UNITED STATES
SECURITIES AND EXCHANGE COMMISSION

WASHINGTON, D.C. 20549

FORM 8-K

CURRENT REPORT
Pursuant to Section 13 or 15(d)
of the Securities Exchange Act of 1934

Date of report (Date of earliest event reported): **January 21, 2025**

Xilio Therapeutics, Inc.

(Exact Name of Registrant as Specified in Charter)

Delaware	**001-40925**	**85-1623397**
(State or Other Jurisdiction of Incorporation)	(Commission File Number)	(IRS Employer Identification No.)

828 Winter Street, Suite 300 **Waltham, Massachusetts** (Address of Principal Executive Offices)	**02451** (Zip Code)

Registrant's telephone number, including area code: **(857) 524-2466**

Not applicable
(Former Name or Former Address, if Changed Since Last Report)

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions (*see* General Instruction A.2. below):

☐ Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)

☐ Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)

☐ Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))

☐ Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

Securities registered pursuant to Section 12(b) of the Act:

Title of each class	Trading symbol(s)	Name of each exchange on which registered
Common stock, par value $0.0001 per share	**XLO**	**Nasdaq Global Select Market**

Indicate by check mark whether the registrant is an emerging growth company as defined in Rule 405 of the Securities Act of 1933 (§230.405 of this chapter) or Rule 12b-2 of the Securities Exchange Act of 1934 (§240.12b-2 of this chapter).

Emerging growth company ☒

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. ☐

Item 7.01 Regulation FD Disclosure.

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

The information in Item 7.01 of this Current Report on Form 8-K, including Exhibit 99.1, is being furnished and shall not be deemed "filed" for purposes of Section 18 of the Securities Exchange Act of 1934, as amended (the "Exchange Act"), or otherwise subject to the liabilities of that section, nor shall it be deemed incorporated by reference in any filing under the Exchange Act or the Securities Act of 1933, as amended, except as expressly set forth by specific reference in such filing.

Item 8.01. Other Events.

On January 21, 2025, the Company issued a press release announcing initial data from its ongoing Phase 2 clinical trial evaluating vilastobart (XTX101) in combination with atezolizumab in patients with advanced solid tumors. These data will be presented in a poster presentation at the American Society of Clinical Oncology (ASCO) 2025 Gastrointestinal Cancer Symposium. The full text of the press release is filed as Exhibit 99.2 to this Current Report on Form 8-K and is incorporated herein by reference. The information contained on, or accessible through, the websites referenced in the press release is not incorporated by reference into this Current Report on Form 8-K and should not be considered to be a part hereof.

Cautionary Note Regarding Forward-Looking Statements

This Current Report on Form 8-K contains forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995, as amended, including, without limitation, statements regarding plans, expectations and anticipated milestones for vilastobart (XTX101), including plans and timing for reporting Phase 2 clinical data for vilastobart in combination with atezolizumab in patients with microsatellite stable colorectal cancer; the potential benefits of vilastobart (as a monotherapy or combination therapy with a PD-(L)1 or other agent) or any of the Company's other current or future product candidates in treating patients as a monotherapy or combination therapy in any indication; the ultimate safety profile of vilastobart; and the Company's strategy, goals and anticipated financial performance, milestones, business plans and focus. The words "aim," "may," "will," "could," "would," "should," "expect," "plan," "anticipate," "intend," "believe," "estimate," "predict," "project," "potential," "continue," "seek," "target" and similar expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words. Any forward-looking statements in this Current Report on Form 8-K are based on management's current expectations and beliefs and are subject to a number of important risks, uncertainties and other factors that may cause actual events or results to differ materially from those expressed or implied by any forward-looking statements contained in this Current Report on Form 8-K, including, without limitation, general market conditions; risks and uncertainties related to: ongoing and planned research and development activities, including initiating, conducting or completing preclinical studies and clinical trials and the timing and results of such preclinical studies or clinical trials; the delay of any current or planned preclinical studies or clinical trials or the development of the Company's current or future product candidates; the Company's ability to obtain and maintain sufficient preclinical and clinical supply of current or future product candidates; the Company's advancement of multiple early-stage immune cell engager programs, including tumor-activated immune cell engagers and tumor-activated effector-enhanced immune cell engagers; initial, preliminary or interim preclinical or clinical data or results (including without limitation, the Phase 2 data for vilastobart and the preliminary investigator-reported preliminary response awaiting radiology confirmation), which may not be replicated in or predictive of future preclinical or clinical data or results; the Company's ability to successfully demonstrate the safety and efficacy of its product candidates and gain approval of its product candidates on a timely basis, if at all; results from preclinical studies or clinical trials for the Company's product candidates, which may not support further development of such product candidates; actions of regulatory agencies, which may affect the initiation, timing and progress of current or future clinical trials; the Company's ability to obtain, maintain and enforce patent and other intellectual property protection for current or future product candidates; the Company's ability to obtain and maintain sufficient cash resources to fund its operations; the impact of international trade policies on the Company's

business, including U.S. and China trade policies; the Company's ability to maintain its clinical trial collaboration with Roche to develop vilastobart in combination with atezolizumab; and the Company's ability to maintain its license agreement with Gilead to develop and commercialize XTX301. These and other risks and uncertainties are described in greater detail in the sections entitled "Risk Factor Summary" and "Risk Factors" in the Company's filings with the U.S. Securities and Exchange Commission ("SEC"), including the Company's most recent Quarterly Report on Form 10-Q and any other filings that the Company has made or may make with the SEC in the future. Any forward-looking statements contained in this Current Report on Form 8-K represent the Company's views only as of the date hereof and should not be relied upon as representing its views as of any subsequent date. Except as required by law, the Company explicitly disclaims any obligation to update any forward-looking statements.

Item 9.01 Financial Statements and Exhibits.

(d) Exhibits.

Exhibit No.	Description
99.1	Corporate slide presentation of Xilio Therapeutics, Inc., dated January 21, 2025
99.2	Press release issued by Xilio Therapeutics, Inc. on January 21, 2025
104	Cover Page Interactive Data File (embedded within the Inline XBRL document and incorporated as Exhibit 101)

SIGNATURES

Pursuant to the requirements of the Securities Exchange Act of 1934, as amended, the registrant has duly caused this report to be signed on its behalf by the undersigned hereunto duly authorized.

XILIO THERAPEUTICS, INC.

Date: January 21, 2025

By: /s/ Christopher Frankenfield
Christopher Frankenfield
Chief Financial Officer and Chief Operating Officer

Exhibit 99.1

Unleashing the Potential of Immuno-Oncology Therapies

January 21, 2025

xilio THERAPEUTICS

Forward-Looking Statements and Disclaimers

This presentation contains forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995, as amended, including, without limitation, statements regarding plans, timing and expectations related to: plans and anticipated milestones for vilastobart (XTX101), XTX301 and Xilio's development candidates, including plans and timing for reporting and results of the Phase 2 clinical data for vilastobart in combination with atezolizumab in patients with microsatellite stable (MSS) colorectal cancer or any of our other clinical programs; the potential to partner vilastobart; the ultimate safety data for any of Xilio's product candidates; the potential benefits of any of Xilio's current or future product candidates in treating patients as a monotherapy or combination therapy; the period in which Xilio expects to have cash to fund its operations; the potential for Xilio to leverage its research platform to develop bispecific and cell engager molecules; and Xilio's strategy, goals and anticipated financial performance, milestones, business plans and focus.

The words "aim," "may," "will," "could," "would," "should," "expect," "plan," "anticipate," "intend," "believe," "estimate," "predict," "project," "potential," "continue," "seek," "target" and similar expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words. Any forward-looking statements in this presentation are based on management's current expectations and beliefs and are subject to a number of important risks, uncertainties and other factors that may cause actual events or results to differ materially from those expressed or implied by any forward-looking statements contained in this presentation, including, without limitation, general market conditions, risks and uncertainties related to ongoing and planned research and development activities, including initiating, conducting or completing preclinical studies and clinical trials and the timing and results of such preclinical studies or clinical trials; the delay of any current or planned preclinical studies or clinical trials or the development of Xilio's current or future product candidates; Xilio's ability to obtain and maintain sufficient preclinical and clinical supply of current or future product candidates; Xilio's advancement of multiple early-stage immune cell engager programs, including tumor-activated immune cell engagers and tumor-activated effector-enhanced immune cell engagers; initial, preliminary or interim preclinical or clinical data or results (including, without limitation, the Phase 2 data for vilastobart and the preliminary investigator-reported response awaiting radiology confirmation), which may not be replicated in or predictive of future preclinical or clinical data or results; Xilio's ability to successfully demonstrate the safety and efficacy of its product candidates and gain approval of its product candidates on a timely basis, if at all; results from preclinical studies or clinical trials for Xilio's product candidates, which may not support further development of such product candidates; actions of regulatory agencies, which may affect the initiation, timing and progress of Xilio's current or future clinical trials; Xilio's ability to obtain, maintain and enforce patent and other intellectual property protection for current or future product candidates; Xilio's ability to obtain and maintain sufficient cash resources to fund its operations; the impact of international trade policies on Xilio's business, including U.S. and China trade policies; Xilio's ability to maintain its clinical trial collaboration with Roche to develop vilastobart in combination with atezolizumab and its license agreement with Gilead to develop and commercialize XTX301.

