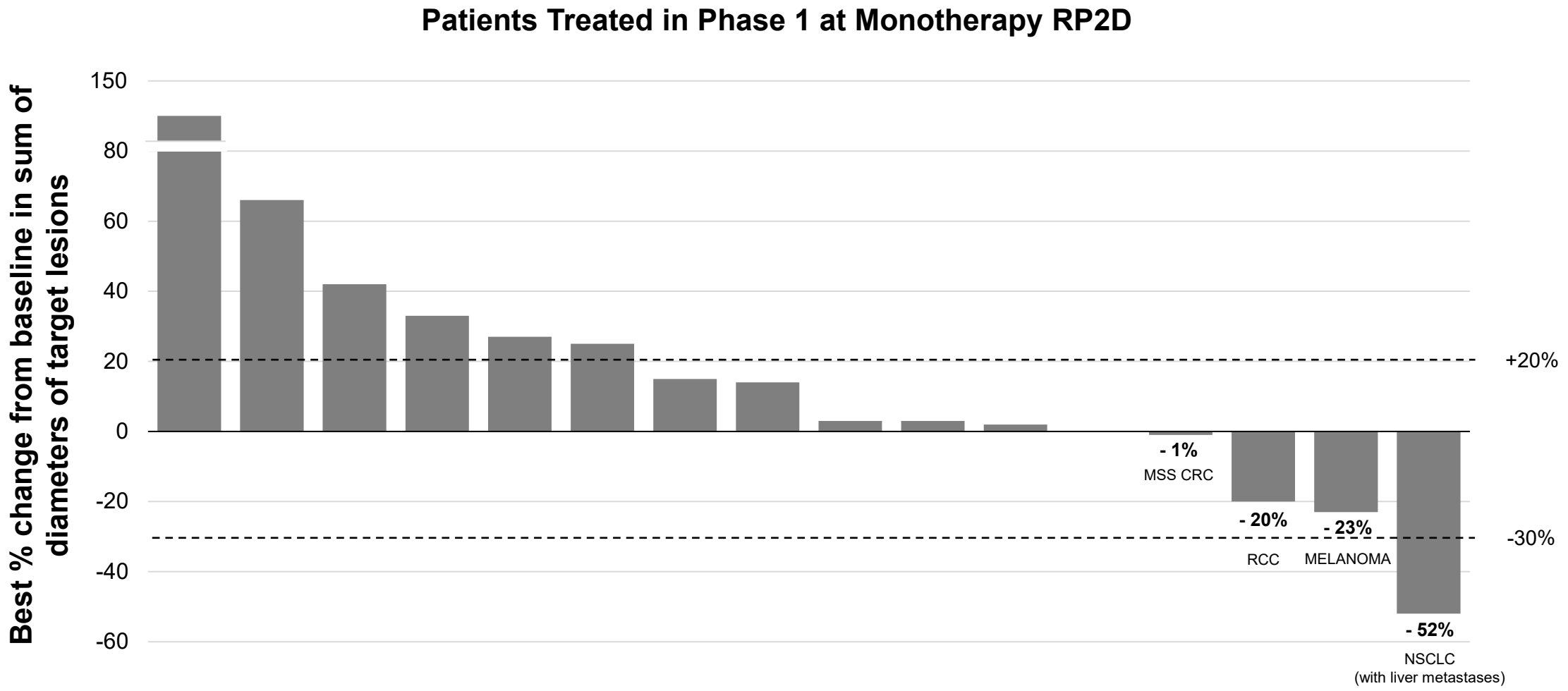
Vilastobart (anti-CTLA-4) 150 mg Q6W Was Generally Well-Tolerated with Minimal TRAEs

AE Category / Term ***All TRAEs with ≥10% incidence in any category or any Grade 3 TRAE***	**Vilastobart 150 mg Q6W (monotherapy RP2D, n=21)**	
	Any	**Grade 3**
Diarrhea	3 (14%)	2 (10%)
Colitis	3 (14%)	2 (10%)
Infusion related reaction	2 (10%)	1 (5%)
Fatigue	3 (14%)	0
Lymphopenia	1 (5%)	1 (5%)
Dermatitis	1 (5%)	1 (5%)
Blood creatine phosphokinase increased	1 (5%)	1 (5%)
Dose reduction due to TRAE	2	
Treatment discontinuation due to TRAE	2	

- ***No Grade 4 or 5 TRAEs were reported for vilastobart at the monotherapy RP2D of 150 mg Q6W***
- ***No endocrine irAEs and limited skin irAEs***
- ***Safety data included long-term administration of vilastobart > 1 year in 1 patient***

Data cutoff date: October 7, 2024

Vilastobart (anti-CTLA-4) 150 mg Q6W Demonstrated Anti-Tumor Activity With Confirmed PR in PD-L1 Negative NSCLC, Including Resolution of Liver Metastases



Data cutoff date: October 7, 2024. n=17 response-evaluable patients
RCC: renal cell carcinoma

Vilastobart (anti-CTLA-4) 150 mg Q6W Demonstrated Deep and Durable Confirmed PR in Patient with PD-L1 Negative NSCLC, Including Resolution of Innumerable Hepatic Metastases

