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): **November 7, 2024**

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 2.02 Results of Operations and Financial Condition.

On November 7, 2024, Xilio Therapeutics, Inc. (the "Company") announced its financial results for the quarter ended September 30, 2024 and other business highlights. The full text of the press release issued in connection with the announcement is furnished as Exhibit 99.1 to this Current Report on Form 8-K and is incorporated by reference herein.

The information in Item 2.02 of this Current Report on Form 8-K, including Exhibit 99.1, is intended to be 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 Securities Act of 1933, as amended (the "Securities Act"), or the Exchange Act, except as expressly set forth by specific reference in such filing.

Item 7.01 Regulation FD Disclosure.

From time to time, 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 99.2 to this Current Report on Form 8-K.

The information in Item 7.01 of this Current Report on Form 8-K, including Exhibit 99.2, is being furnished and shall not be deemed "filed" for purposes of Section 18 of 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, except as expressly set forth by specific reference in such filing.

Item 8.01 Other Events.

On November 7, 2024, the Company issued a press release announcing initial data from Phase 1C of its ongoing clinical trial evaluating vilastobart (XTX101) in combination with atezolizumab in patients with advanced solid tumors. These data are being presented in a late-breaker poster presentation at the Society for Immunotherapy of Cancer 39th Annual Meeting. The full text of the press release is filed as Exhibit 99.3 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 or any of the Company's other current or future product candidates in treating patients as a monotherapy or combination therapy; 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 1C

data for vilastobart), 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	Press release issued by Xilio Therapeutics, Inc. on November 7, 2024
99.2	Corporate slide presentation of Xilio Therapeutics, Inc. dated November 7, 2024
99.3	Press release issued by Xilio Therapeutics, Inc. on November 7, 2024
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: November 7, 2024

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

Xilio Therapeutics Announces Pipeline and Business Updates and Third Quarter 2024 Financial Results

Will present initial Phase 1C dose escalation data for vilastobart (XTX101), a tumor-activated, Fc-enhanced anti-CTLA-4, in combination with atezolizumab, in a late-breaker poster presentation at the SITC Annual Meeting

Expect to report initial Phase 2 data in microsatellite stable colorectal cancer (MSS CRC) for vilastobart in combination with atezolizumab in the fourth quarter of 2024

Expect to report Phase 1 data for XTX301, a tumor-activated IL-12, in the fourth quarter of 2024

WALTHAM, Mass., November 7, 2024 – 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 pipeline progress and business updates and reported financial results for the third quarter ended September 30, 2024.

"Throughout the third quarter, our team continued to drive execution across all stages of our pipeline, including advancing our clinical development programs for vilastobart, a tumor-activated, Fc-enhanced anti-CTLA-4, and XTX301, a tumor-activated IL-12, toward key data milestones and potential value inflection points," said René Russo, Pharm.D., president and chief executive officer of Xilio. "We look forward to sharing initial data from our Phase 1C dose escalation trial of vilastobart in combination with atezolizumab as part of a late-breaker poster presentation at the SITC Annual Meeting. In addition, we continue to advance multiple promising research-stage programs, including XTX501, our tumor-activated PD-1/IL-2, and tumor-activated immune cell engagers."

Pipeline and Business Updates

Vilastobart (XTX101): tumor-activated anti-CTLA-4

Vilastobart is an investigational tumor-activated, Fc-enhanced, high affinity binding anti-CTLA-4 antibody designed to block CTLA-4 and deplete regulatory T cells when activated in the tumor microenvironment (TME).

- Xilio will present initial Phase 1C dose escalation data for vilastobart in combination with atezolizumab in a late-breaker poster presentation at the Society for Immunotherapy of Cancer (SITC) 39th Annual Meeting taking place in Houston, Texas, from November 6-10, 2024.
- In addition, Xilio continues to enroll patients in its ongoing Phase 2 clinical trial evaluating vilastobart in combination with atezolizumab in patients with metastatic MSS CRC, including patients with and without liver metastases.
- Xilio expects to report initial Phase 2 data for vilastobart in combination with atezolizumab in approximately 20 patients with MSS CRC in the fourth quarter of 2024 and in a total of approximately 40 patients with MSS CRC in the first quarter of 2025.

XTX301: tumor-activated, engineered IL-12

XTX301 is an investigational tumor-activated, engineered IL-12 molecule designed to potently stimulate anti-tumor immunity and reprogram the TME of poorly immunogenic "cold" tumors towards an inflamed, or "hot," state.

- Xilio continues to enroll patients in Phase 1A monotherapy dose escalation and Phase 1B monotherapy dose expansion of its ongoing Phase 1 clinical trial of XTX301 in patients with advanced solid tumors.
- Xilio plans to report safety, pharmacokinetic and pharmacodynamic data from the ongoing Phase 1 clinical trial for XTX301 in the fourth quarter of 2024.

Tumor-Activated Bispecific and Immune Cell Engager Programs

Xilio is leveraging its proprietary platform to advance a pipeline of research-stage programs for tumor-activated bispecific and immune cell engager molecules, including tumor-activated immune cell engagers and tumor-activated effector-enhanced immune cell engagers.

- XTX501 is a tumor-activated bispecific PD-1/IL-2 designed to selectively stimulate PD-1 positive antigen-experienced T cells and enhance their function. XTX501 incorporates masking designed to overcome IL-2 receptor-mediated clearance and peripheral activity. Xilio is currently advancing initial investigational new drug (IND)-enabling activities for XTX501.
- Xilio will present preclinical data from its tumor-activated SELECTIVE EFFECTOR-ENHANCED CELL ENGAGER (SEECR) format in a poster session at the SITC Annual Meeting. Details on the poster presentation can be found here.

Third Quarter 2024 Financial Results

- **Cash Position:** Cash and cash equivalents were $61.3 million as of September 30, 2024, compared to $44.7 million as of December 31, 2023.
- **License Revenue:** License revenue was $2.3 million for the quarter ended September 30, 2024, which consisted of revenue recognized under the license agreement and stock purchase agreement with Gilead. No license revenue was recognized for the quarter ended September 30, 2023.
- **Research & Development (R&D) Expenses:** R&D expenses were $10.8 million for the quarter ended September 30, 2024, compared to $11.1 million for the quarter ended September 30, 2023. The decrease was primarily driven by decreased clinical development activities for XTX202, a tumor-activated, IL-2, decreased spending related to early-stage programs and indirect research and development costs and decreased personnel-related costs, partially offset by increased clinical development activities for vilastobart and XTX301.
- **General & Administrative (G&A) Expenses:** G&A expenses were $6.3 million for
for each of the quarters ended September 30, 2024 and September 30, 2023.
- **Net Loss:** Net loss was $14.0 million for the quarter ended September 30, 2024, compared to $16.7 million for the quarter ended September 30, 2023.

Financial Guidance

Based on its current operating plans, Xilio anticipates that its existing cash and cash equivalents as of September 30, 2024, will be sufficient to fund its operating expenses and capital expenditure requirements through the end of the second quarter of 2025.

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 XTX301 and the Phase 1 Clinical Trial

XTX301 is an investigational tumor-activated IL-12 designed to potently stimulate anti-tumor immunity and reprogram the tumor microenvironment (TME) of poorly immunogenic “cold” tumors towards an inflamed or “hot” state. In March 2024, Xilio entered into an exclusive license agreement with Gilead Sciences, Inc. for Xilio’s tumor-activated IL-12 program, including XTX301. Xilio is currently evaluating the safety and tolerability of XTX301 as a monotherapy in patients with advanced solid tumors in a first-in-human, multi-center, open-label Phase 1 clinical trial. Please refer to NCT05684965 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.).

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including IND-enabling activities, 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, 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 (XTX101) 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.

TECENTRIQ is a registered trademark of Genentech USA, Inc., a member of the Roche Group.

Xilio Investor and Media Contact

Scott Young
Vice President, Investor Relations and Corporate Communications
investors@xiliotx.com

XILIO THERAPEUTICS, INC.
Condensed Consolidated Balance Sheets
(In thousands)

(Unaudited)

	September 30, 2024	December 31, 2023
Assets		
Cash and cash equivalents	$ 61,259	$ 44,704
Other assets	13,399	16,222
Total assets	74,658	60,926
Liabilities and Stockholders' Equity		
Liabilities		
Deferred revenue	34,504	—
Other liabilities	19,180	24,099
Total liabilities	53,684	24,099
Stockholders' equity	20,974	36,827
Total liabilities and stockholders' equity	74,658	60,926

XILIO THERAPEUTICS, INC.
Condensed Consolidated Statements of Operations and Comprehensive Loss
(In thousands, except share and per share data)

(Unaudited)

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2024	**2023**	**2024**	**2023**
License revenue	$ 2,263	$ —	$ 4,620	$ —
Operating expenses [1]				
Research and development	10,759	11,051	32,375	40,400
General and administrative	6,307	6,310	18,261	20,603
Restructuring	(41)	—	937	—
Total operating expenses	17,025	17,361	51,573	61,003
Loss from operations	(14,762)	(17,361)	(46,953)	(61,003)
Other income, net	742	613	1,805	2,254
Net loss and comprehensive loss	$ (14,020)	$ (16,748)	$ (45,148)	$ (58,749)
Net loss per share, basic and diluted	$ (0.22)	$ (0.61)	$ (0.91)	$ (2.14)
Weighted average common shares outstanding, basic and diluted	63,465,063	27,523,821	49,762,800	27,475,579

(1) Operating expenses include the following amounts of non-cash stock-based compensation expense:

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2024	**2023**	**2024**	**2023**
Research and development expense	$ 384	$ 548	$ 1,275	$ 1,670
General and administrative expense	1,190	1,313	3,643	3,782
Total stock-based compensation expense	$ 1,574	$ 1,861	$ 4,918	$ 5,452

# # #

Unleashing the Potential of Immuno-Oncology Therapies

November 7, 2024

Forward-Looking Statements and Disclaimers

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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 researc 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 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 int 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 US Inc., a member of the Roche Group.