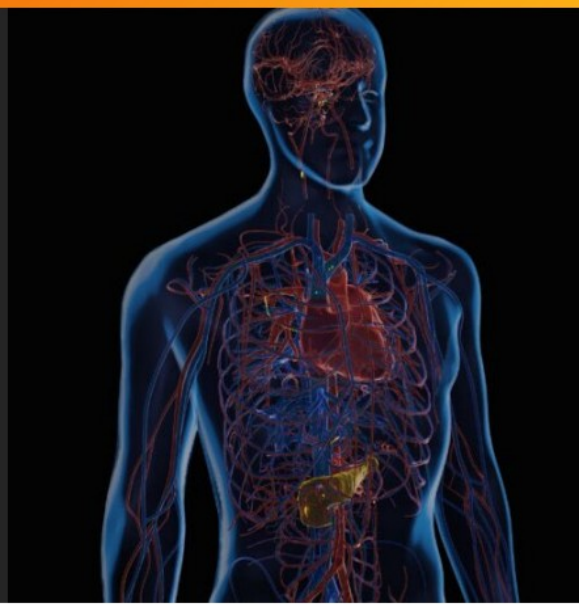
These and other risks and uncertainties are described in greater detail in the sections entitled "Risk Factor Summary" and "Risk Factors" in Xilio's filings with the U.S. Securities and Exchange Commission (SEC), including Xilio's most recent Quarterly Report on Form 10-Q and any other filings that Xilio has made or may make with the SEC in the future. Any forward-looking statements contained in this presentation represent Xilio's views only as of the date hereof and should not be relied upon as representing its views as of any subsequent date. Except as required by law, Xilio explicitly disclaims any obligation to update any forward-looking statements.

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

This presentation contains trademarks, trade names and service marks of other companies, which are the property of their respective owners. TECENTRIQ is a registered trademark of Genentech USA Inc., a member of the Roche Group.

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

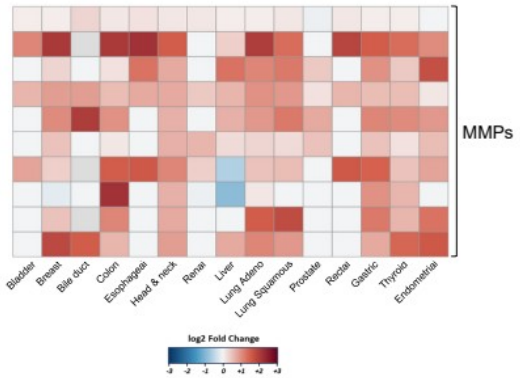
Xilio believes the next revolution in I-O therapy will **harness the power of the body's immune system** by **leveraging the dysregulated biology of the tumor against itself**



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

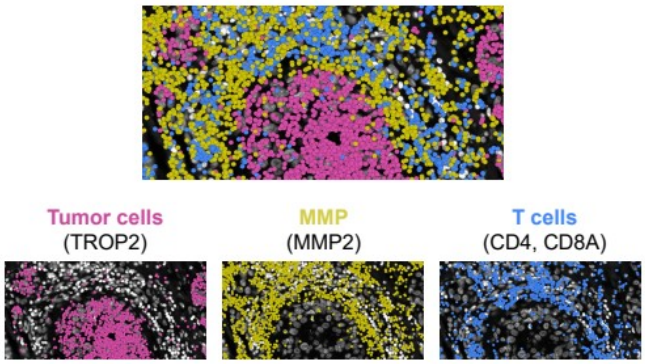
MMPs are dysregulated broadly across solid tumors

MMP mRNA expression in tumor vs. normal tissue



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

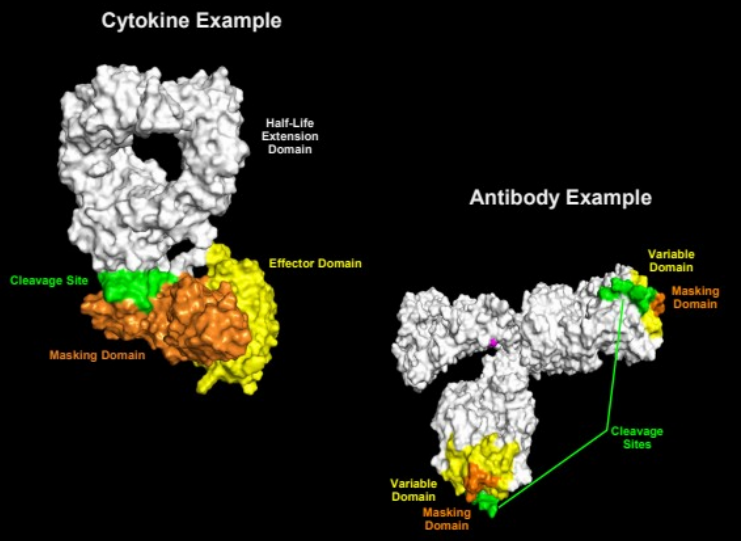
In situ mRNA expression in human breast cancer



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

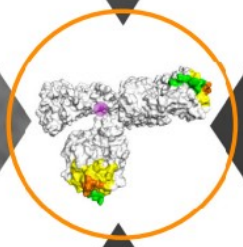
Program	Tumor Types	Mechanism of Action	Discovery	IND-Enabling	Phase 1	Phase 2	Phase 3	Partnerships
Vilastobart (XTX101) [1]	Metastatic MSS CRC	anti-CTLA-4 + PD-L1						**Co-funded clinical collaboration with Roche**
XTX301 [2]	Advanced Solid Tumors	IL-12						**Exclusive global option with Gilead**
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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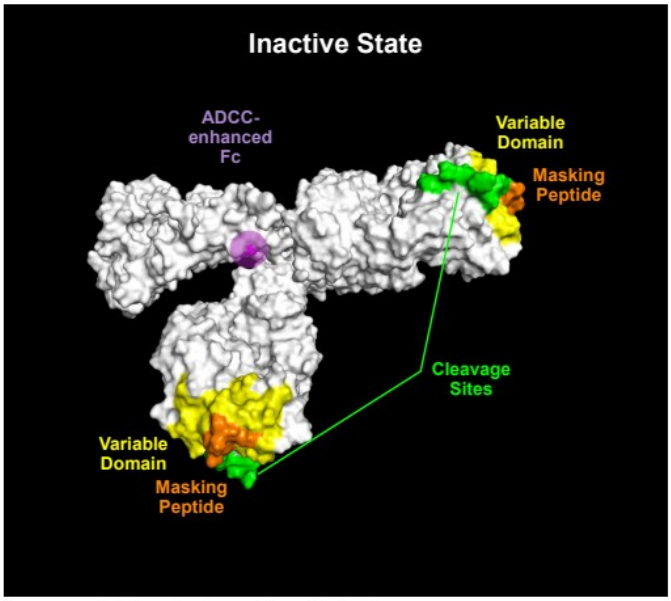
Vilastobart: Tumor-Activated, High Affinity Binding, Fc-Enhanced Anti-CTLA-4 in Phase 2 Development



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

Highlights from Previously Reported Data

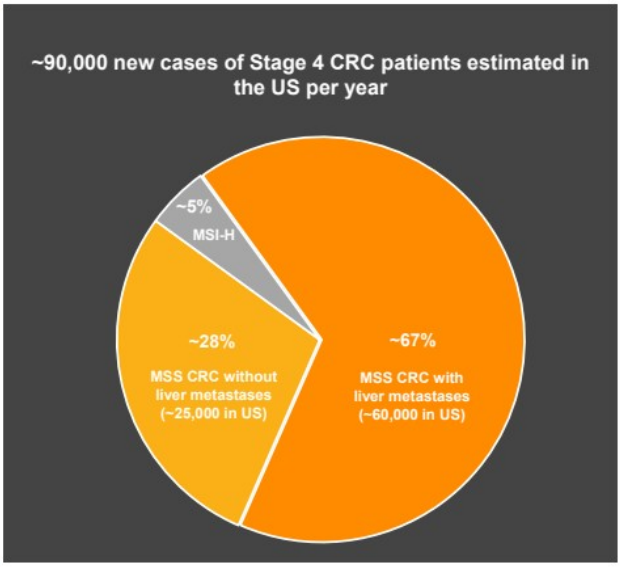
- High affinity binding, 10x potency of ipilimumab in preclinical studies [1]
- Fc mutations for enhanced effector function (ADCC), improved T cell priming and Treg depletion
- On-treatment biopsies in Phase 1 monotherapy demonstrated >70% activated molecule in tumor with <15% activated molecule in periphery
- 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