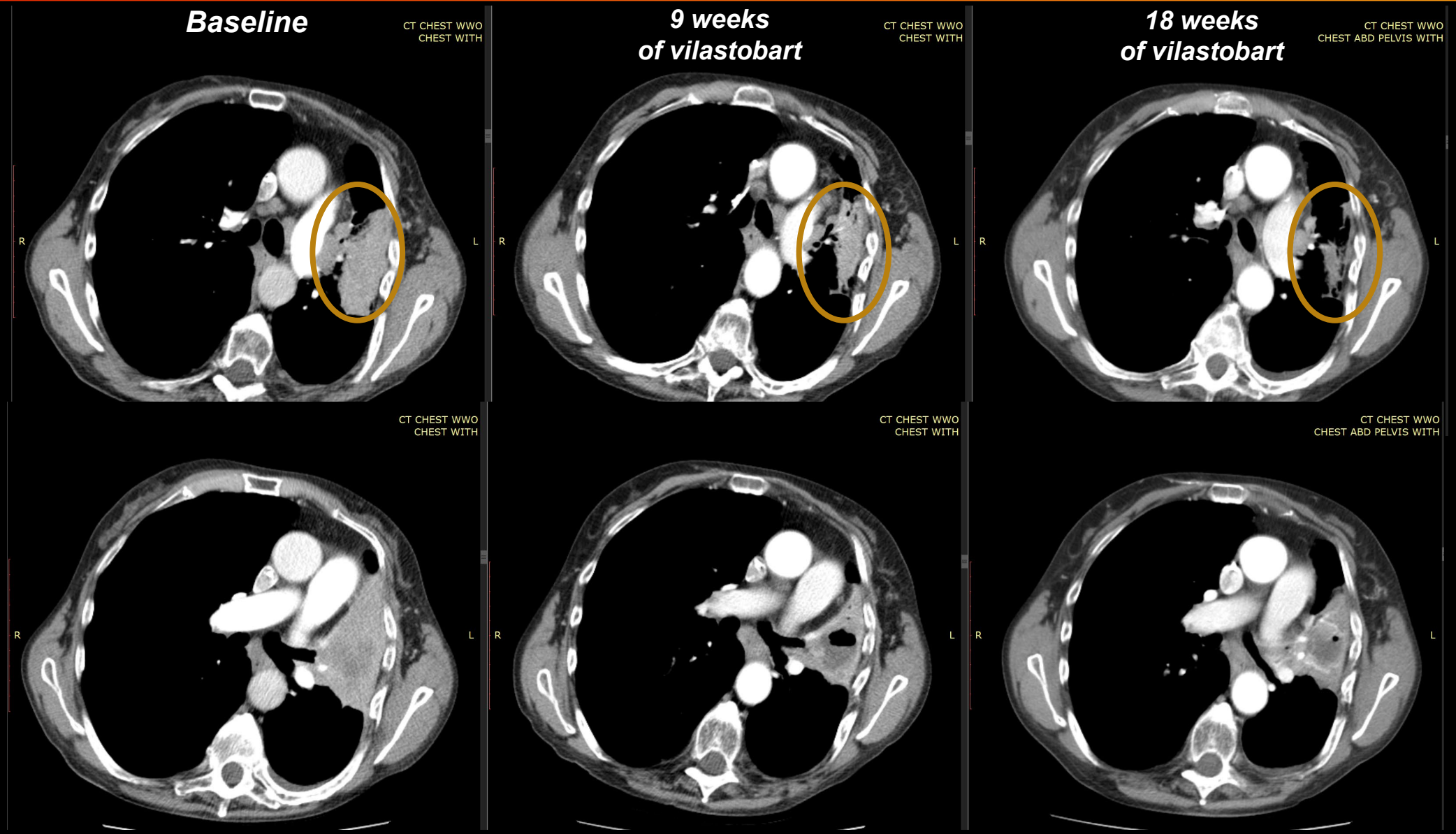
PD-L1 Negative Stage 4 NSCLC

- 66 year-old female
- Progressed after 1 prior line of treatment (paclitaxel and carboplatin)
- Administered vilastobart at 150 mg Q6W (monotherapy RP2D) for 7 doses (36 weeks)

	Screening	1st follow-up *(9 weeks)*	4th follow-up *(36 weeks)*
Sum of diameters	93.0	60.0	45.0
Change		**- 35%**	**- 52%**

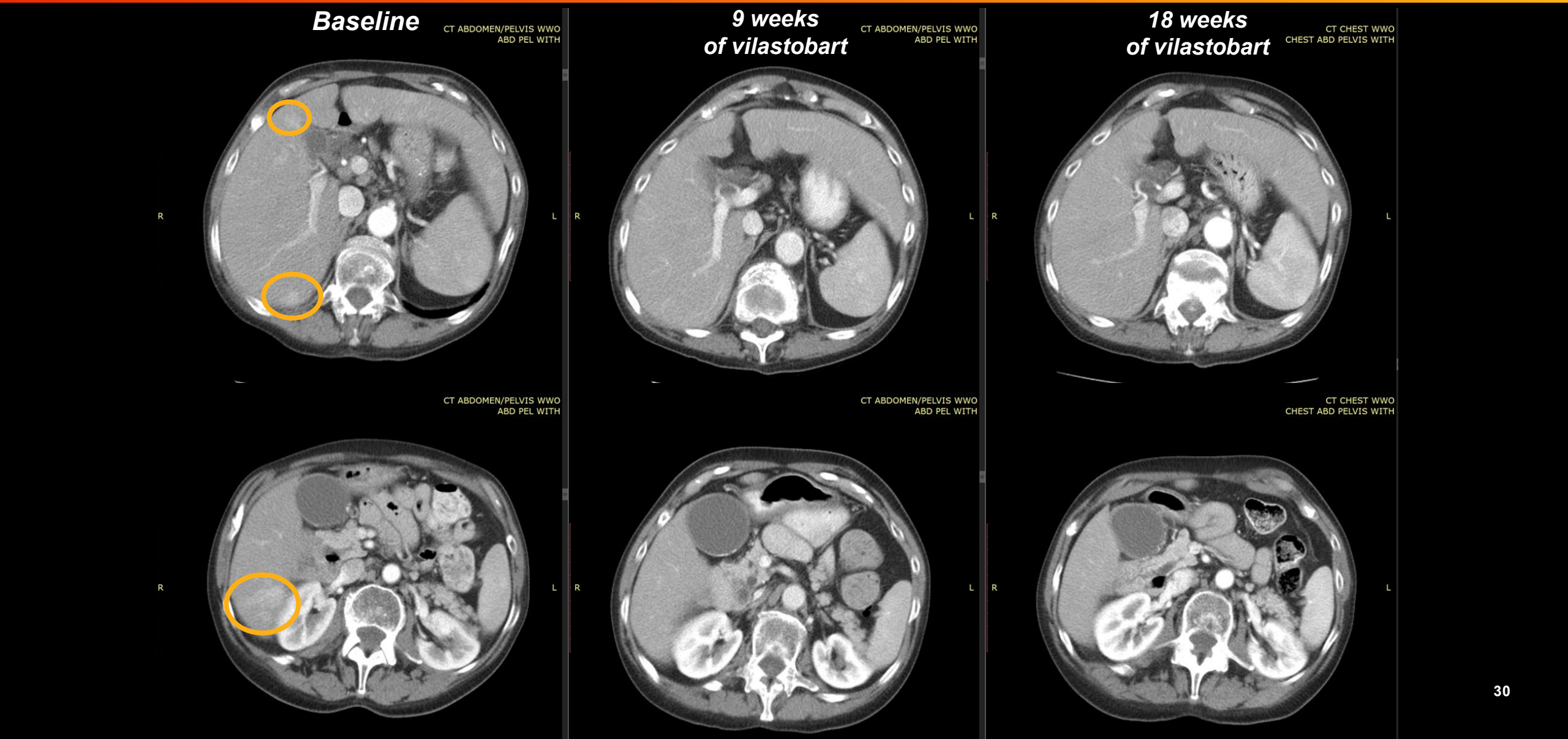
Data cutoff date: October 7, 2024

Vilastobart (anti-CTLA-4) 150 mg Q6W Demonstrated Deep and Durable Confirmed PR Through 36 Weeks in a Patient with PD-L1 Negative NSCLC



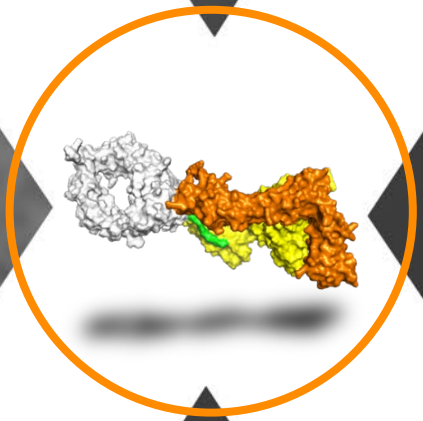
52% Reduction (Sum of Diameters) Through 36 Weeks

Vilastobart (anti-CTLA-4) 150 mg Q6W Demonstrated Durable Resolution of Hepatic Metastases Through 36 Weeks in a Patient with PD-L1 Negative NSCLC