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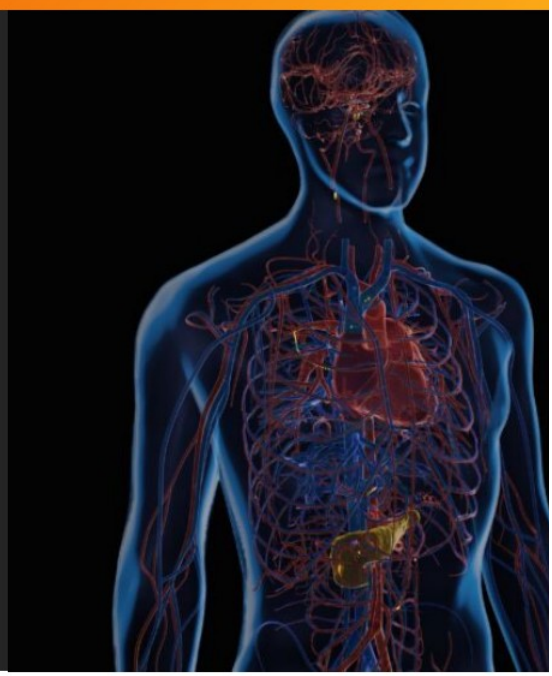
Immuno-Oncology Therapy is the Key to Curative Potential, But Continues to Be Limited by Systemic Toxicity

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**



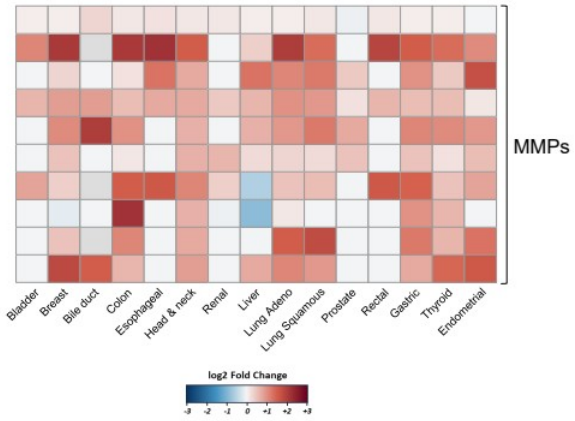
xilio THERAPEUTICS

I-O: immuno-oncology

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

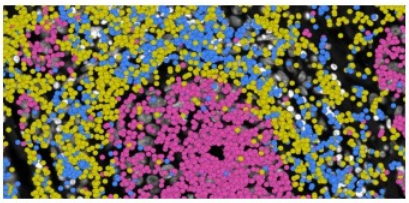
MMPs are dysregulated broadly across solid tumors

MMP mRNA expression in tumor vs. normal tissue

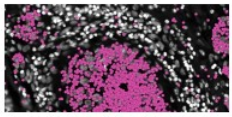


MMPs and immune cells co-localize at the invasive edge of tumors

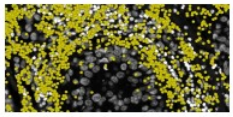
In situ mRNA expression in human breast cancer



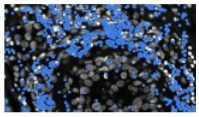
Tumor cells (TROP2)



MMP (MMP2)



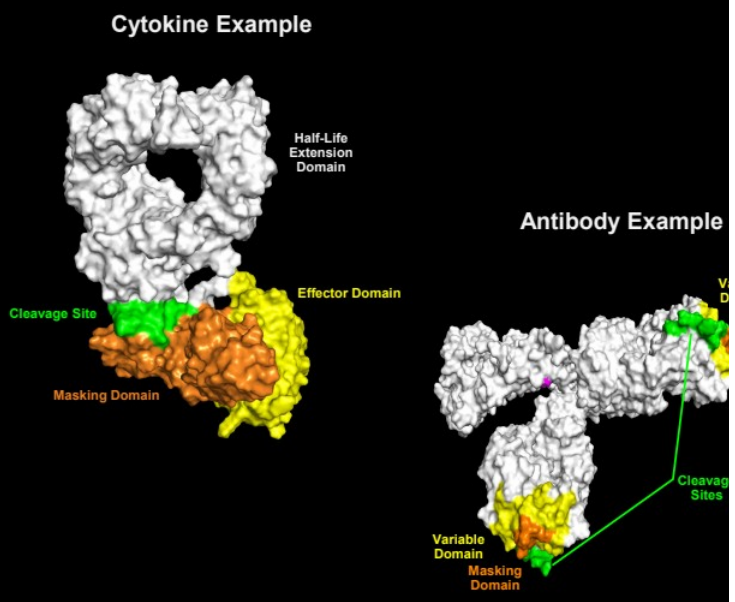
T cells (CD4, CD8A)



Left panel: Heatmap summarizing RNA expression changes of genes encoding for selected MMPs (bottom) in tumor vs. adjacent normal samples from multiple TCGA studies (x-axis). Color intensity tracks with log2-transformed fold changes (log2FC). Pre-processed TCGA data were obtained from UCSC Xena. **Right panel:** Spatial gene expression analysis using Xenium platform (10X Genomics) showing expression of TROP2 (TACSTD2, pink), MMP2 (yellow), CD4 and CD8A (blue) in a human breast cancer sample. https://www.10xgenomics.com/products/xenium-in-situ/human-breast-dataset-explorer; Xenium Explorer Version 1.2.0; Instrument Analysis Version: Xenium- 1.0.1
MMP: matrix metalloproteases

Xilio's Tumor-Activated Approach Has Been Successfully Applied in the Clinic Acro 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