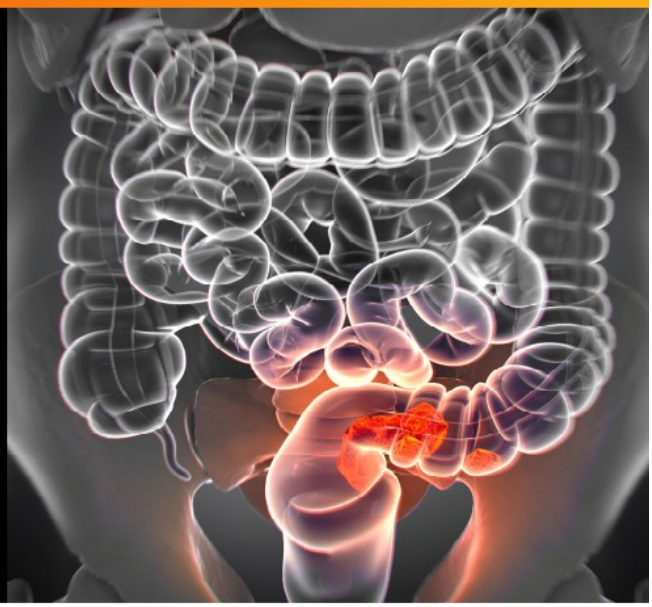
- CRC is 2nd in cancer-related deaths in the US and leading cause of cancer-related death in men younger than 50 in the US (1)
- CRC is 3rd in total annual new cases globally, with ~1.9M new cases and ~900,000 deaths related to CRC globally (2)
- >25% of Stage 4 CRC patients have MSS CRC without liver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

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

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%

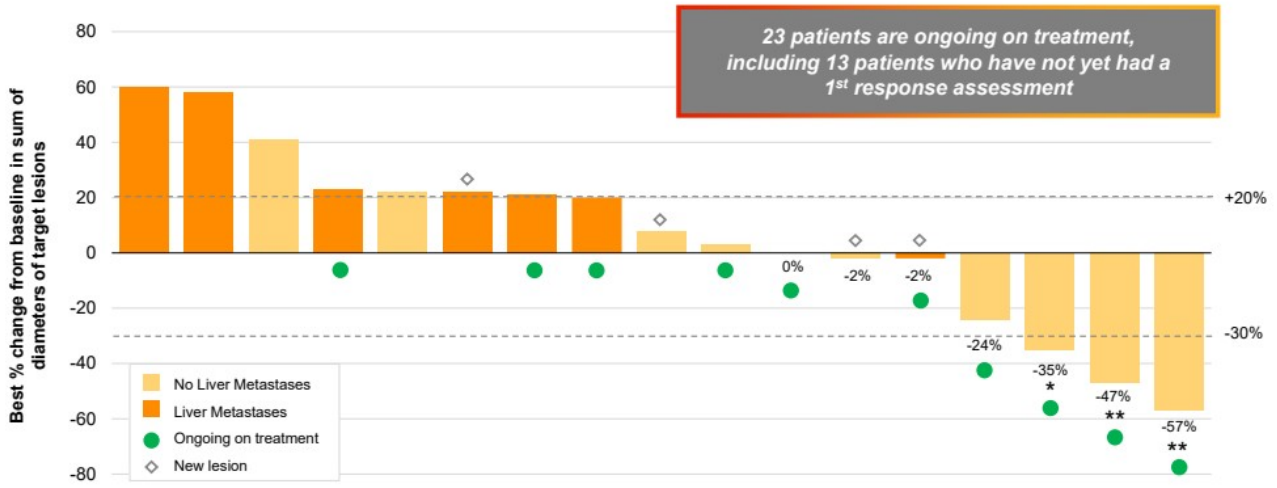
One additional patient (with peritoneal metastasis) had significant reduction in tumor burden (24% reduction) and is currently ongoing on treatment

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

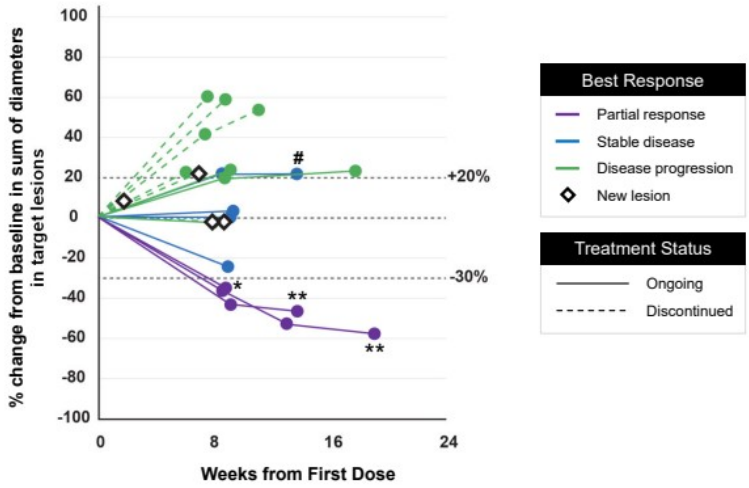
Anti-Tumor Activity in MSS CRC Patients, Including 3 PRs (2 Confirmed), Demonstrated for Combination of Vilastobart (anti-CTLA-4) and Atezolizumab



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).

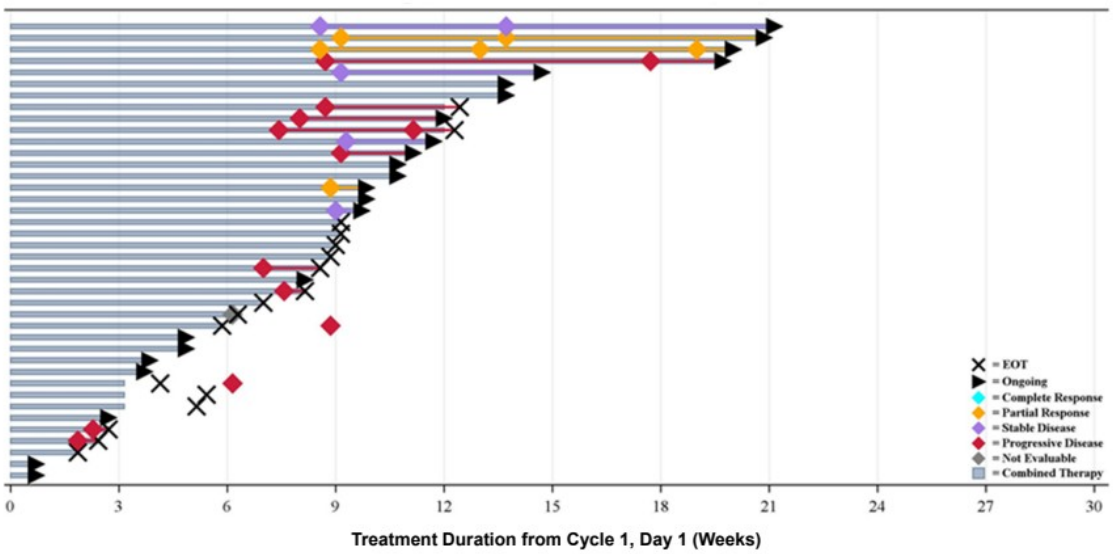
Confirmed PRs in MSS CRC Patients Without Liver Metastases Deepening Through Up to 18 Weeks To Date



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).