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

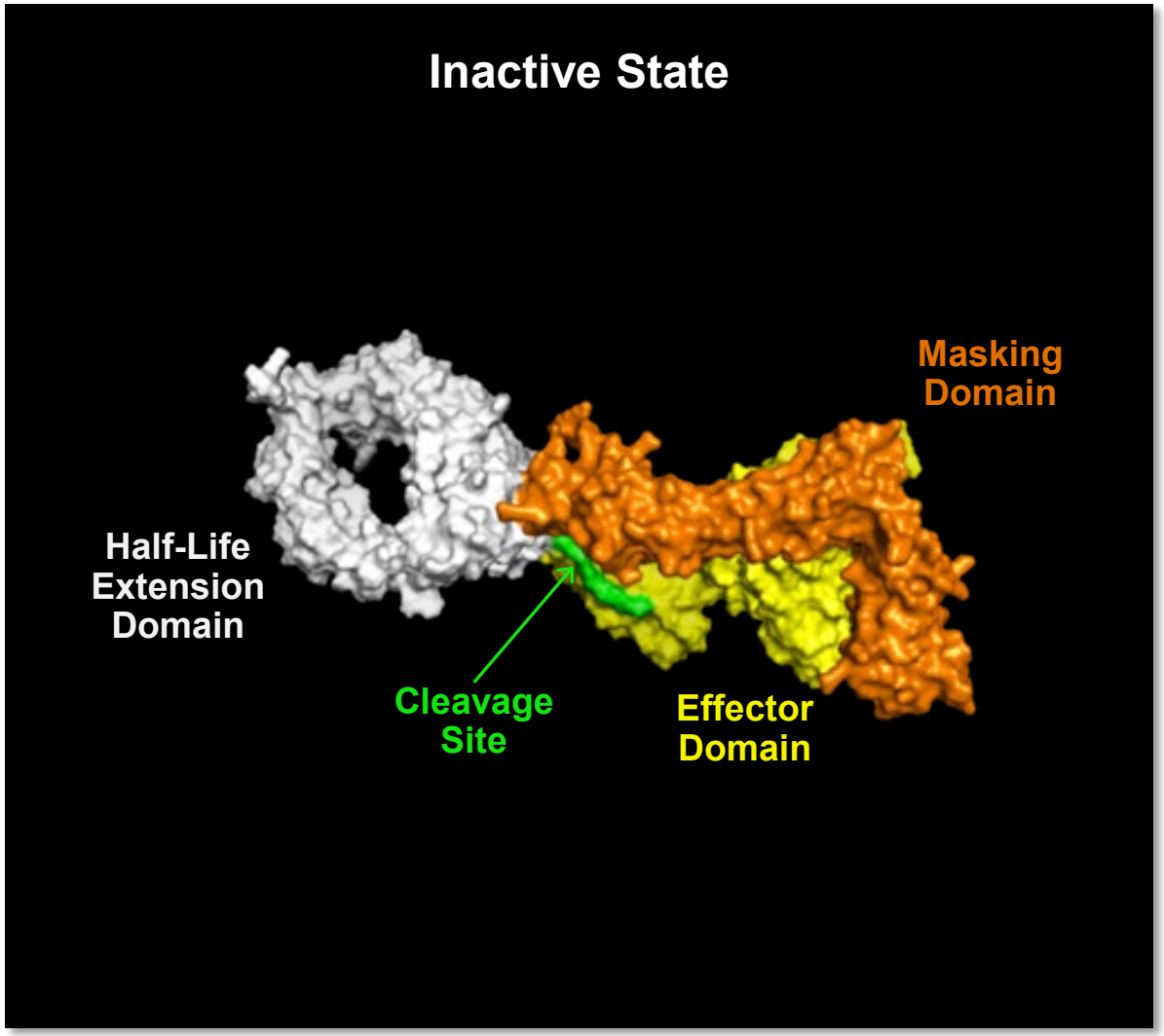
Capable of polarizing CD4 T-cells towards Th1 phenotype, thus driving cellular immunity against infection and cancer

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)
- Efficient activation by human tumors demonstrated *ex vivo*
- Robust anti-tumor activity and tumor-selective PD *in vivo* in preclinical model
- Potential for broad therapeutic index supported by robust preclinical data
- Generally well-tolerated with no DLTs observed in Phase 1 dose escalation to date

Entered Into Partnership with Gilead in March 2024, Designed to Explore Broad Potential of IL-12 Across Solid Tumors

$43.5M

total upfront payments

($30M cash payment +
$13.5M initial equity investment at a premium ($1.97/share)

Up to $604M

additional contingent payments:

- **Includes up to $29M prior to transition fee for up to $11.5M in additional equity investments (1) and 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 (2)

GILEAD
Creating Possible

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1. Subject to 19.9% ownership cap. In April 2024, Xilio received aggregate gross proceeds of approximately $3.3 million from an additional private placement with Gilead under the stock purchase agreement and is eligible to receive up to approximately $8.2 million in additional gross proceeds from up to two additional equity investments by Gilead.
2. If Gilead elects not to transition responsibilities for development and commercialization, the agreement will automatically terminate.

XTX301 Phase 1

Monotherapy Dose Escalation Initial Data

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XTX301 Monotherapy Phase 1 Ongoing: No DLTs Reported To Date at Doses Equivalent to >100x MTD for Systemically Active rhIL-12

XTX301 Phase 1 Trial Design

Phase 1A
Monotherapy Dose Escalation

- Advanced solid tumors
- 3+3 design with optional dose expansion (up to 10 patients per cohort)

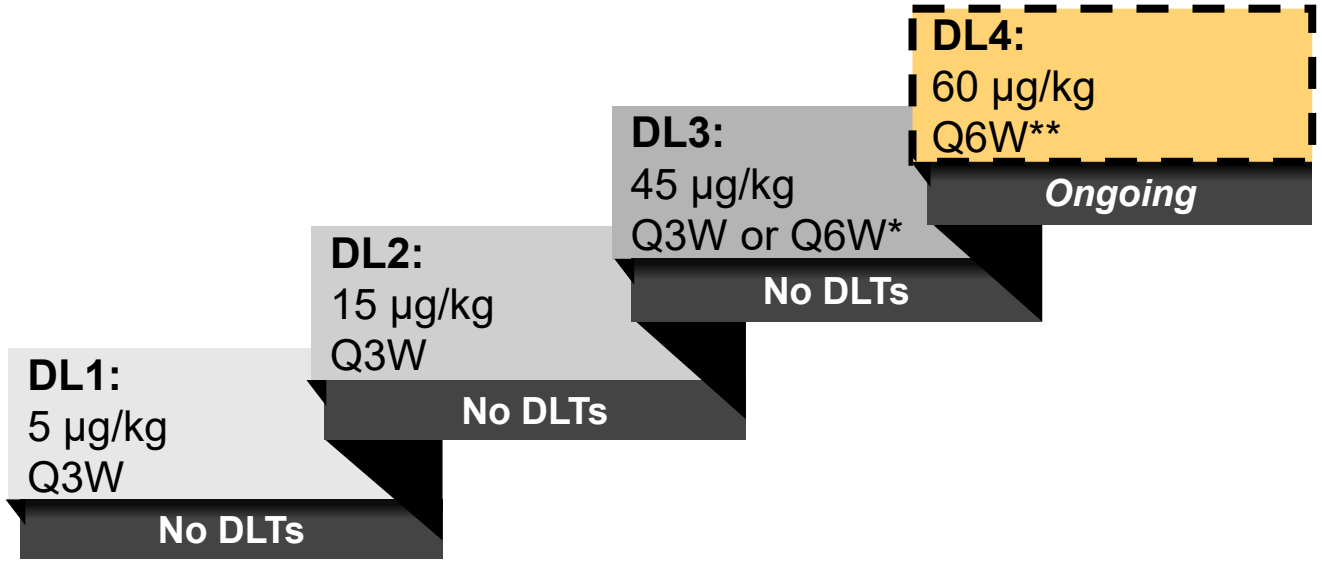
Enrollment Ongoing
*Current dose: 60 µg/kg Q6W ***