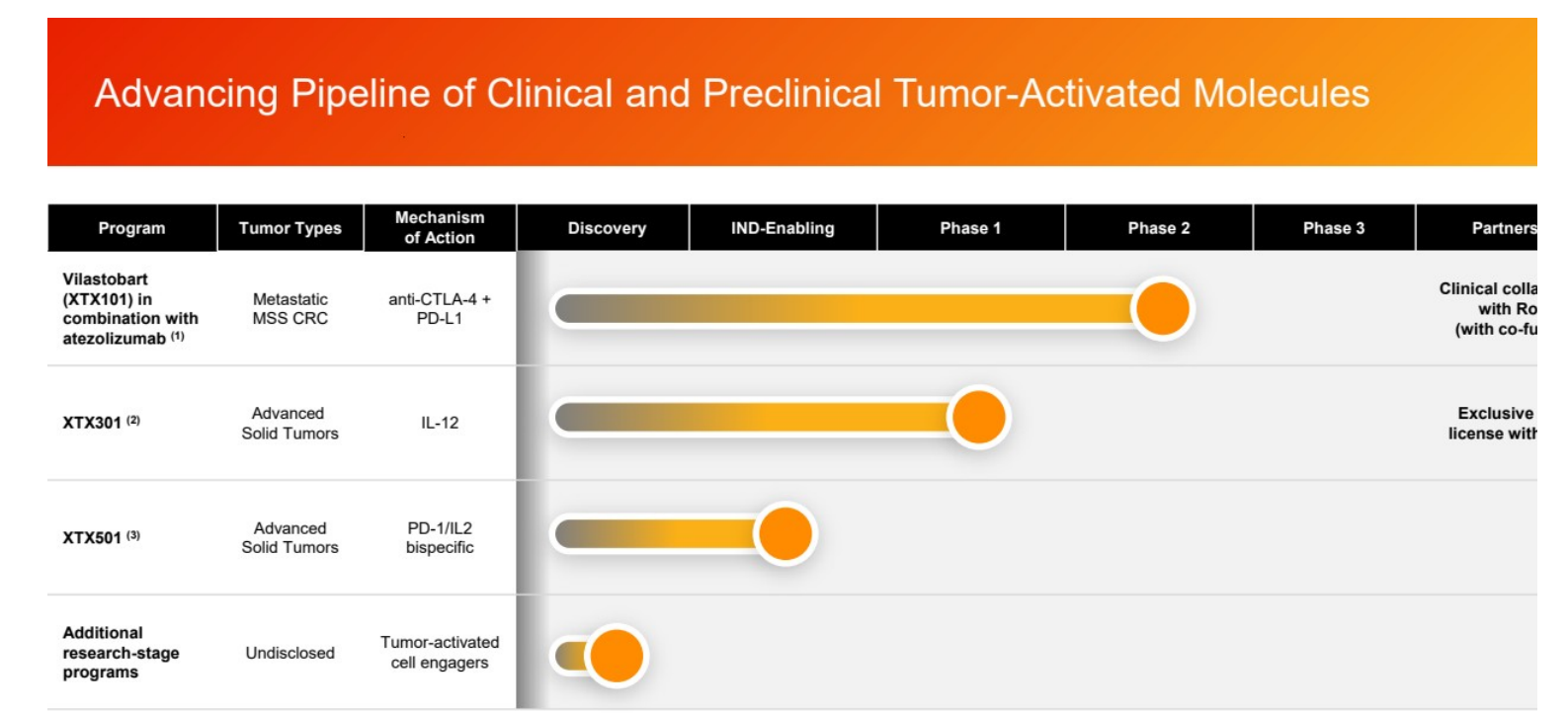


xilio THERAPEUTICS

TME: tumor microenvironment

Advancing Pipeline of Clinical and Preclinical Tumor-Activated Molecules

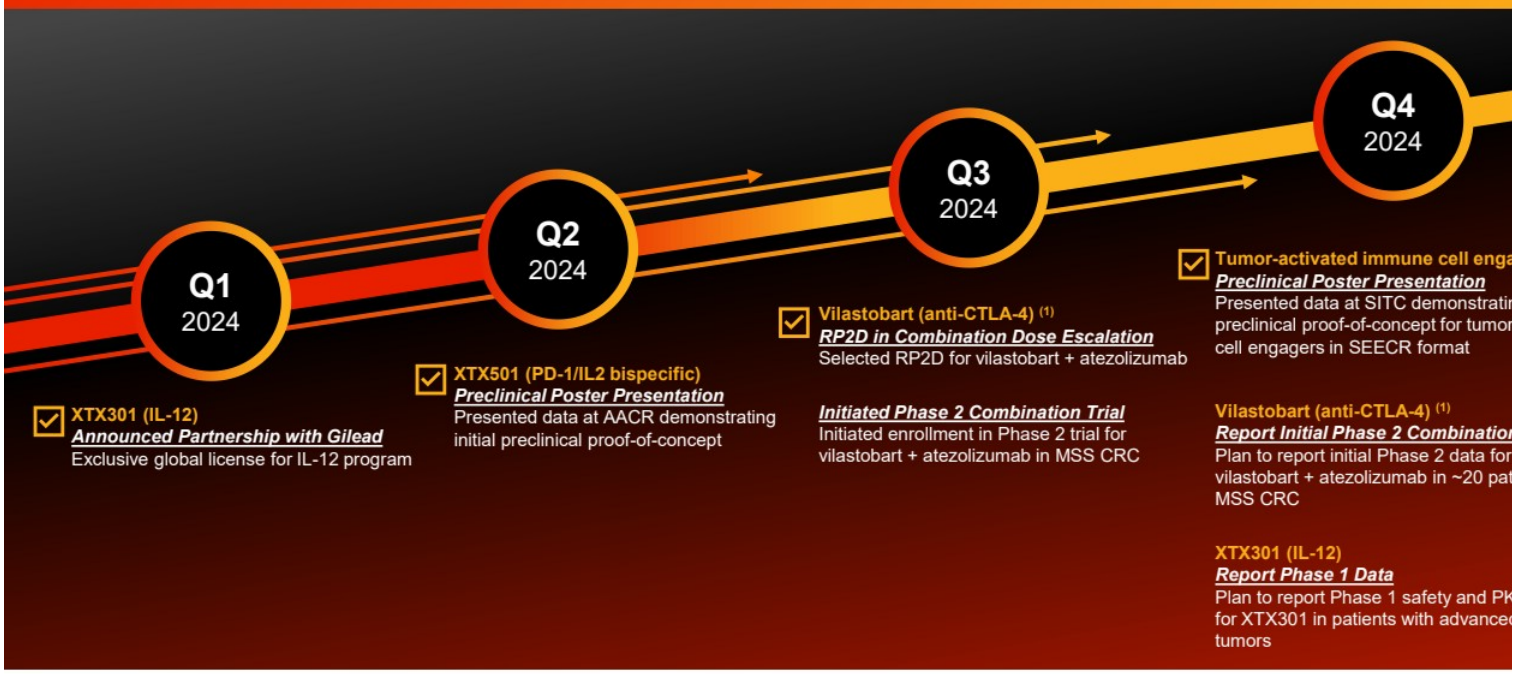
Program	Tumor Types	Mechanism of Action	Discovery	IND-Enabling	Phase 1	Phase 2	Phase 3	Partners
Vilastobart (XTX101) in combination with atezolizumab [1]	Metastatic MSS CRC	anti-CTLA-4 + PD-L1						**Clinical colla with Ro (with co-fu**
XTX301 [2]	Advanced Solid Tumors	IL-12						**Exclusive license with**
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

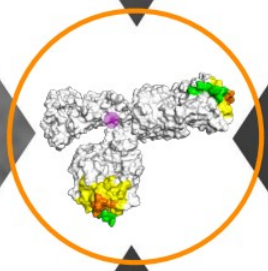
Positioned for Multiple Anticipated Key Clinical Milestones in Q4 2024



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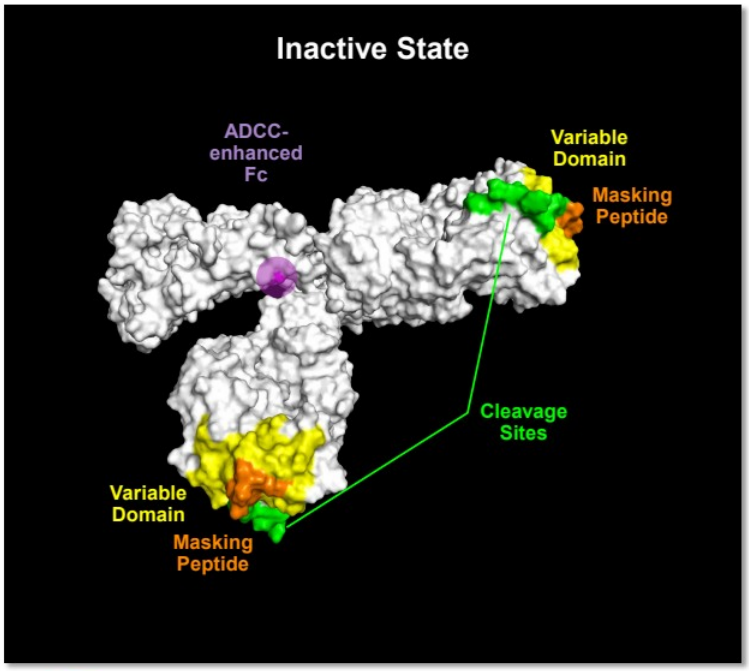
Vilastobart: Tumor-Activated, High Affinity Binding, Fc-Enhanced Anti-CTLA-4



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 a PD-L1 negative NSCLC patient, including resolution innumerable liver metastases

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* 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 CR in Co-Funded Clinical Collaboration with Roche

Phase 2 Combination Proof-of-Concept Trial	***Anticipated Near-Term Phase 2 Data Milestones***
Metastatic MSS CRC patients with and without liver metastases vilastobart at 100 mg Q6W + atezolizumab at 1200 mg Q3W	❑ Initial data (n = ~20 total) in MSS CRC in Q4 2024 ❑ Additional data (n = ~40 total) in MSS CRC in Q1 2025

Currently Enrolling

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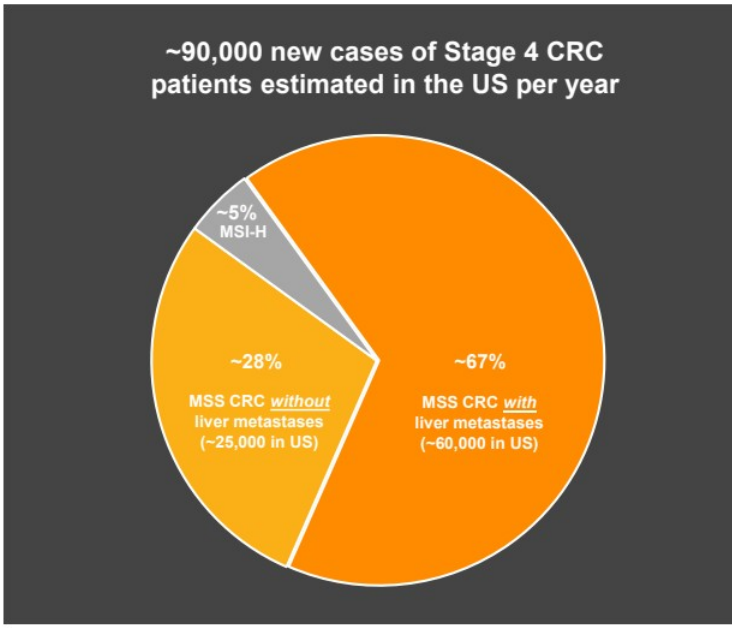
Q3W: once every three weeks; Q6W: once every six weeks

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

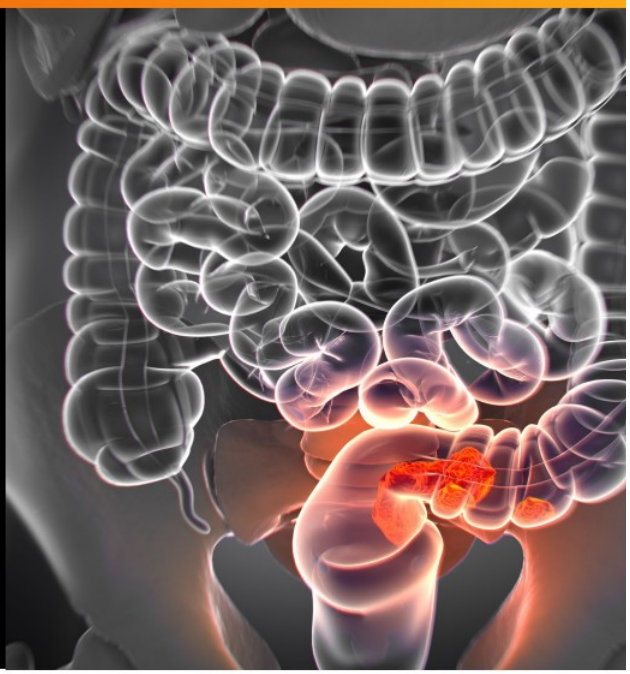
- CRC is 2nd in cancer-related deaths in the US and leading cause of cancer-related death in men younger than 50 in the US (1)
- CRC is 3rd in total annual new cases globally, with ~1.9M new cases and ~900,000 deaths related to CRC globally (2)
- >65% of Stage 4 CRC patients present with liver metastases,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