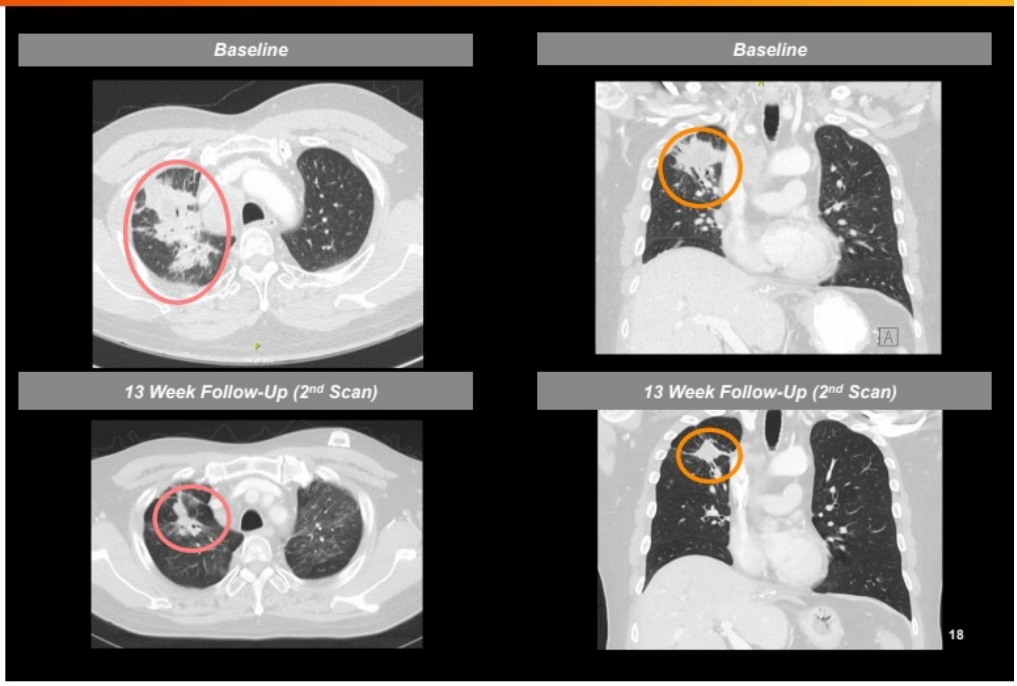
23 Patients Ongoing on Treatment with Combination of Vilastobart (anti-CTLA-4) and Atezolizumab, Including 13 Patients Who Have Not Yet Had a First Response Assessment



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

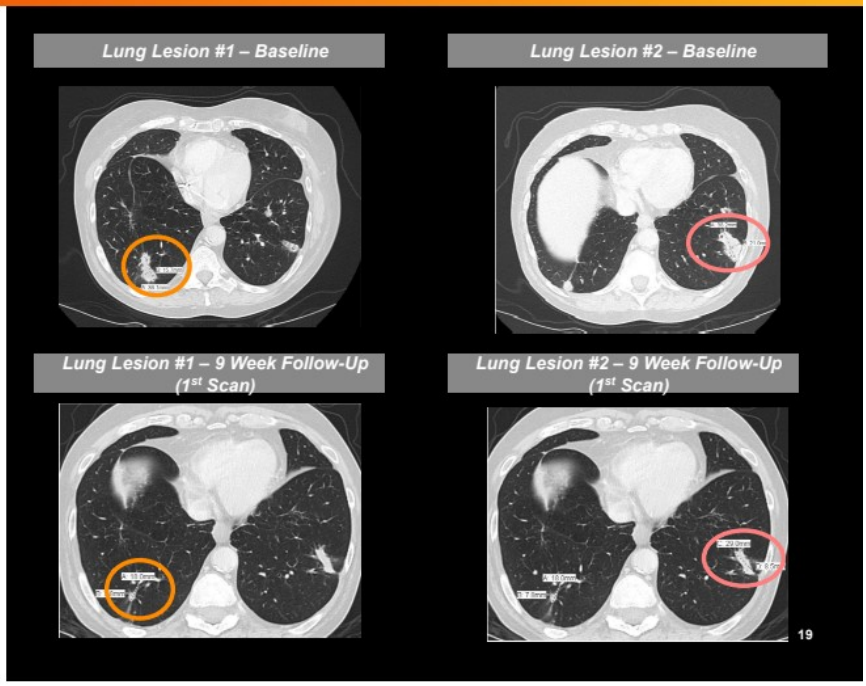


CEA: carcinoembryonic antigen; ctDNA: circulating tumor DNA

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

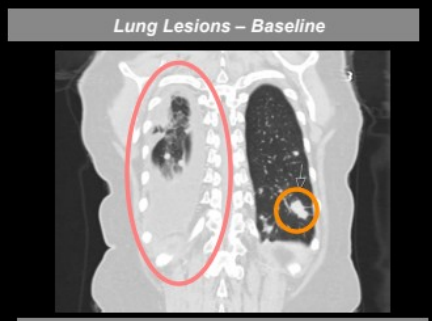
- 63 year-old female
- 2 prior lines of therapy:
  - FOLFOX
  - 5FU and irinotecan
- PR (confirmed) and continues to deepen:
  - 37% reduction (1st scan, 9 weeks)
  - 53% reduction (2nd scan, 13 weeks)
  - 57% reduction (3rd scan, 18 weeks)
- Accompanied by:
  - 100% decrease in ctDNA while on treatment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

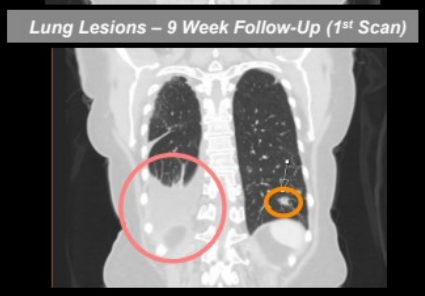
	Screening	C3	C4	C5	C7
CEA value (ng/ml)	192.9	23.6		3.5 (normal)	1.9 (normal)
Target lesions	74 mm		47 mm	35 mm	32 mm



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

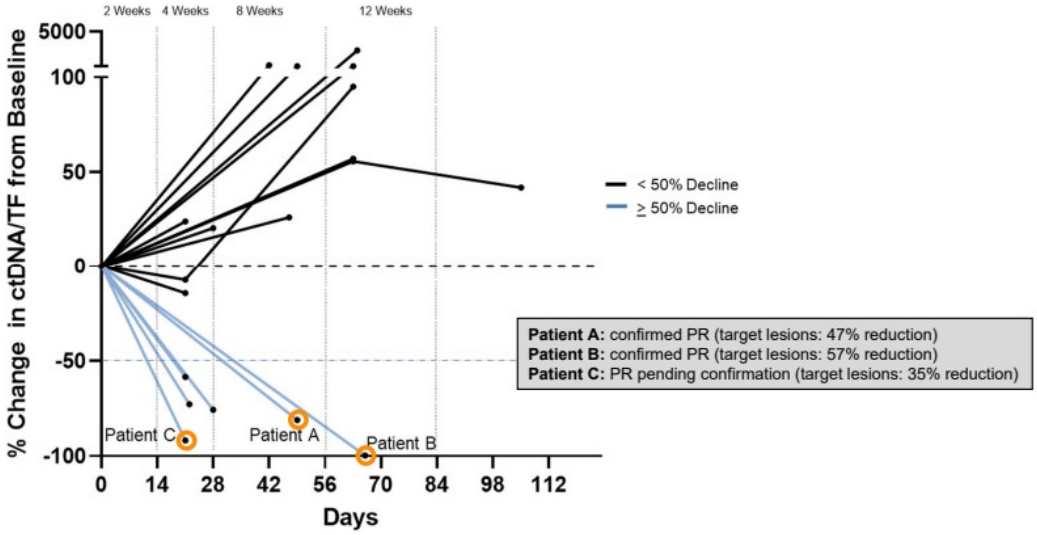
- 67 year-old female
- 6 prior lines of therapy:
  - FOLFOX
  - Capecitabine + bevacizumab
  - 5FU + bevacizumab
  - 5FU + panitumumab
  - FOLFIRI + panitumumab
  - 5FU + panitumumab
- PR (pending confirmation)* with 35% reduction at 9 weeks
- Accompanied by:
  - Substantial decrease in ctDNA
  - Decrease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





* 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



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.

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
x·ilio
THERAPEUTICS®

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

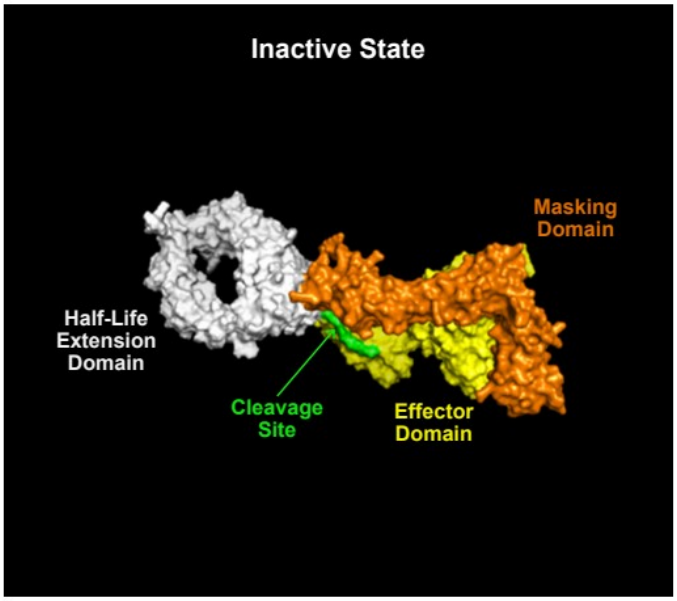
Capable of polarizing CD4 T-cells towards Th1 phenotype, thus driving cellular immunity against infection and cancer

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.