Phase 1B
Monotherapy PD Cohort

- n = up to 40
- Selected solid tumors

Enrollment Ongoing
*Current dose: 45 µg/kg Q6W ***

XTX301 Phase 1 Monotherapy Dose Escalation



- Generally well-tolerated with no DLTs reported to date
- XTX301 is administered in the outpatient setting

As of August 5, 2024
* Q6W dosing schedule evaluated at DL3 based on emerging PK data for XTX301 half-life in inactive state
** Preceded by a single priming dose of XTX301 at 15 µg/kg
DL1: dose level 1; DL2: dose level 2; DL3: dose level 3; DL4: dose level 4; MTD: maximum tolerated dose; rHIL: recombinant human Interleukin 12

XTX301 Phase 1 Monotherapy Data Anticipated in Q4 2024

- Demonstrated dose-dependent anti-tumor activity without significant body weight loss *in vivo*
- Preferentially activated in tumors vs. plasma in vivo and patient tumors vs. plasma *ex vivo*
- Generally well-tolerated with no DLTs observed to date
  - Enrollment ongoing in Phase 1 monotherapy dose escalation and dose expansion
  - Currently evaluating XTX301 at 60 µg/kg Q6W in dose escalation *
- Entered into partnership with Gilead in March 2024 designed to explore broad potential of IL-12 across solid tumors

Q4 2024

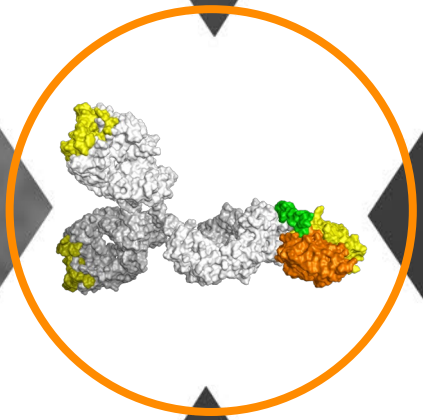
Next Anticipated Milestone

- Report Phase 1 safety and PK/PD data

As of August 5, 2024
* Preceded by a single priming dose of XTX301 at 15 µg/kg

XTX501

PD1/IL2 bispecific



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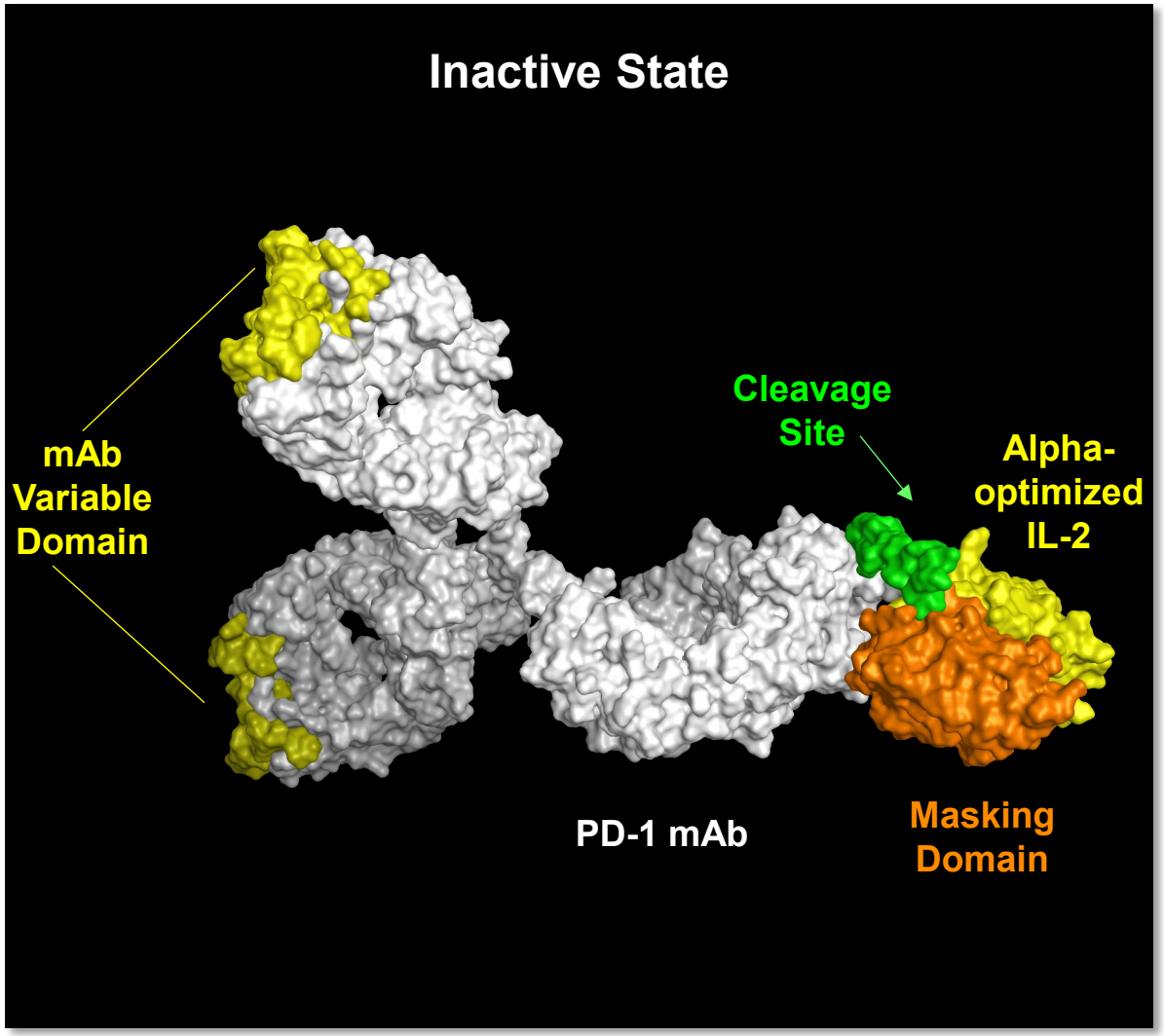
XTX501: Tumor-Activated PD1/IL2 Bispecific