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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%)

83% of patients had ≥3 prior lines of treatment

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
Continuing on Treatment	**7**
Discontinued Treatment	**10**
Progressive Disease	1
Adverse Events	2
Consent Withdrawal	4
Death	0
Investigator Decision	3

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

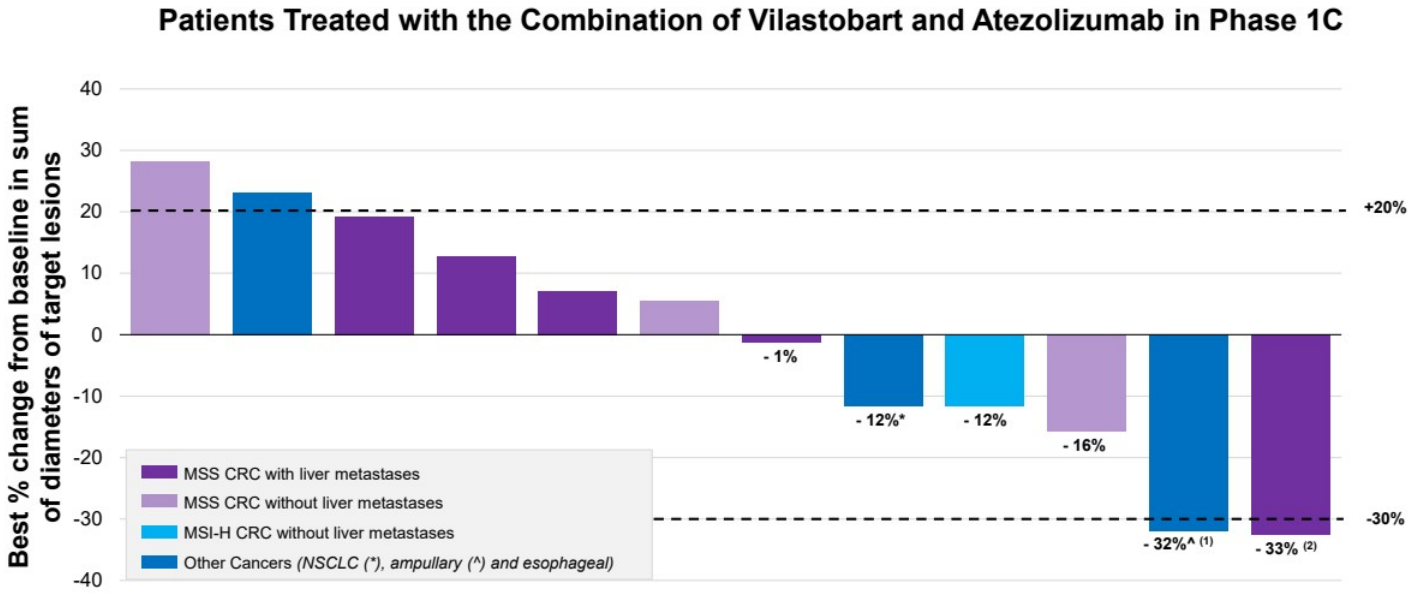
Combination of Vilastobart (anti-CTLA-4) and Atezolizumab Was Generally Well-Tolerated with Minimal irAEs

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

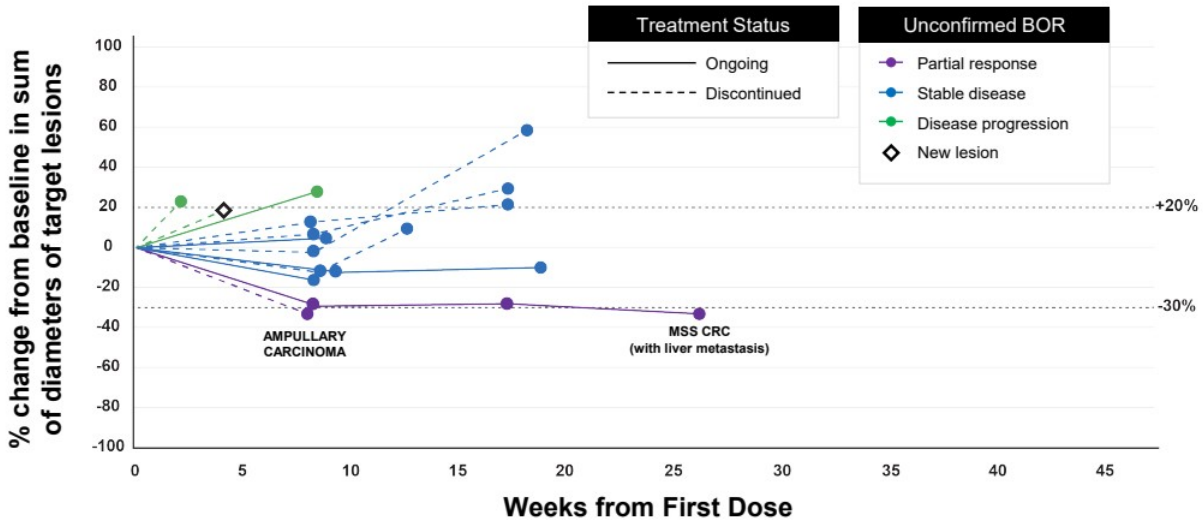
Combination of Vilastobart (anti-CTLA-4) and Atezolizumab Demonstrated Anti-Tumor Activity in Cold Tumors, Including a Sustained Tumor Reduction in a MSS CRC Patient with Metastatic Liver Disease



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

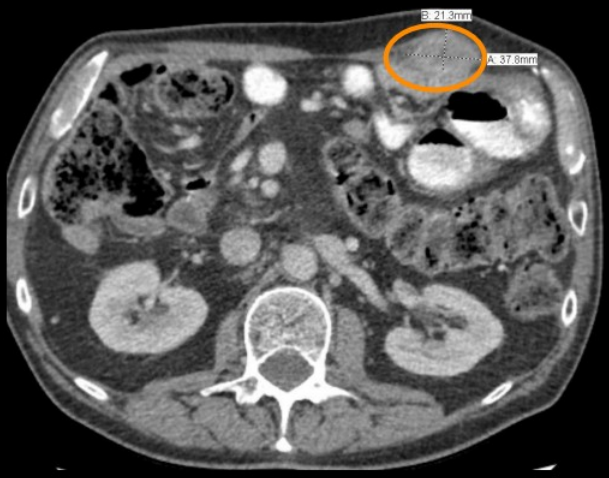
- 76 year-old male
- 2 prior lines of therapy:
  - Gemcitabine + nab-Paclitaxel
  - 5-fluorouracil + Irinotecan Liposome + Leucovorin
- Administered vilastobart (150 mg Q6W) + atezolizumab (1200 mg Q3W)
- Significant CA 19-9 decrease after a single cycle of the combination

	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**

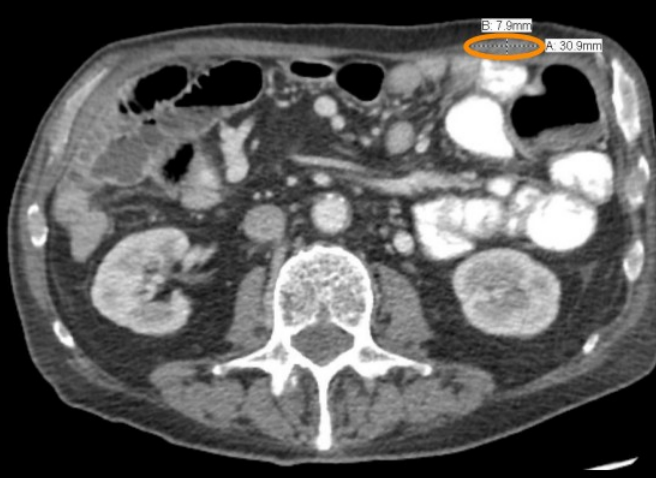
Data cutoff date: October 7, 2024
* Patient withdrew consent prior to confirmatory scan.
C1D1: cycle 1, day 1

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)

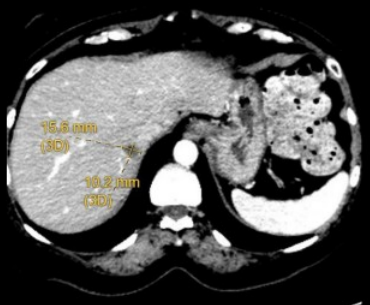
	Screening	1st follow-up (9 weeks)	2nd follow-up (18 weeks)	3rd follow- (27 week
Sum of diameters	98.4 mm	70.5 mm	71.0 mm	66.3 mm
Change		- 28%	- 28%	- 33%

Including full resolution of target lesion in the liver

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

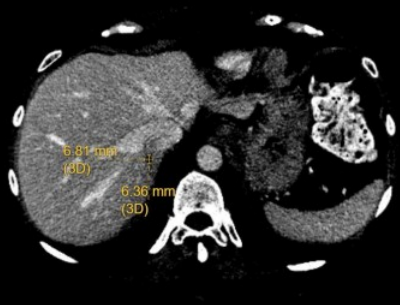
PR (Unconfirmed)* Including Resolution of Liver Metastatic Lesion in Patient With MSS CRC (33% Reduction in Sum of Diameters)

Target Liver Lesion – Baseline



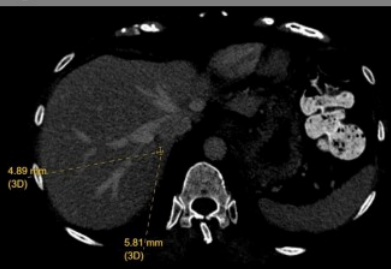
15.6 mm

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 202

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Data cutoff date: October 7, 2024