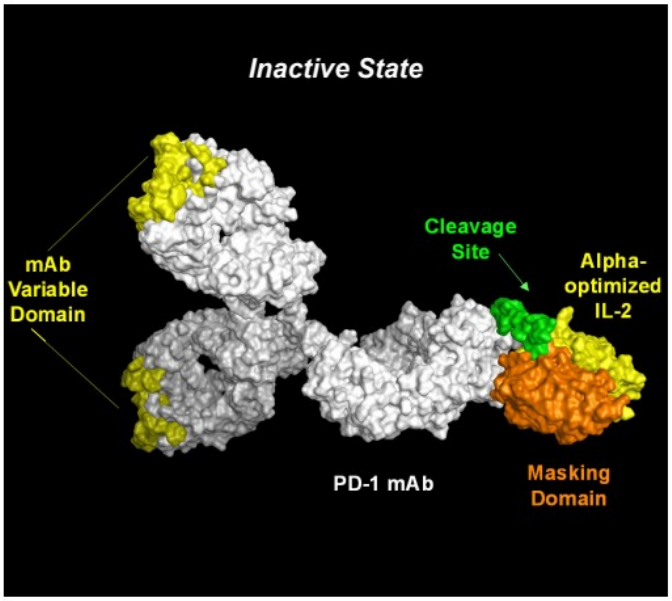

XTX501
PD1/IL2 bispecific
xilio
THERAPEUTICS

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

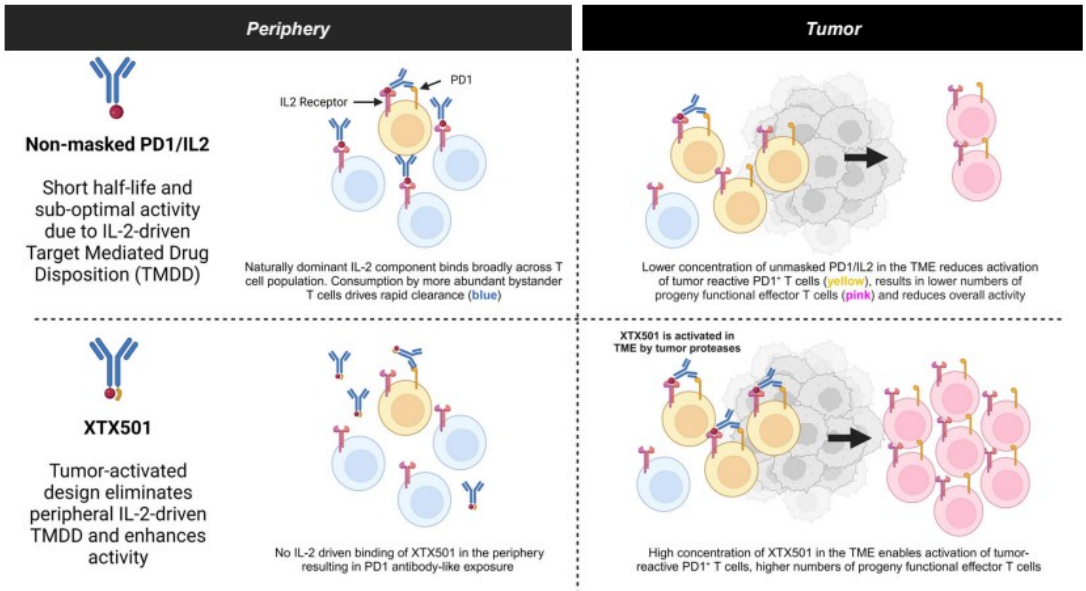
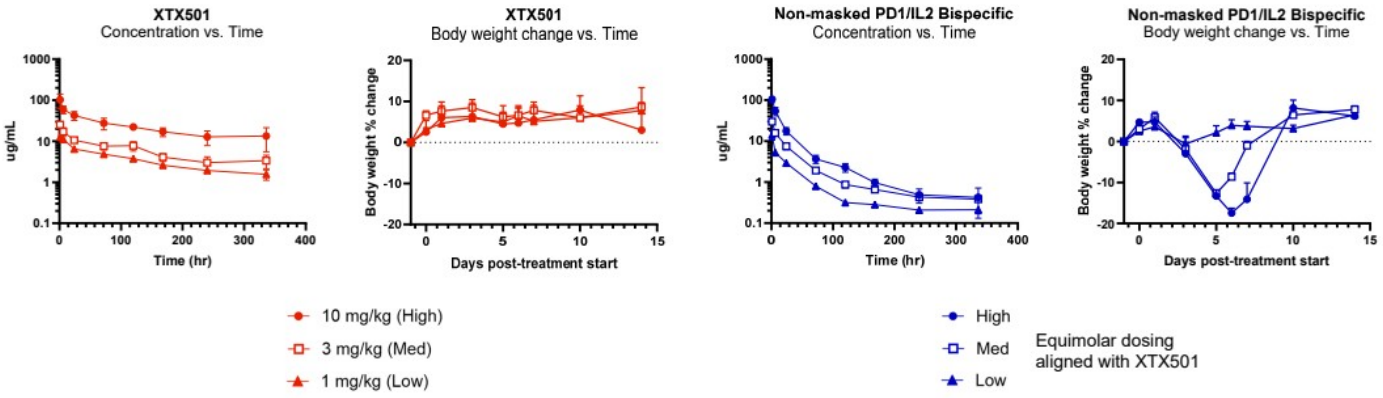


Figure generated using BioRender.com.

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

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

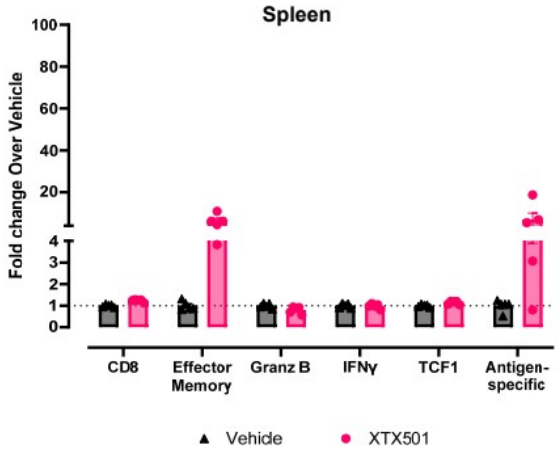
Non-Masked PD1/IL2 Bispecific Was Rapidly Cleared and Poorly Tolerated



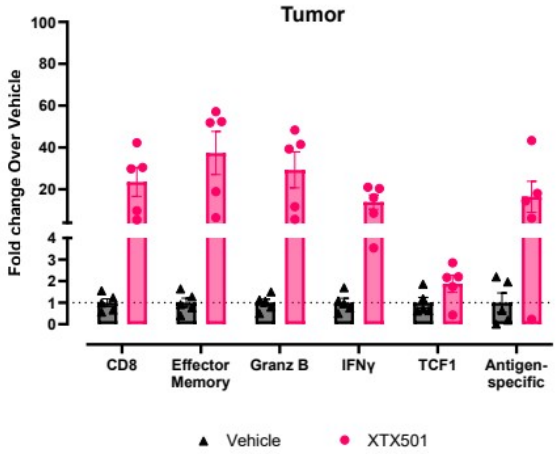
XTX501 exposure after a single 10, 3 or 1 mg/kg intravenous injection in non-tumor bearing C57BL/6-hFcRn mice. Non-masked PD1/IL2 exposure after a single equal molar dose of 9.25, 2.75 or 0.92 mg/kg intravenous injection in non-tumor bearing C57BL/6-hFcRn mice. Body weight data are displayed until day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