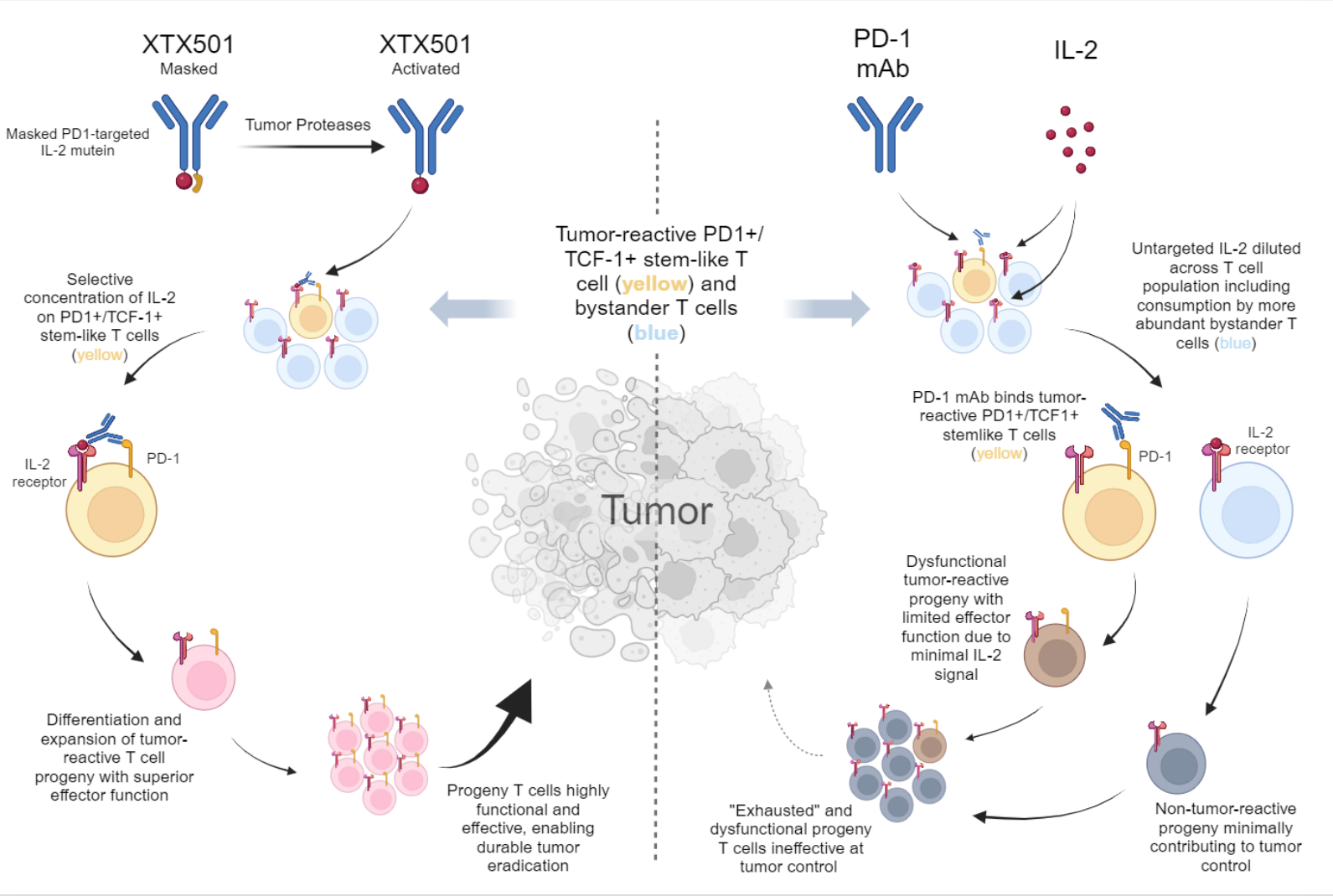


Demonstrated Synergistic Anti-Tumor Activity, Antibody-Like PK and Favorable Tolerability in NHP

- 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 Designed to Induce a Differentiated, Enhanced Immune Response to Cancer Compared to PD-(L)1 Monotherapy or PD-(L)1 + IL-2 Combination

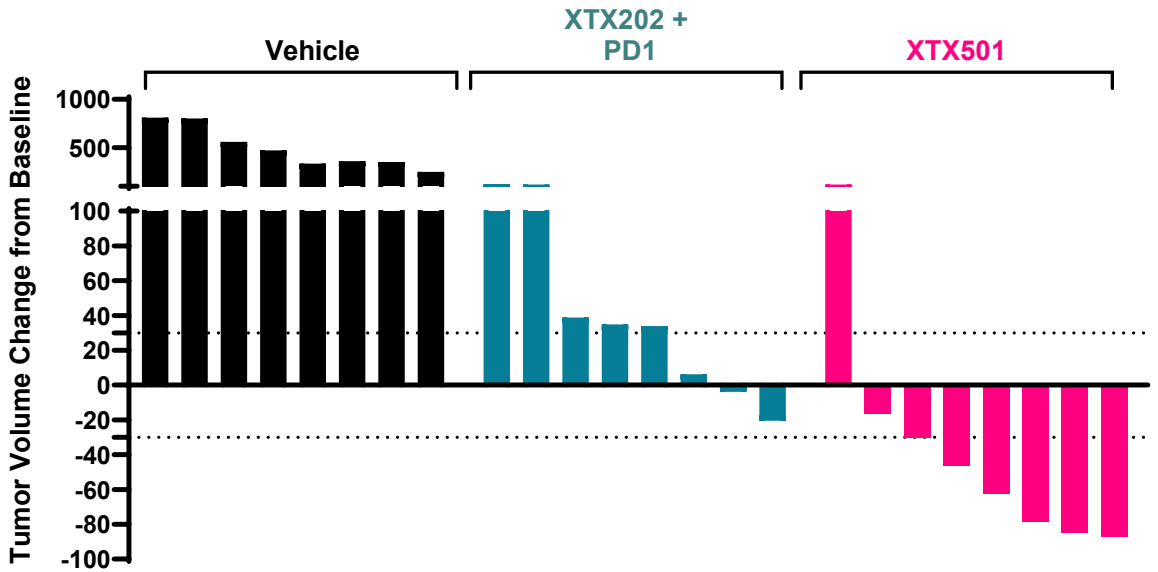


- Targeted delivery of IL-2 to PD1+ cells selectively enhances IL-2 signaling on tumor-reactive, stem-like T cells
- Drives unique differentiation program in progeny effector T cells endowing them with superior effector function and anti-tumor activity
- Not achievable with PD-(L)1 monotherapy or IL-2 combo since no concurrent selective targeting of tumor-reactive cells

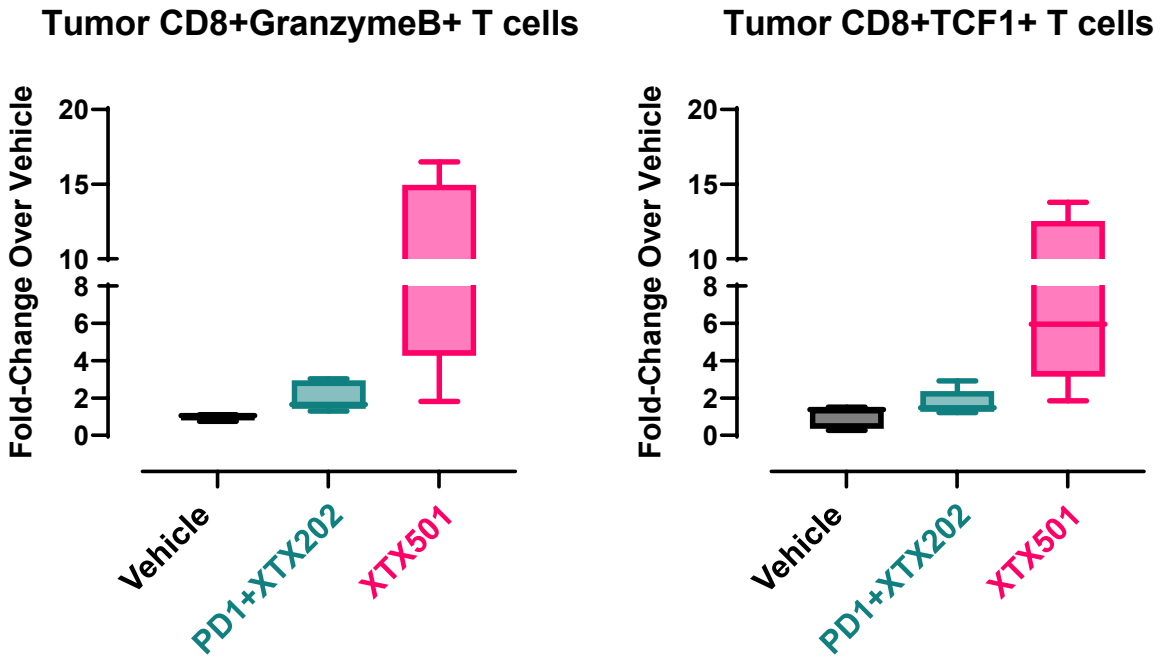
Figure adapted from Deak et al., OncoImmunology, 2023. Figure generated using BioRender.com.