Vilastobart (XTX101)

Phase 1 Monotherapy Clinical Data

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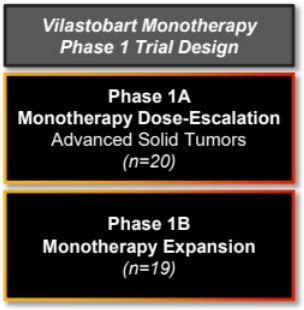
Phase 1 Monotherapy Trial for Vilastobart (anti-CTLA-4) Included Patients With a Wide Range of Advanced/Refractory Solid Tumors



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 (
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

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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*

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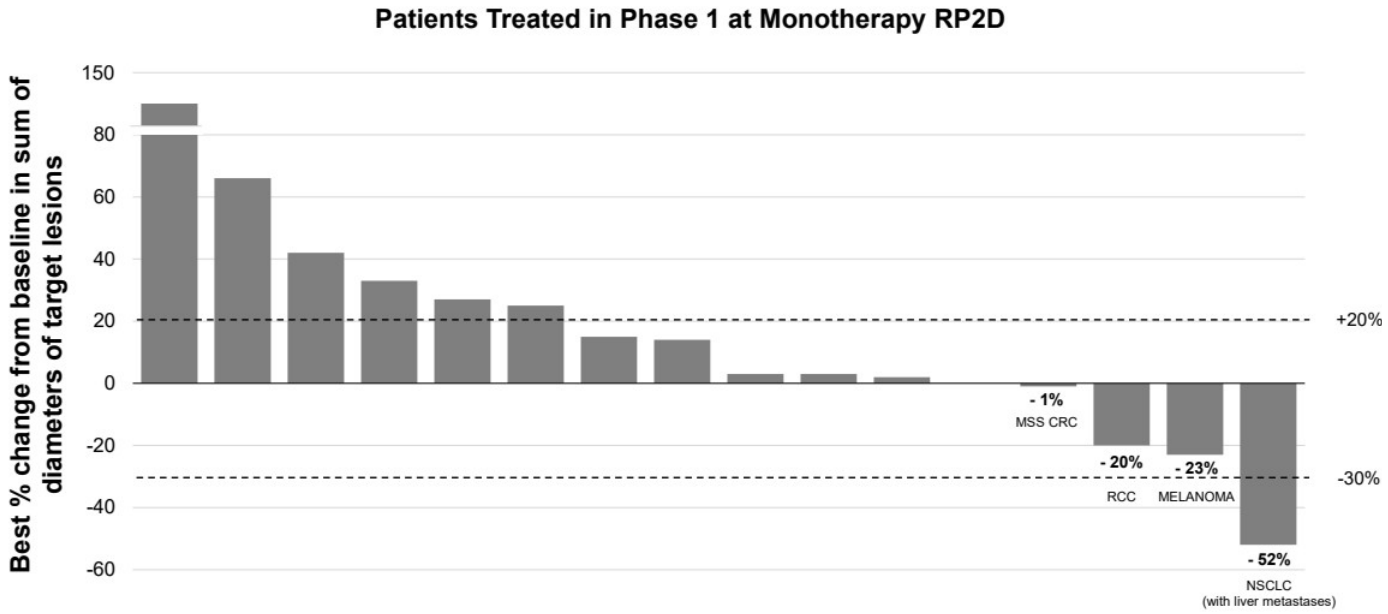
Data cutoff date: October 7, 2024

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



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 Confirme 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-u *(36 weeks*
Sum of diameters	93.0	60.0	45.0
Change		**- 35%**	**- 52%**

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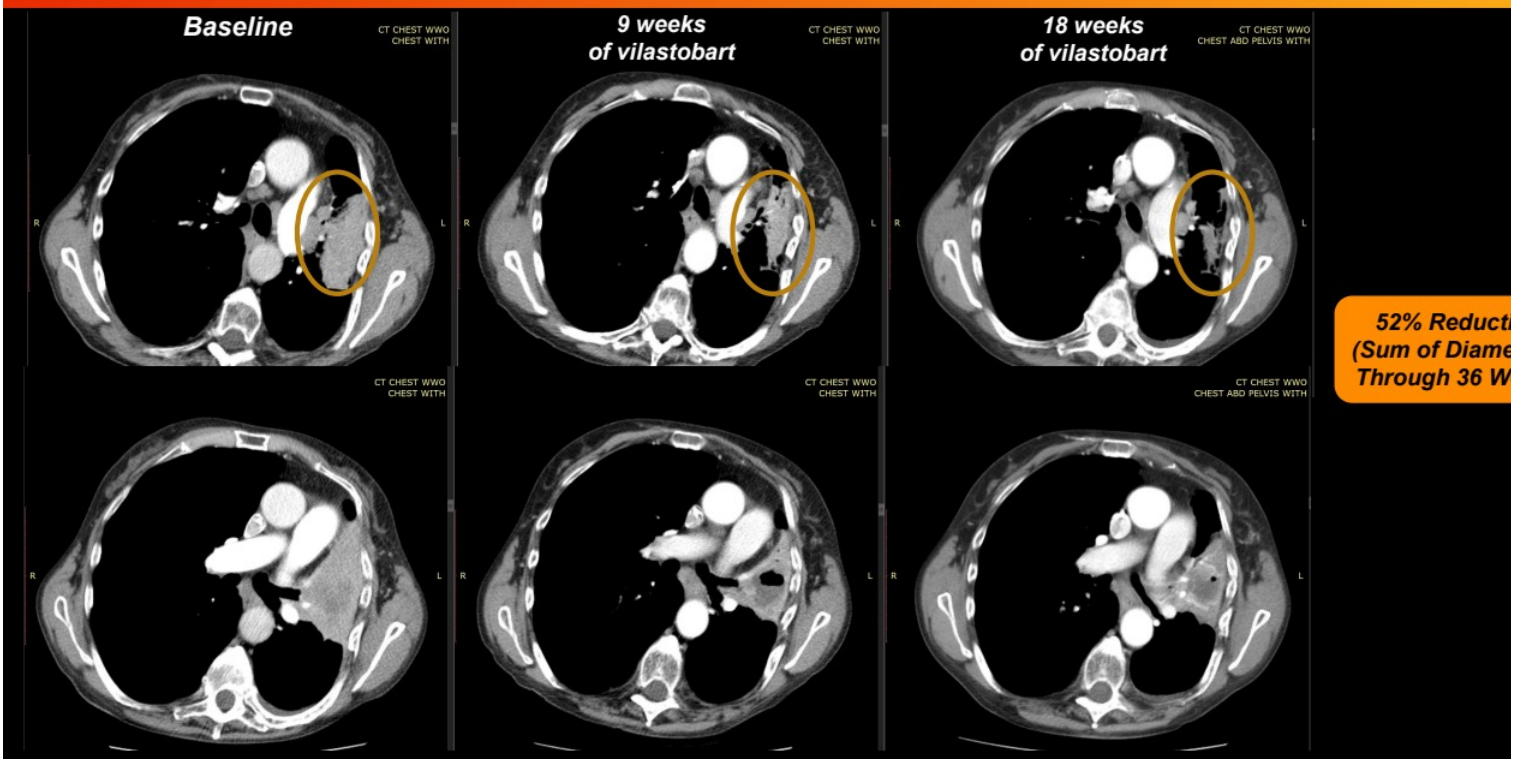
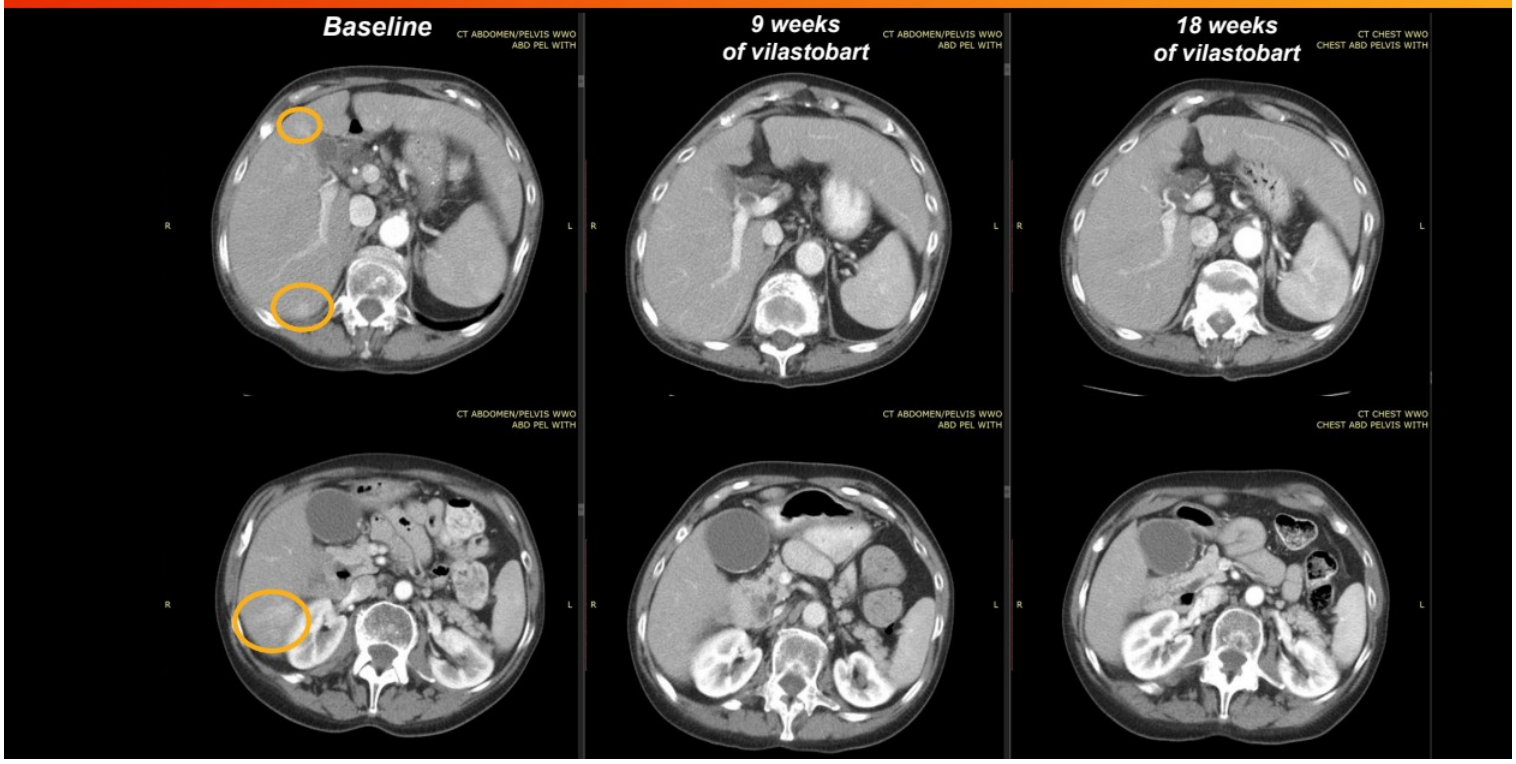
Data cutoff date: October 7, 2024