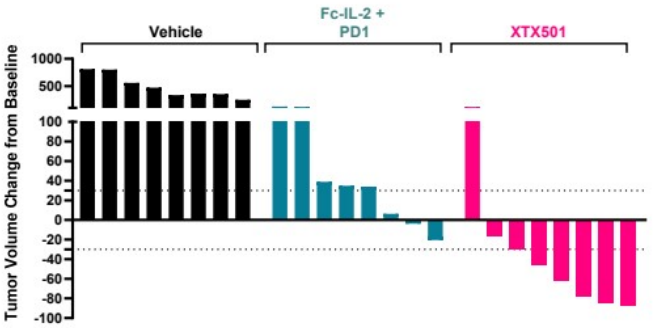
XTX501 Treatment Demonstrated Robust Increases in Activated T Cell Populations in Tumor



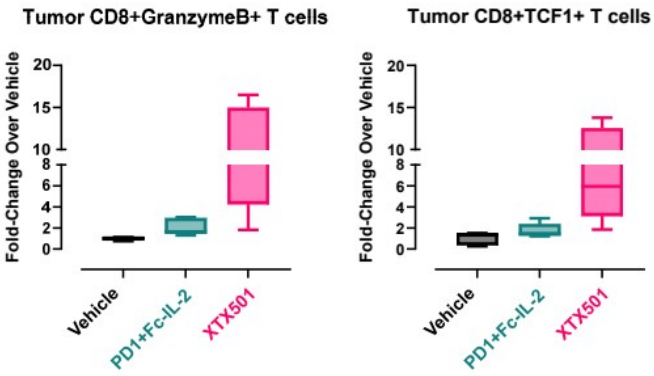
Female C57BL/6 hPD-1 mice (n=5 in each treatment group) were inoculated with 0.5x106 MC38 tumor cells subcutaneously in the right flank. On day 0, 3 mice received XTX501 bispecific or vehicle. The percentage of cells for each immune phenotype was calculated as percentage of live CD45+ cells and the ratio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

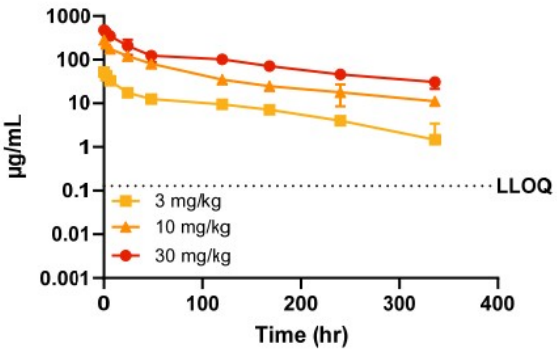


Left panel: Female C57BL/6 hPD-1 mice (n=8 in each treatment group) were inoculated with MB49 tumor cells. On day 0, 5 mice received vehicle or equimolar doses of anti-PD1 antibody (pembrolizumab) plus XTX202 (Masked βγIL-2), or XTX501. Tumor volume change on day 12 post treatment relative to baseline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

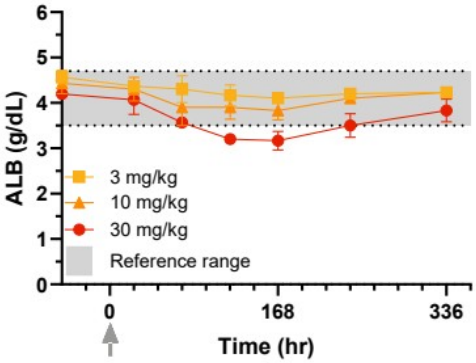
Single Dose PK Study in NHP
Tolerable Up to 30 mg/kg

XTX501 Concentration Over Time



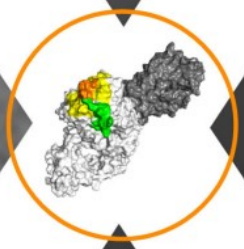
Minimal Effects of XTX501 on Serum Albumin
(i.e., No Signs of Vascular Leak Syndrome)

Serum Albumin Concentration Over Time



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



x·ilio THERAPEUTICS®

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

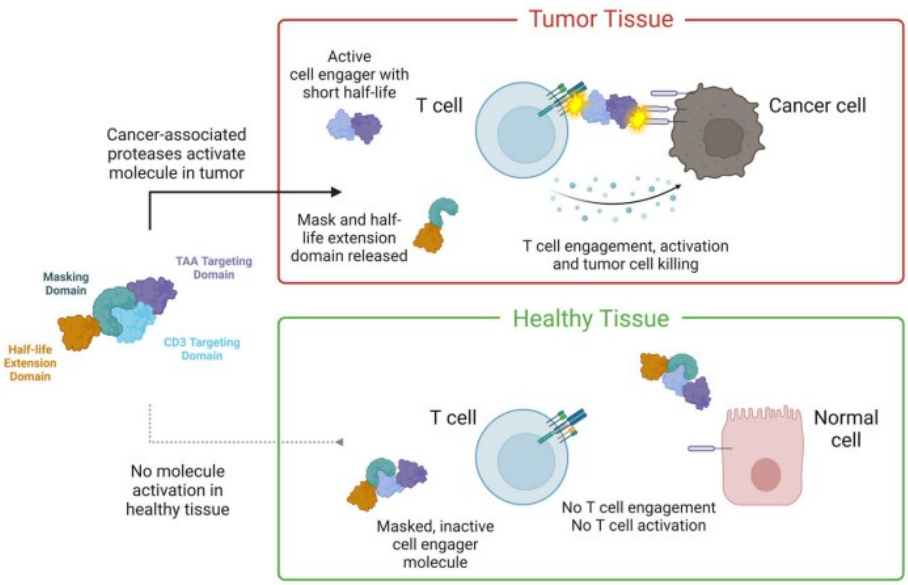


Figure generated using BioRender.com.

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

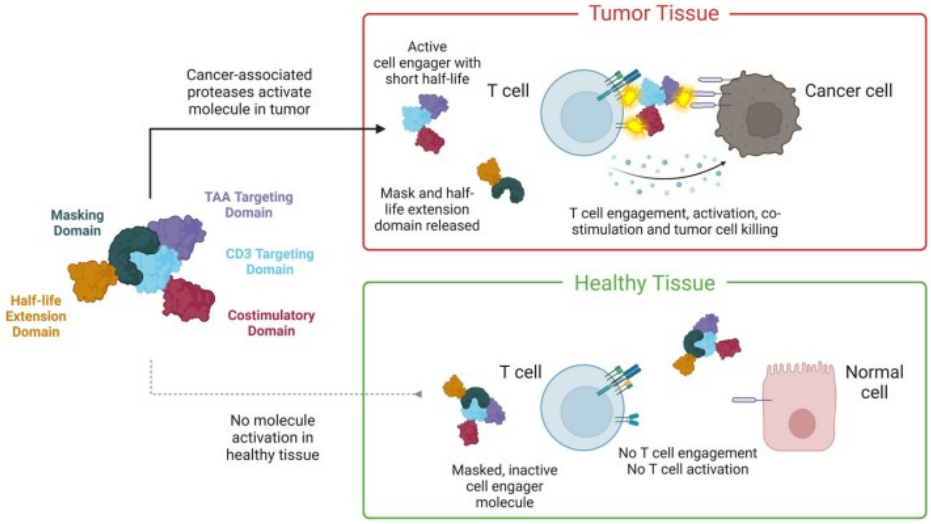
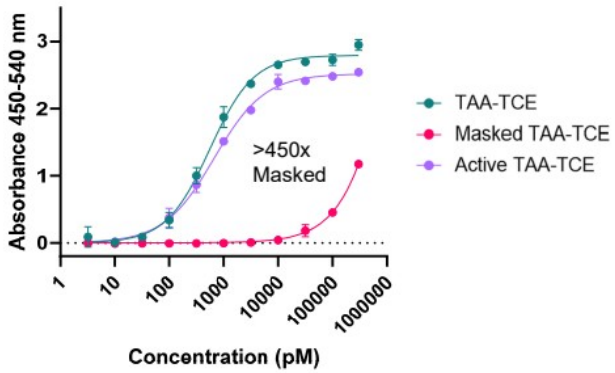


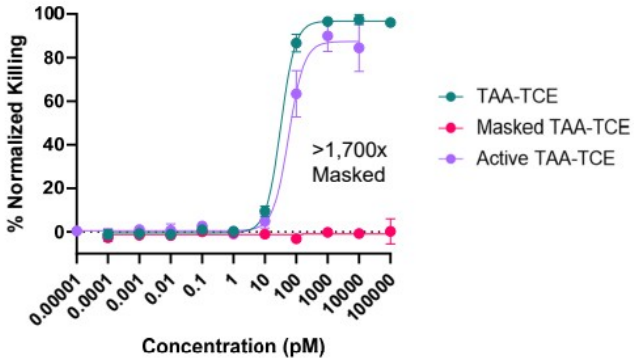
Figure generated using BioRender.com.