XTX501 Demonstrated Differentiated Pharmacology vs PD1 or PD1+XTX202 Indicative of Enhanced Anti-Tumor Immunity

Robust Preclinical Monotherapy Activity Beyond XTX202 + PD1 Combination

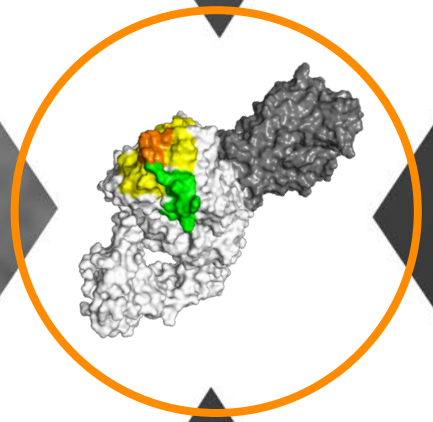


XTX501 Increased Intra-tumoral Cytotoxic and TCF1+ Stem-like T cells



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 analog of XTX501 with minimal variance in amino acid sequence.

Cell Engager Programs



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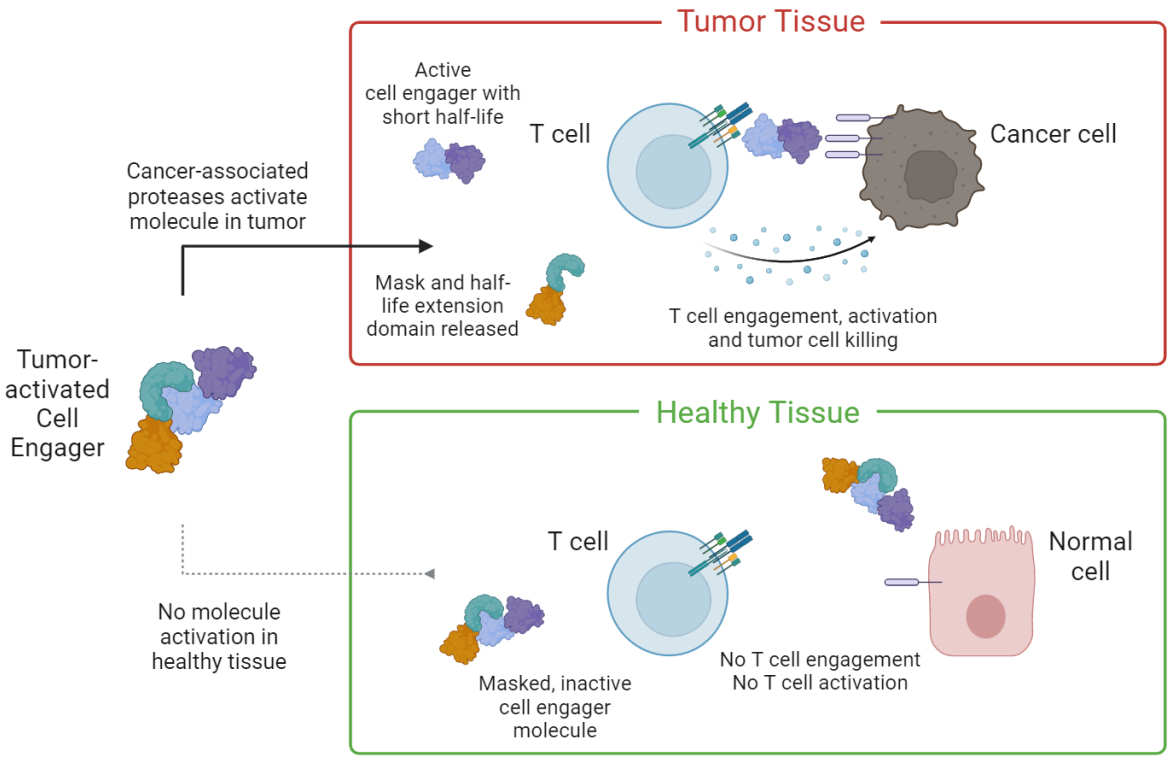
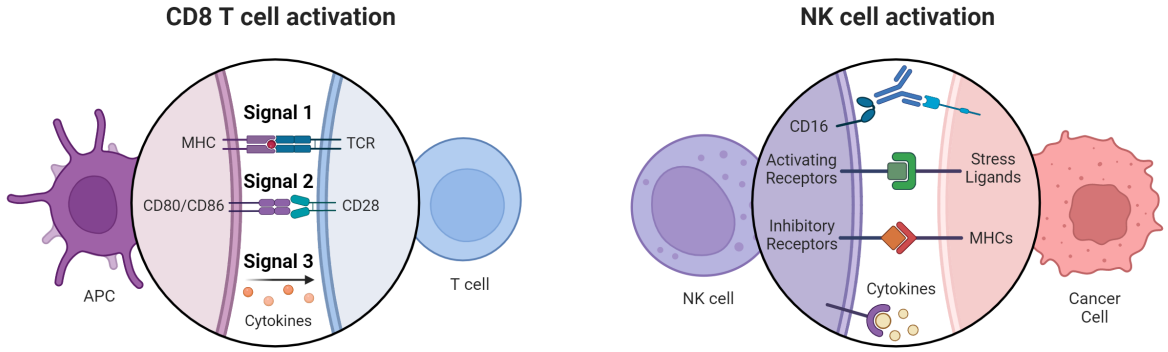
Xilio is Developing Tumor-Activated Cell Engagers Built on Our Validated Masking Approach and Conditional Half-Life Optimization

Advanced Tumor-Activated Cell EngageR ("ATACR" molecules)



Selective Effector-Enhanced Cell EngageR (SEECR molecules)