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

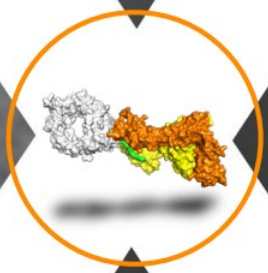


Vilastobart (anti-CTLA-4) 150 mg Q6W Demonstrated Durable Resolution of Hepat Metastases Through 36 Weeks in a Patient with PD-L1 Negative NSCLC



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

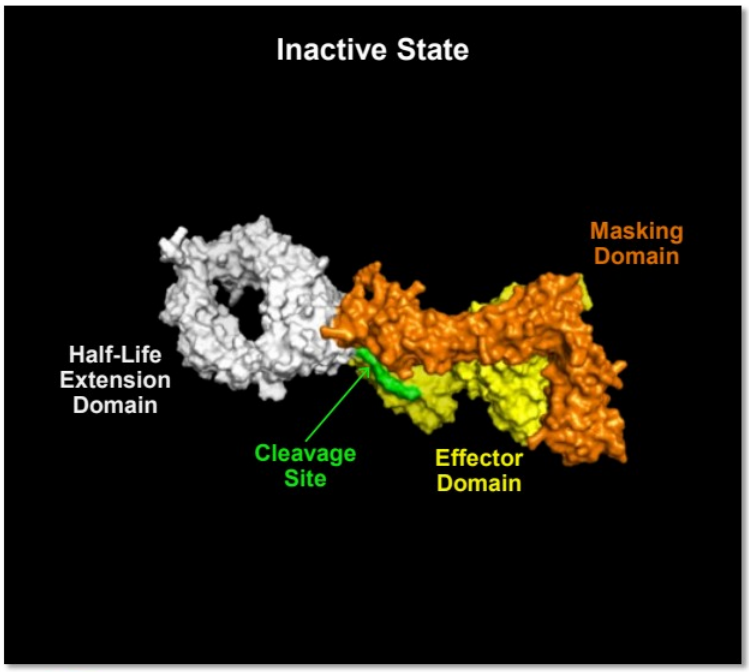
Capable of polarizing CD4 T-cells towards Th1 phenotype, thus driving cellular immunity against infection and cancer

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

Demonstrated si
agent objectiv
responses in pati
but poorly tolera
(MTD <500 ng/k
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 ha 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 vi* in preclinical model
- Potential for broad therapeutic index supported by robu preclinical data
- Generally well-tolerated with no DLTs observed in Phas 1 dose escalation to date

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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-activat IL-12 program, including XTX301

- Xilio responsible for clinical development of XTX30 in ongoing Phase 1 trial through initial planned Pha 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)

GILEA
Creating

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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

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 vi*
- 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 I 12 across solid tumors

Q4 2024

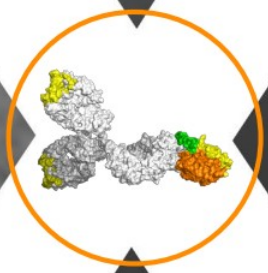
Next Anticipated Milestone

- 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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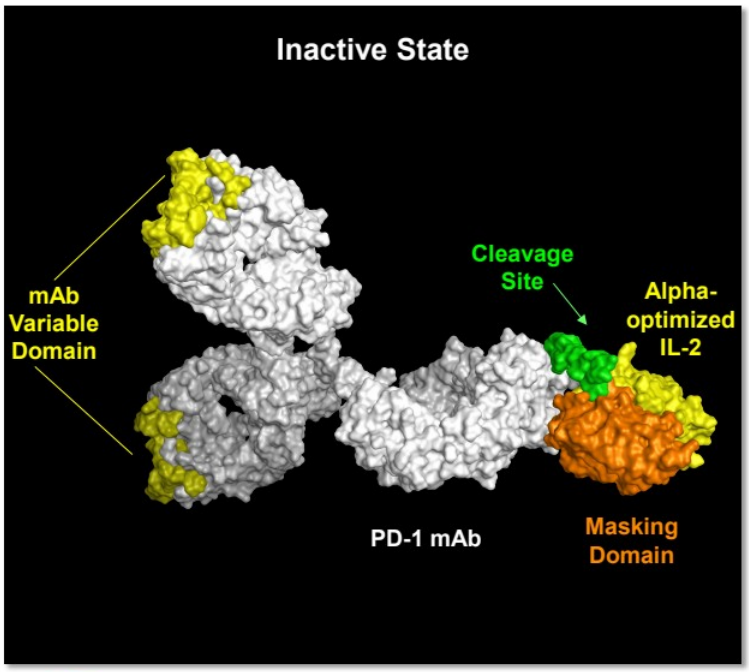
XTX501: Tumor-Activated PD1/IL2 Bispecific

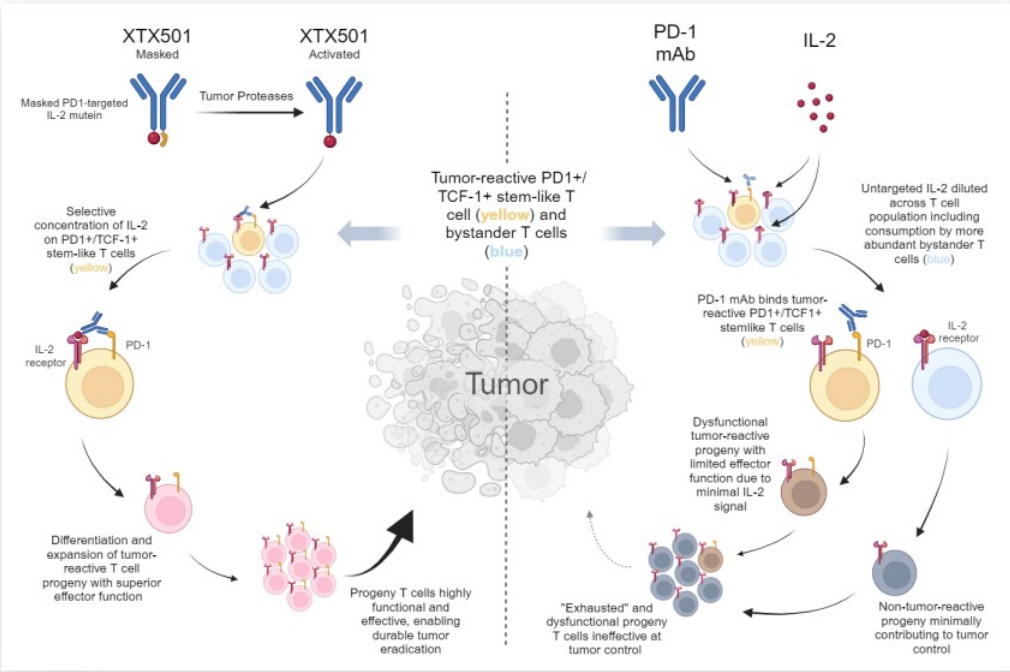


Demonstrated Synergistic Anti-Tumor Activity Antibody-Like PK and Favorable Tolerability i NHP

- 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 tolerabil in NHP

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

XTX501 Designed to Induce a Differentiated, Enhanced Immune Response Cancer Compared to PD-(L)1 Monotherapy or PD-(L)1 + IL-2 Combination

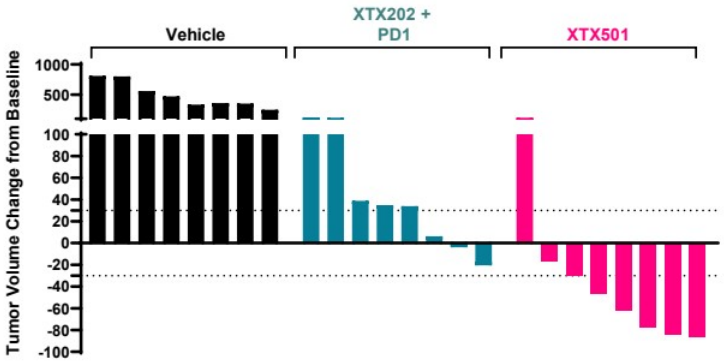


- Targeted delivery of IL-2 to PD1+ cells selectively enhance IL-2 signaling on tumor-reactiv stem-like T cells
- Drives unique differentiation program in progeny effector T cells endowing them with superior effector function and anti-tumor activity
- Not achievable with PD-(L)1 monotherapy or IL-2 combo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

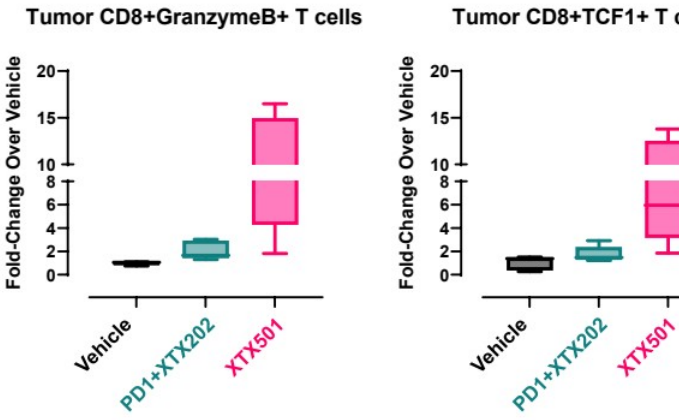
Figure adapted from Deak et al., OncoImmunology, 2023. Figure generated using BioRender.com.