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

Demonstrated Protease-Dependent Binding to CD3 by ELISA



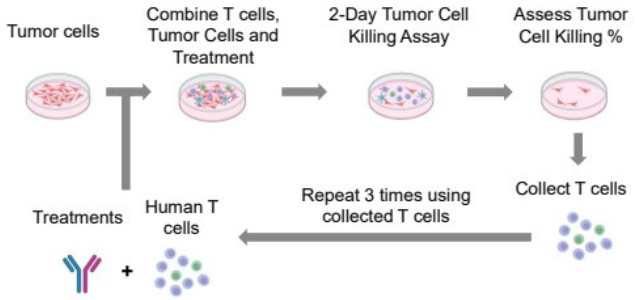
Confirmed Protease-Dependent Activity in Primary T Cell Assay



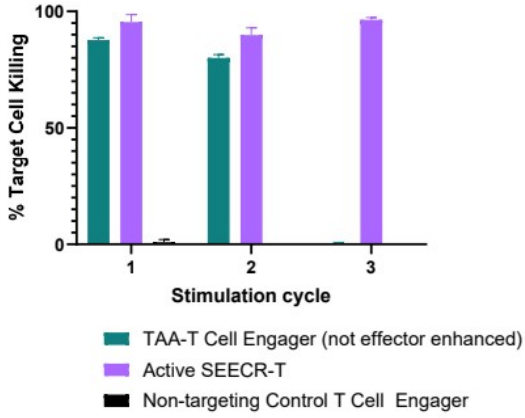
Left panel: Protease dependent CD3-binding demonstrated via TAA-TCEs bound to immobilized CD3 in an ELISA. **Right panel:** Protease-dependent tumor cell killing. Active TAA-TCEs led to killing in co-culture assay. A375 tumor cells were cultured overnight before addition of expanded T cells at a 5:1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



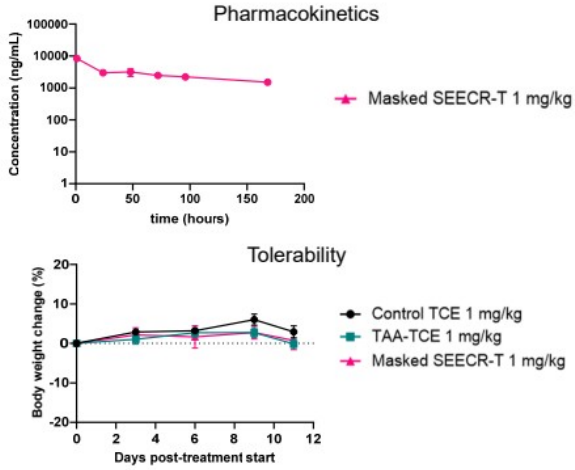
SEECR Format Enabled Sustained Tumor Cell Killing Over Multiple Rounds



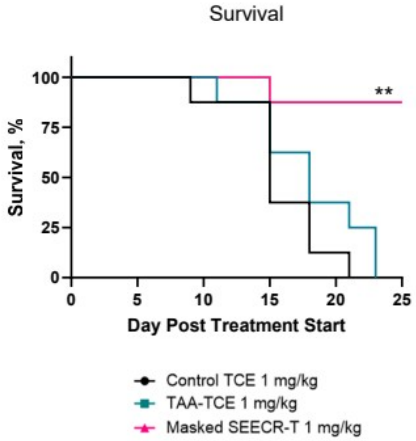
Human T cells were incubated over three consecutive rounds with indicated test articles and A431 cancer cells and percent tumor cell killing was assessed using a luminescence readout.

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
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.

Exhibit 99.2

Xilio Therapeutics Announces Initial Phase 2 Data for Vilastobart (XTX101), a Tumor-Activated Anti-CTLA-4, in Combination with Atezolizumab in Patients with Metastatic Microsatellite Stable Colorectal Cancer

27% preliminary response rate observed in heavily pre-treated microsatellite stable colorectal cancer (MSS CRC) patients without liver metastases

Responses were accompanied by decreases in levels of carcinoembryonic antigen (CEA) and circulating tumor DNA (ctDNA) and improvement in clinical symptoms

Data continue to demonstrate differentiated safety and tolerability profile for the combination with low incidence of immune-related adverse events

Xilio Therapeutics to host investor conference call and webcast on Wednesday, January 22, 2025, at 8:30 am ET

WALTHAM, Mass., January 21, 2025 – Xilio Therapeutics, Inc. (Nasdaq: XLO), a clinical-stage biotechnology company discovering and developing tumor-activated immuno-oncology therapies for people living with cancer, today announced initial data from its ongoing Phase 2 clinical trial evaluating vilastobart (XTX101), a tumor-activated, Fc-enhanced, high affinity binding anti-CTLA-4, in combination with atezolizumab (Tecentriq®) in patients with metastatic microsatellite stable colorectal cancer (MSS CRC). The data will be presented in a poster session (abstract #206) at the American Society of Clinical Oncology 2025 Gastrointestinal Cancer Symposium (ASCO GI) being held January 23-25, 2025, in San Francisco.

“We are very encouraged by the initial Phase 2 proof-of-concept data for the combination of vilastobart and atezolizumab in heavily pre-treated patients with MSS colorectal cancer, including partial responses accompanied by marked decreases in tumor biomarkers and improvement in clinical symptoms,” said Katarina Luptakova, M.D., chief medical officer of Xilio. “We believe these data highlight the important contribution of vilastobart in this combination, as PD-(L)1 inhibitors alone have demonstrated no meaningful efficacy in patients with MSS CRC to date. The preliminary evidence of anti-tumor activity, together with continued evidence of a well-tolerated safety profile, support the potential for the combination in MSS colorectal cancer, as well as in other tumors that have traditionally been resistant to treatment with immunotherapy. We look forward to sharing additional Phase 2 data, including further follow-up, in patients with metastatic MSS CRC in the middle of this year.”

“These preliminary Phase 2 data for the combination of vilastobart and atezolizumab show clear responses for patients with MSS colorectal cancer, an area of very high and increasing unmet medical need,” said J. Randolph Hecht, M.D., Professor of Clinical Medicine at the David Geffen School of Medicine at UCLA, Director of the UCLA Gastrointestinal Oncology Program and the lead author for the presentation at ASCO GI. “I am excited to see these initial data highlighting the potential for vilastobart, a tumor-activated anti-CTLA-4, in combination with PD-(L)1 inhibitors to have clinically meaningful benefit in a classically immunotherapy-resistant major malignancy.”

Data from Phase 2 Trial for Vilastobart (XTX101), a Tumor-Activated Anti-CTLA-4, in Combination with Atezolizumab in Patients with Metastatic MSS CRC

As of a data cutoff date of January 13, 2025, 40 patients with metastatic MSS CRC had been treated with the combination of vilastobart at a dose of 100 mg once every six weeks (Q6W) and atezolizumab at 1200 mg once every three weeks (Q3W). The median age was 55 years (ranging from 25 to 82 years), and patients

were heavily pre-treated, with 70% of patients having previously received three or more prior lines of anti-cancer therapy.

Preliminary Anti-Tumor Activity Data

In patients without liver metastases, the preliminary objective response rate (ORR) was 27% with three partial responses (PRs), including two confirmed PRs. Responses were accompanied by decreases in levels of carcinoembryonic antigen (CEA) and circulating tumor DNA (ctDNA) as well as improvement in clinical symptoms.

As of the data cutoff date, 18 patients had at least one imaging scan reported and were evaluable for response assessment (per RECIST version 1.1 criteria), including 11 patients without liver metastases and seven patients with liver metastases.

In response-evaluable MSS CRC patients without liver metastases, investigators reported three PRs (two confirmed, one pending confirmation), with each patient ongoing on treatment as of the data cutoff date:

- PR (confirmed) with a 47% decrease in the sum of diameters of target lesions at 13 weeks accompanied by a decrease in levels of the serum tumor marker CEA, a multi-log fold decrease in levels of ctDNA and improvement of clinical symptoms, such as cough. CEA is a serum biomarker that is often elevated in many malignancies, including colorectal cancer, and ctDNA is a biomarker found in the bloodstream of patients with cancer.

- PR (confirmed) that continued to deepen over time with a 57% reduction in the sum of diameters of target lesions at 18 weeks accompanied by a multi-log fold decrease in ctDNA to undetectable levels and significant decrease in levels of the serum tumor marker CEA to normal values.

- PR (pending confirmation) with a 35% decrease in the sum of diameters of target lesions at nine weeks accompanied by a decrease in levels of the tumor marker CEA to normal values, a substantial decrease in levels of ctDNA and improvement of clinical symptoms, such as cough. For this patient, the initial response on CT imaging was assessed by the investigator and the radiology assessment is pending.