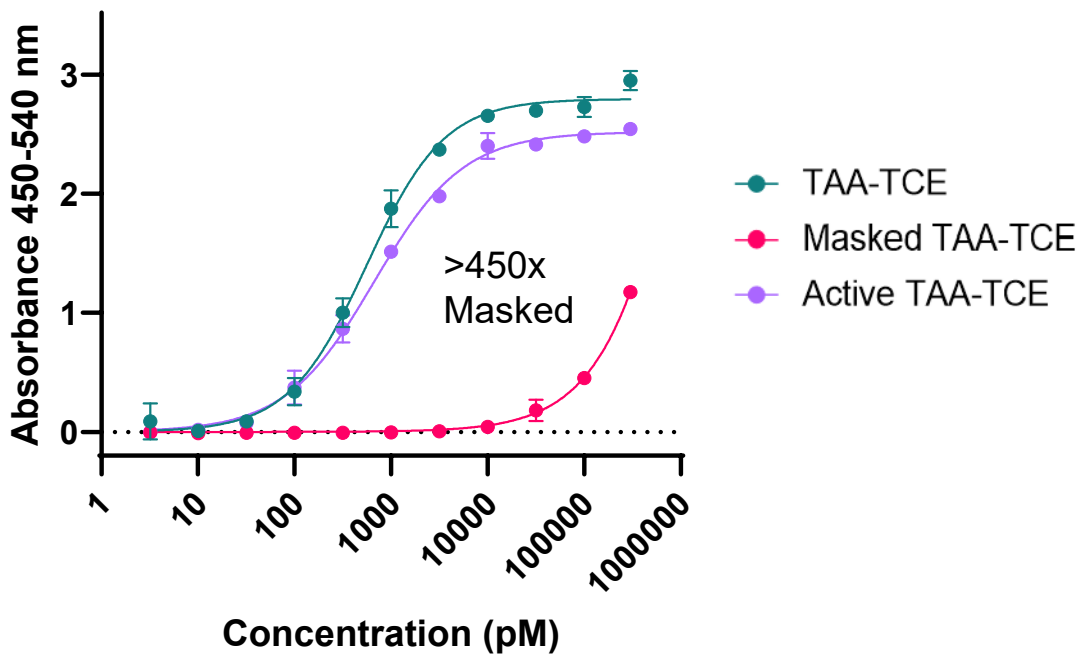
Design Goals

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

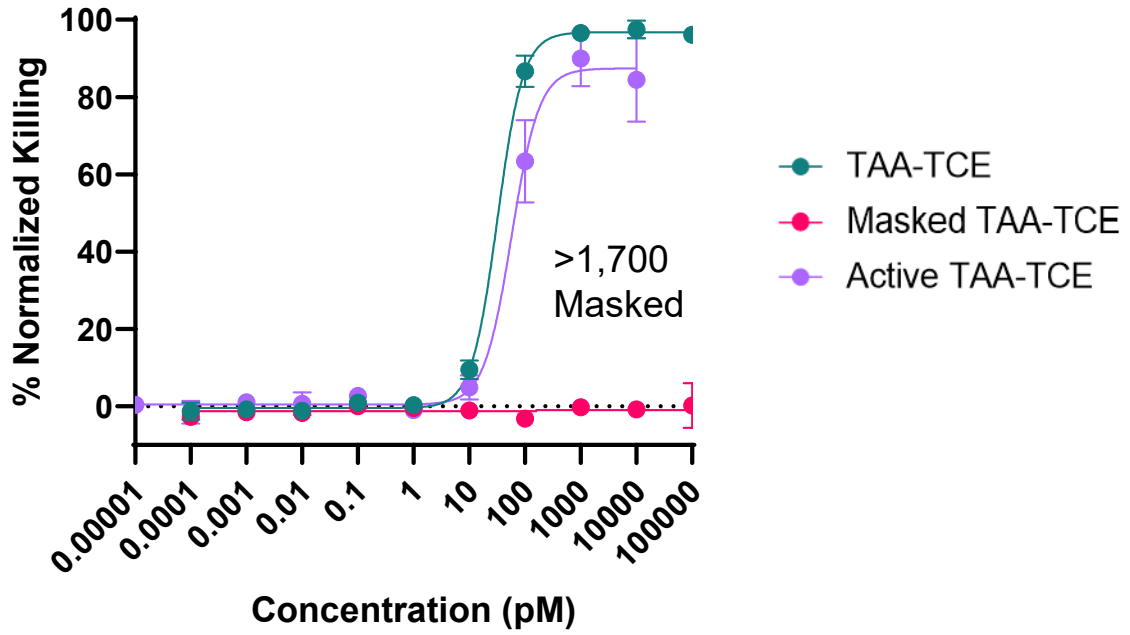
Illustrations generated using Biorender.com

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

Demonstrated Protease-Dependent Binding to CD3 by ELISA



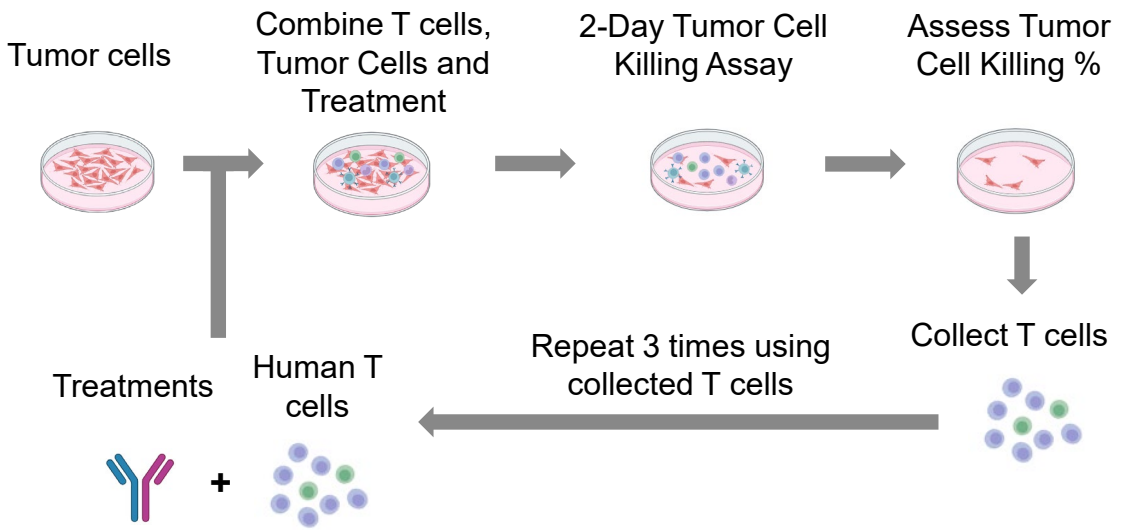
Confirmed Protease-Dependent Activity in Primary T Cell Assay



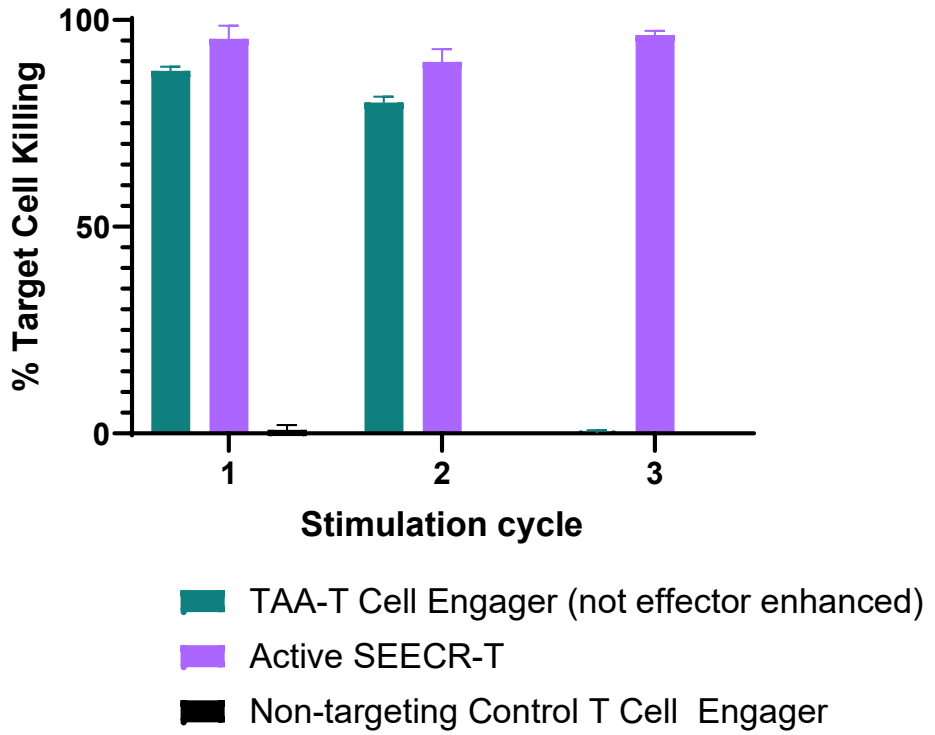
Left panel: Protease dependent CD3-binding demonstrated via TAA-TCEs bound to immobilized CD3 in an ELISA. **Right panel:** Protease-dependent tumor cell killing. Active TAA-TCEs led to killing in co-culture assay. A375 tumor cells were cultured overnight before addition of expanded T cells at a 5:1 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