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

Robust Preclinical Monotherapy Activity Beyond XTX202 + PD1 Combination

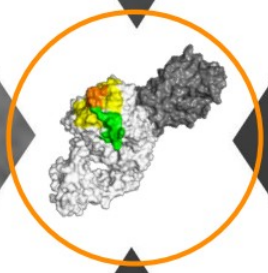


XTX501 Increased Intra-tumoral Cytotoxic a TCF1+ Stem-like T cells



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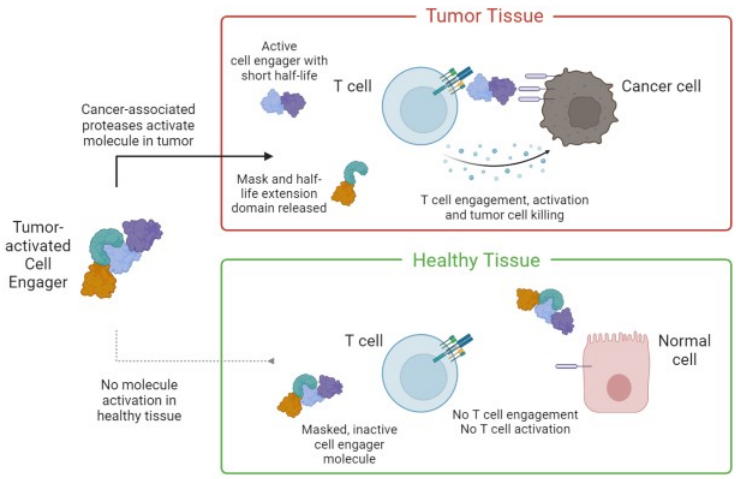
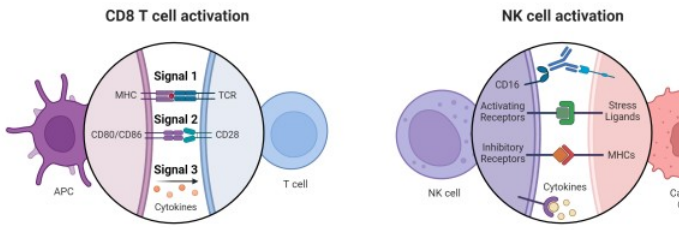
Xilio is Developing Tumor-Activated Cell Engagers Built on Our Validated Masking Approach and Conditional Half-Life Optimization

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



Selective Effector-Enhanced Cell EngageR (SEECR molecules)



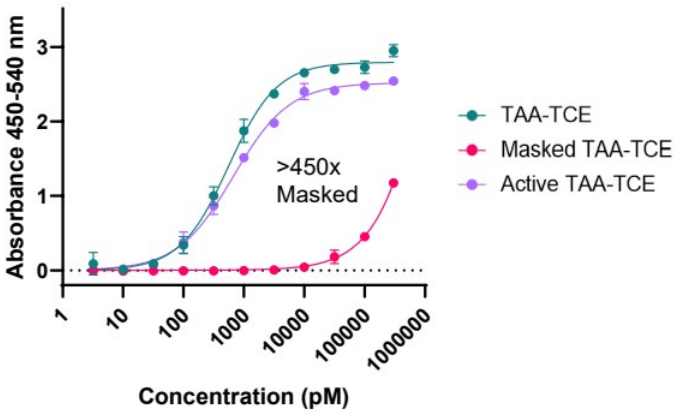
Design Goals

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

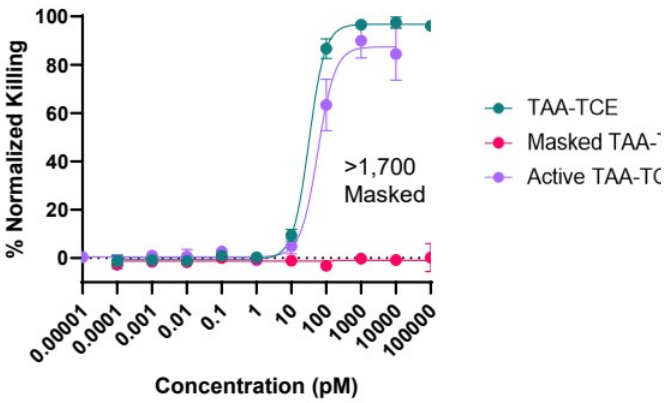
Illustrations generated using Biorender.com

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

Demonstrated Protease-Dependent Binding to CD3 by ELISA



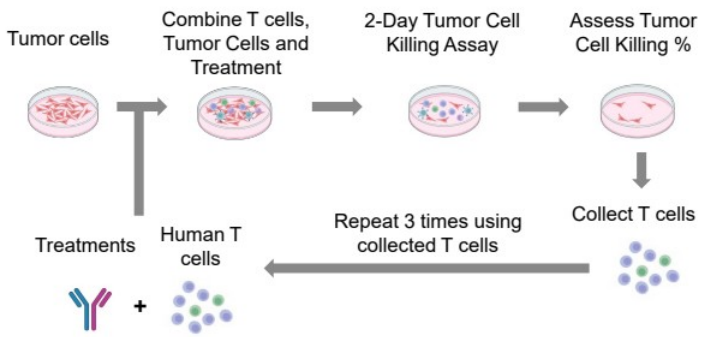
Confirmed Protease-Dependent Activity in Primary T Cell Assay



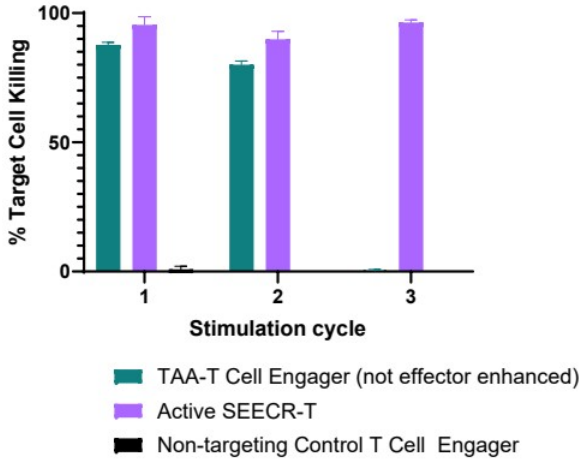
Left panel: Protease dependent CD3-binding demonstrated via TAA-TCEs bound to immobilized CD3 in an ELISA. **Right panel:** Protease-dependent tumor cell killing. Active TAA-TCEs led to killing in co-culture assay. A375 tumor cells were cultured overnight before addition of expanded T cells at a 5:1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



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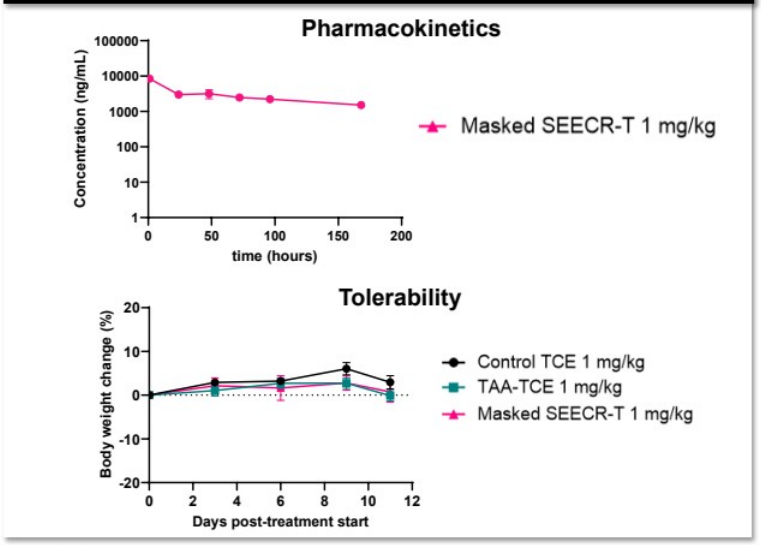
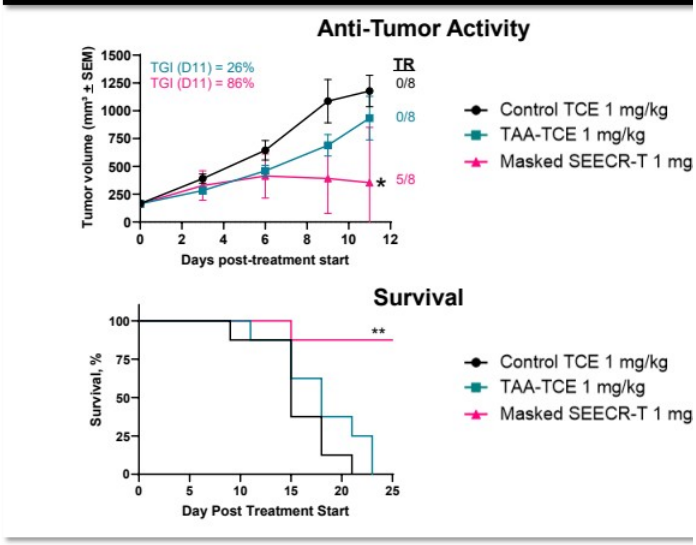
Human T cells were incubated over three consecutive rounds with indicated test articles and A431 cancer cells and percent tumor cell killing was assessed using a luminescence readout.