In addition, an MSS CRC patient without liver metastases but with a peritoneal metastasis had a 24% decrease in the sum of diameters of target lesions assessed by CT imaging at their initial nine-week scan accompanied by a decrease in levels of the serum tumor marker CEA to normal values. This patient was ongoing on treatment as of the data cutoff date.

Investigators reported stable disease in three patients without liver metastases and one patient with liver metastases, representing a preliminary disease control rate of 55% and 14%, respectively, and highlighting additional evidence of anti-tumor activity for the combination.

As of the data cutoff date, 23 patients were ongoing on treatment, including 13 patients who had not yet had a first response assessment.

Preliminary Safety Data

Safety data continue to support the potential for vilastobart to be a differentiated next-generation anti-CTLA-4 in combination with PD-(L)1 inhibitors. Consistent with the tumor-selective design for vilastobart, the combination was generally well-tolerated, with patients experiencing a low incidence of immune-related adverse events (irAEs) and only 5% of patients reporting colitis.

As of the data cutoff date, 40 patients were evaluable for safety. Across all patients treated:

- Investigators reported only six patients with Grade 3 or 4 treatment-related adverse events (AEs), including only two Grade 4 treatment-related AEs (laboratory abnormalities of thrombocytopenia and neutropenia, one patient each), and no Grade 5 treatment-related AEs.
- No patients experienced a dose reduction for vilastobart due to an AE, and only three patients discontinued treatment for the combination of vilastobart and atezolizumab due to a treatment-related AE.
- Investigators reported minimal endocrine irAEs (5%) and limited skin irAEs (13%), and the incidence of endocrine and skin irAEs was consistent with the incidence reported for atezolizumab alone.
- The most common treatment-related AEs (≥10% incidence) of any grade reported by investigators were the following: fatigue (30%); diarrhea (20%); infusion-related reactions (13%, with 8% deemed related to vilastobart and 5% deemed related to atezolizumab); pyrexia (10%); aspartate aminotransferase (AST) increase (10%); and alanine aminotransferase (ALT) increase (10%).
- The only Grade 3 treatment-related AE with ≥5% incidence reported by investigators was colitis (5%). Non-laboratory Grade 3 treatment-related AEs (<5% incidence) consisted of the following: maculopapular rash and febrile neutropenia in one patient; lower gastrointestinal hemorrhage in one patient with thrombocytopenia; and one patient with Triple M overlap syndrome (myocarditis, myositis and myasthenia gravis).

Clinical Development Plans for Vilastobart

The Phase 2 clinical trial evaluating vilastobart in combination with atezolizumab in patients with MSS CRC is currently ongoing, and Xilio expects to report updated data from the Phase 2 trial in the middle of 2025, including additional response assessments and follow-up.

These initial Phase 2 proof-of-concept data demonstrate the potential for vilastobart as a combination therapy in patients with MSS CRC and a range of other tumor types, including “cold” tumors historically resistant to immunotherapy. Based on these data, Xilio plans to seek opportunities for partnering to prioritize and expand further development beyond the initial Phase 2 proof-of-concept trial in MSS CRC.

In addition, Xilio continues to enroll patients in Phase 1C dose escalation and evaluate the combination of vilastobart at the 150 mg Q6W dose level and atezolizumab at 1200 mg Q3W.

Investor Conference Call Information

Xilio will host a conference call and webcast tomorrow (Wednesday, January 22, 2025) at 8:30 am ET to discuss the initial Phase 2 data for the combination of vilastobart and atezolizumab. Viewers can access the webcast by using this link. Listeners who require dial-in access should register here to receive a unique PIN and information to join the call. Listeners are encouraged to join at least 15 minutes prior to the scheduled start time. The webcast will also be accessible under “Events & Presentations” in the

Investors & Media section of the Xilio Therapeutics website at https://ir.xiliotx.com. A replay of the webcast will be archived on the website for 30 days following the presentation.

About Vilastobart (XTX101) and the Phase 1/2 Combination Clinical Trial

Vilastobart is an investigational tumor-activated, Fc-enhanced, high affinity binding anti-CTLA-4 monoclonal antibody designed to block CTLA-4 and deplete regulatory T cells when activated in the tumor microenvironment (TME). In 2023, Xilio entered into a co-funded clinical trial collaboration with Roche to evaluate vilastobart in combination with atezolizumab (Tecentriq®) in a multi-center, open-label Phase 1/2 clinical trial. Xilio is currently evaluating the safety of the combination in Phase 1C dose escalation in patients with advanced solid tumors and the safety and efficacy of the combination in Phase 2 in patients with metastatic microsatellite stable colorectal cancer with and without liver metastases. Please refer to NCT04896697 on www.clinicaltrials.gov for additional details.

About Xilio Therapeutics

Xilio Therapeutics is a clinical-stage biotechnology company discovering and developing tumor-activated immuno-oncology (I-O) therapies with the goal of significantly improving outcomes for people living with cancer without the systemic side effects of current I-O treatments. The company is using its proprietary platform to advance a pipeline of novel, tumor-activated clinical and preclinical I-O molecules that are designed to optimize the therapeutic index by localizing anti-tumor activity within the tumor microenvironment, including tumor-activated cytokines, antibodies, bispecifics and immune cell engagers. Learn more by visiting www.xiliotx.com and follow us on LinkedIn (Xilio Therapeutics, Inc.).

Cautionary Note Regarding Forward-Looking Statements

This press release contains forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995, as amended, including, without limitation, statements regarding plans, expectations and anticipated milestones for vilastobart (XTX101), including plans and timing for reporting Phase 2 clinical data for vilastobart in combination with atezolizumab in patients with MSS CRC; the potential benefits of vilastobart (as a monotherapy or combination therapy with a PD-(L)1 or other agent) or any of Xilio's other current or future product candidates in treating patients as a monotherapy or combination therapy in any indication; the ultimate safety profile of vilastobart; and Xilio's strategy, goals and anticipated financial performance, milestones, business plans and focus. The words "aim," "may," "will," "could," "would," "should," "expect," "plan," "anticipate," "intend," "believe," "estimate," "predict," "project," "potential," "continue," "seek," "target" and similar expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words. Any forward-looking statements in this press release are based on management's current expectations and beliefs and are subject to a number of important risks, uncertainties and other factors that may cause actual events or results to differ materially from those expressed or implied by any forward-looking statements contained in this press release, including, without limitation, general market conditions; risks and uncertainties related to ongoing and planned research and development activities, including initiating, conducting or completing preclinical studies and clinical trials and the timing and results of such preclinical studies or clinical trials; the delay of any current or planned preclinical studies or clinical trials or the development of Xilio's current or future product candidates; Xilio's ability to obtain and maintain sufficient preclinical and clinical supply of current or future product candidates; Xilio's advancement of multiple early-stage immune cell engager programs, including tumor-activated immune cell engagers and tumor-activated effector-enhanced immune cell engagers; initial, preliminary or interim preclinical or clinical data or results (including without limitation, the Phase 2 data for vilastobart and the preliminary investigator-reported PR awaiting radiology confirmation), which may not be replicated in or predictive of future preclinical or clinical data or results; Xilio's ability to successfully demonstrate the safety and

efficacy of its product candidates and gain approval of its product candidates on a timely basis, if at all; results from preclinical studies or clinical trials for Xilio's product candidates, which may not support further development of such product candidates; actions of regulatory agencies, which may affect the initiation, timing and progress of current or future clinical trials; Xilio's ability to obtain, maintain and enforce patent and other intellectual property protection for current or future product candidates; Xilio's ability to obtain and maintain sufficient cash resources to fund its operations; the impact of international trade policies on Xilio's business, including U.S. and China trade policies; Xilio's ability to maintain its clinical trial collaboration with Roche to develop vilastobart in combination with atezolizumab; and Xilio's ability to maintain its license agreement with Gilead to develop and commercialize XTX301. These and other risks and uncertainties are described in greater detail in the sections entitled "Risk Factor Summary" and "Risk Factors" in Xilio's filings with the U.S. Securities and Exchange Commission (SEC), including Xilio's most recent Quarterly Report on Form 10-Q and any other filings that Xilio has made or may make with the SEC in the future. Any forward-looking statements contained in this press release represent Xilio's views only as of the date hereof and should not be relied upon as representing its views as of any subsequent date. Except as required by law, Xilio explicitly disclaims any obligation to update any forward-looking statements.

This press release contains hyperlinks to information that is not deemed to be incorporated by reference in this press release.

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