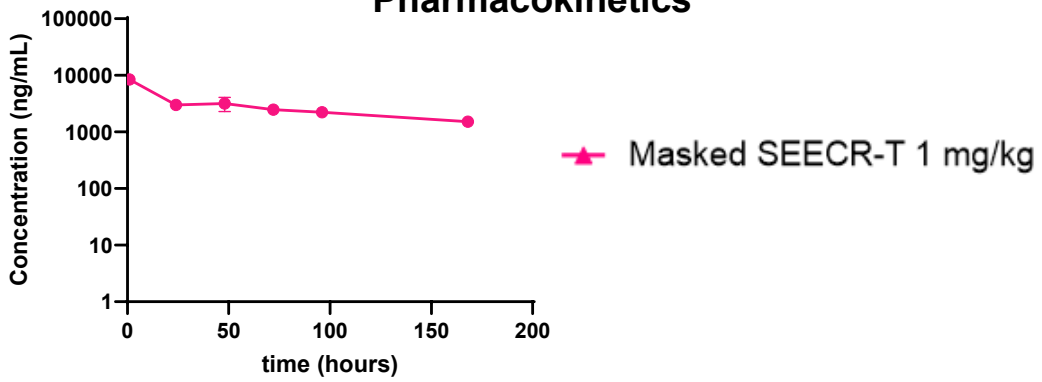


Human T cells were incubated over three consecutive rounds with indicated test articles and A431 cancer cells and percent tumor cell killing was assessed using a luminescence readout.

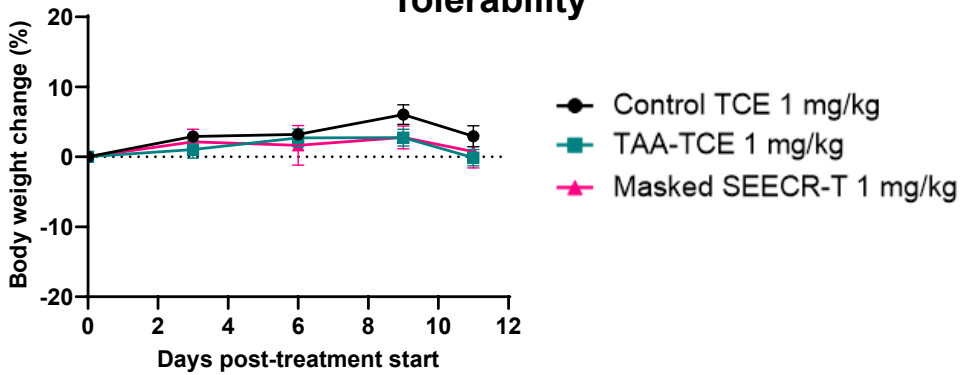
SEECR Molecule Demonstrated Potent Anti-Tumor Activity, Antibody-Like PK and was Well-Tolerated in Murine Models

SEECR Featured Antibody-Like PK and Tolerability Comparable to Control

Pharmacokinetics

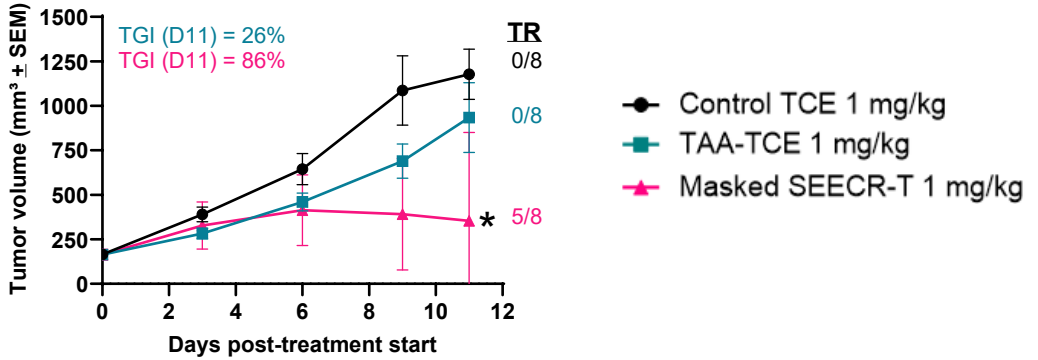


Tolerability

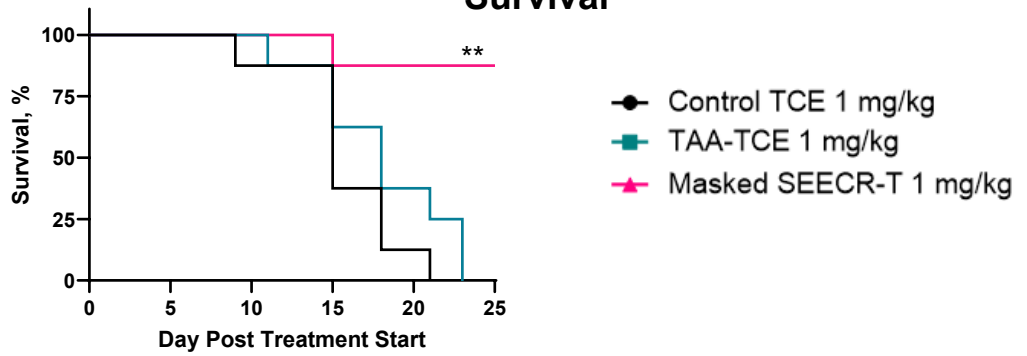


SEECR Showed Significantly Enhanced Activity and Survival Compared to Standard TCE

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

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Deep Expertise to Build a Transformational Immuno-Oncology Company

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

CHRIS FRANKENFIELD
Chief Financial and Operating Officer

ULI BIALUCHA, PH.D.
Chief Scientific Officer

KATARINA LUPTAKOVA, M.D.
Chief Medical Officer

SCOTT COLEMAN, PH.D.
Chief Development Officer

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

Q3 2024 Financial Results
Anticipate Cash Runway Through End of Q2 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

Xilio is working to deliver highly potent, localized immunotherapies in cancer and beyond

Xilio Therapeutics is a Differentiated I-O Company with a Proprietary Tumor-Activated Platform and the Team to Deliver

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