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



SEECR Showed Significantly Enhanced Activity a Survival Compared to Standard TCE



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,
Chief Development Officer

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

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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	$44.7

Statement of Operations

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

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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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Xilio Therapeutics Announces Initial Clinical Trial Data from Phase 1C Dose Escalation for Vilastobart (XTX101), a Tumor-Activated Anti-CTLA-4, in Combination with Atezolizumab in Patients with Advanced Solid Tumors

Combination of vilastobart and atezolizumab demonstrated encouraging early evidence of anti-tumor activity, including unconfirmed partial responses observed in two patients with difficult-to-treat, immunologically "cold" tumors

Complete resolution of a metastatic liver lesion observed in a patient with microsatellite stable colorectal cancer (MSS CRC)

Safety data indicated combination of vilastobart and atezolizumab was generally well-tolerated and support the potential of vilastobart to be a differentiated next-generation anti-CTLA-4 in combination with PD-(L)1 inhibitors

Continue to anticipate initial data from Phase 2 trial for combination of vilastobart and atezolizumab in metastatic MSS CRC patients with and without liver metastases in fourth quarter of 2024

Xilio Therapeutics to host investor conference call and webcast today at 4:30 pm EST

WALTHAM, Mass., November 7, 2024 – 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 clinical data from its ongoing Phase 1C clinical trial evaluating vilastobart (XTX101), a tumor-activated, Fc-enhanced, high affinity binding anti-CTLA-4, in combination with atezolizumab (Tecentriq®) in patients with advanced solid tumors. The data will be presented in a late-breaker poster presentation (abstract #1455) on November 8, 2024, at the Society for Immunotherapy of Cancer (SITC) 39th Annual Meeting taking place in Houston, Texas.

"These Phase 1 combination data for vilastobart and atezolizumab provide promising initial clinical evidence of the potential for the combination in patients with traditionally immunotherapy-resistant tumors, or "cold" tumors, including MSS colorectal cancer," said René Russo, Pharm.D., president and chief executive officer of Xilio. "In particular, we are encouraged by the potentially differentiated safety profile and two unconfirmed partial responses, including complete resolution of a metastatic liver lesion observed in a patient with MSS colorectal cancer. The majority of metastatic MSS colorectal cancer patients have liver metastases, which have proven to be resistant to existing immuno-oncology treatments, including combination treatments, and represent a significant unmet need. We look forward to sharing initial Phase 2 data for the combination of vilastobart and atezolizumab in patients with metastatic MSS colorectal cancer with and without liver metastases later this year."

"With the increasing incidence of MSS colorectal cancer, particularly in younger adults, the lack of effective treatment options for these patients represents one of the most significant challenges in oncology today," said Diwakar Davar, M.D., Associate Professor of Medicine, Clinical Director of the Melanoma Program and Medical Oncologist/Hematologist at the UPMC Hillman Cancer Center and the lead author of the study. "These initial combination data for vilastobart are encouraging as they show early evidence of meaningful anti-tumor activity in patients with traditionally immunotherapy-resistant tumors and highlight the potential for vilastobart to be a differentiated, next-generation anti-CTLA-4 in combination with PD-(L)1 inhibitors in MSS colorectal cancer and other tumors."

Data from Phase 1C Dose Escalation for Vilastobart (XTX101), a Tumor-Activated Anti-CTLA-4, in Combination with Atezolizumab

As of a data cutoff date of October 7, 2024, 17 patients had been treated with the combination of vilastobart at doses ranging from 75 mg to 150 mg once every six weeks (Q6W) and atezolizumab at 1200 mg once every three weeks (Q3W). Across all patients treated:

- Tumor types included MSS CRC (n=12) and microsatellite instability high (MSI-H) CRC, non-small cell lung cancer (NSCLC), esophageal cancer, ampullary carcinoma and cancer of the abdomen (n=1 each).
- The median age was 69 years (ranging from 39 to 77 years), and patients were generally heavily pre-treated.
- 83% of patients previously received three or more prior lines of anti-cancer therapy.

As of the data cutoff date, seven patients were continuing on treatment with the combination of vilastobart and atezolizumab, and 10 patients had discontinued treatment.

Initial Safety Data

Safety data support the potential for vilastobart to be a differentiated next-generation anti-CTLA-4 in combination with PD-(L)1 inhibitors—combination was generally well-tolerated with patients experiencing minimal immune-related adverse events

- Across all dose levels, no Grade 4 or Grade 5 treatment-related adverse events (AEs) were reported by investigators. In addition, no endocrine immune-related AEs (irAEs) and limited skin irAEs were reported by investigators. Only one patient (6%) experienced a dose reduction due to a treatment-related AE, and only one patient (6%) discontinued treatment of both vilastobart and atezolizumab due to a treatment-related AE.
- Across all dose levels, investigators reported Grade 3 treatment-related AEs in only three patients: alanine aminotransferase (ALT) increase (12%); diarrhea, colitis and blood alkaline phosphatase (ALP) increase (6% each). Of these Grade 3 treatment-related AEs, two patients at the 150 mg dose level for vilastobart had dose-limiting toxicities: one patient with Grade 3 colitis and diarrhea and one patient with Grade 3 ALT increase and blood ALP increase.
- Across all dose levels, the most common treatment-related AEs (≥10% incidence) of any grade reported by investigators were the following: infusion-related reactions (59%); aspartate aminotransferase (AST) increase, ALT increase and lipase increase (18% each); diarrhea, fatigue and blood ALP increase (12% each). Of the 10 patients with infusion-related reactions, four patients experienced reactions related to vilastobart, three patients experienced reactions related to atezolizumab and three patients experienced reactions related to the combination.

Initial Anti-Tumor Activity Data

Encouraging early evidence of anti-tumor activity, including partial responses (unconfirmed) in two patients with difficult-to-treat, immunologically "cold" tumors, including one patient with MSS CRC and a metastatic liver lesion

- ***Patient with MSS CRC and a metastatic liver lesion:*** A patient with MSS CRC and a metastatic liver lesion achieved a partial response (pending confirmation) per Response Evaluation Criteria in Solid Tumors (RECIST) (33% reduction in the sum of diameters of target lesions), including full resolution of the liver lesion. The patient previously progressed on five prior lines of therapy and was administered the combination of vilastobart at the 150 mg Q6W dose level and atezolizumab (1200 mg Q3W).
- ***Patient with ampullary carcinoma:*** A patient with ampullary carcinoma achieved a partial response (unconfirmed) per RECIST (32% reduction in the sum of diameters of target lesions) accompanied by a substantial decrease in the serum tumor marker CA 19-9 (from 700.2 at baseline to 40.8 after 6 weeks of treatment). CA 19-9 associated antigen levels are often significantly elevated in patients with pancreatic cancer. The patient previously progressed on two prior lines of therapy and was administered the combination of vilastobart at the 150 mg Q6W dose level and atezolizumab (1200 mg Q3W). The patient withdrew consent prior to undergoing a confirmatory scan.

Clinical Development Plans for Vilastobart

The initial Phase 1C data supported the selection of an initial recommended Phase 2 dose (RP2D) for vilastobart at 100 mg Q6W in combination with atezolizumab at 1200 mg Q3W. In addition, Xilio continues to enroll patients in Phase 1C dose escalation for the combination of vilastobart at the 150 mg Q6W dose level and atezolizumab at 1200 mg Q3W.

Xilio is currently enrolling patients in its ongoing Phase 2 clinical trial evaluating the combination of vilastobart and atezolizumab at the initial combination RP2D in patients with metastatic MSS CRC, including patients with and without liver metastases.

Xilio expects to report initial Phase 2 data for the combination in approximately 20 patients with metastatic MSS CRC in the fourth quarter of 2024 and additional Phase 2 data for the combination in a total of approximately 40 patients with metastatic MSS CRC in the first quarter of 2025.

Investor Conference Call Information

Xilio will host a conference call and webcast at 4:30 pm ET today (November 7, 2024) to discuss the Phase 1C dose escalation data for the combination of vilastobart and atezolizumab. Members of Xilio's management team will be joined by Aparna Parikh, M.D., Director of Colorectal Medical Oncology Research and Director of the Young Adult Colorectal Cancer Program at The Massachusetts General Hospital Cancer Center. The conference call may be accessed by dialing (800) 715-9871 (domestic) or (646) 307-1963 (international) and referring to conference ID 7645770. A webcast of the call will also be available 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 or any of Xilio's other current or future product candidates in treating patients as a monotherapy or combination therapy; 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 1C data for vilastobart), 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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Investor and Media Contact

Scott Young
Vice President, Investor Relations and Corporate Communications
investors@xiliotx.com