#### **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): December 18, 2024

# Xilio Therapeutics, Inc. (Exact Name of Registrant as Specified in Charter)

Delaware (State or Other Jurisdiction of Incorporation)

001-40925 (Commission File Number)

85-1623397 (IRS Employer Identification No.)

> 02451 (Zip Code)

828 Winter Street, Suite 300

Waltham, Massachusetts
(Address of Principal Executive Offices)

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

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

	Common stock, par value \$0.0001 per share	XLO	Nasdag Global Select Market			
	Title of each class	Trading symbol(s)	Name of each exchange on which registered			
Secu	rities registered pursuant to Section 12(b) of the Act:					
	Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))					
	Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))					
	Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)					
	Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)					
	ek the appropriate box below if the Form 8-K filing is intended to uction A.2. below):	simultaneously satisfy the filing obligation of the reg	istrant under any of the following provisions (see General			

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.  $\Box$ 

#### Item 3.02. Unregistered Sales of Equity Securities.

As previously disclosed, in connection with Xilio Development, Inc., a wholly-owned subsidiary of Xilio Therapeutics, Inc. (the "Company"), entering into an exclusive license agreement with Gilead Sciences, Inc. ("Gilead"), on March 27, 2024, the Company entered into a stock purchase agreement (the "Stock Purchase Agreement") with Gilead pursuant to which the Company agreed to issue and sell up to an aggregate of \$25.0 million of the Company's common stock to Gilead (or at Gilead's election, prefunded warrants in lieu of shares of common stock) in an initial private placement and up to three additional private placements through March 2025. In March 2024, the Company initially issued and sold 6,860,223 shares of common stock to Gilead at a purchase price of \$1.97 per share and received approximately \$13.5 million in aggregate gross proceeds, and in April 2024, the Company issued and sold an additional 485,250 shares of its common stock at a purchase price of \$0.76 per share and received approximately \$3.3 million in aggregate gross proceeds.

On December 18, 2024, the Company issued and sold an aggregate of 1,759,978 shares of common stock at a purchase price of \$1.04 per share and a prefunded warrant to purchase up to an aggregate of 6,092,816 shares of common stock (collectively, the "Securities") at a purchase price of \$1.0399 per share underlying such prefunded warrant and received approximately \$8.2 million in aggregate gross proceeds. Upon the closing of the sale of the Securities, the Company has issued and sold to Gilead an aggregate of approximately \$25.0 million in common stock and prefunded warrants to purchase common stock, representing the maximum aggregate investment under the Stock Purchase Agreement.

The prefunded warrants issued in April 2024 and December 2024, respectively, are exercisable any time at an exercise price of \$0.0001 per share, subject to Gilead not being deemed a beneficial owner of greater than 19.9% of the Company's common stock upon the exercise of the prefunded warrants.

The issuance and sale of the Securities has not been registered under the Securities Act of 1933, as amended (the "Securities Act"), or any state securities laws. Based in part upon the representations of Gilead in the Stock Purchase Agreement, the Company has relied on the exemption from the registration requirements of the Securities Act under Section 4(a)(2) thereof for a transaction by an issuer not involving any public offering.

The foregoing descriptions of the Securities Purchase Agreement and the Prefunded Warrant are qualified in their entirety by reference to the complete text of the Stock Purchase Agreement and the form of prefunded warrant, copies of which are attached hereto as Exhibits 10.1 and 4.1, respectively, and incorporated by reference into this Item 3.02.

#### 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 Company has included its website address in this Current Report on Form 8-K solely as an inactive textual reference. A copy of the presentation is furnished as Exhibit 99.1 to this Current Report on Form 8-K.

The information in this Item 7.01 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 or the Exchange Act, except as expressly set forth by specific reference in such filing.

#### Item 8.01. Other Events.

Phase 1 Clinical Data for XTX301 (IL-12)

On December 19, 2024, the Company issued a press release announcing preliminary data from its ongoing Phase 1 clinical trial evaluating XTX101, a tumor-activated IL-12, in patients with advanced solid tumors. 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.

#### Financial Guidance

After giving effect to the proceeds from the additional private placement to Gilead on December 18, 2024, and based on the Company's current operating plans, the Company now anticipates that its existing cash and cash equivalents will be sufficient to fund its operating expenses and capital expenditure requirements into the third quarter of 2025.

#### Cautionary Note Regarding Forward Looking Statements

This Form 8-K contains forward-looking statements that involve estimates, assumptions, risks and uncertainties. Forward-looking statements include, but are not limited to, statements related to the period in which the Company expects to have eash to fund its operations, and the Company's strategy, goals and anticipated financial performance, milestones, business plans and focus. The risks and uncertainties relating to the Company and the transactions include general market conditions and other risks detailed from time to time in the Company's filings with the SEC, including in its Quarterly Report on Form 10-Q for the quarter ended September 30, 2024. Any forward-looking statements contained in this 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
4.1	Form of Prefunded Warrant (incorporated by reference to Exhibit 4.1 to the Registrant's Current Report on Form 8-K (File No. 001-40925), filed with the
	Securities and Exchange Commission on March 28, 2024)
10.1	Common Stock Purchase Agreement, dated March 27, 2024, between Xilio Therapeutics, Inc. and Gilead Sciences, Inc. (incorporated by reference to
	Exhibit 10.2 to the Registrant's Quarterly Report on Form 10-Q for the quarter ended March 31, 2024, field with the Securities and Exchange Commission
	on May 14, 2024)
99.1	Corporate investor presentation of Xilio Therapeutics, Inc., dated December 19, 2024
99.2	Press release issued by Xilio Therapeutics, Inc. on December 19, 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: December 19, 2024

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

# Unleashing the Potential of Immuno-Oncology Therapies

**December 19, 2024** 



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## 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 Phase 2 clinical data vilastobart in combination with atezolizumab in patients with microsatellite stable (MSS) colorectal cancer; the potential benefits of any of Xilio's current or future product candidates in treating patients 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," "project," "project," "potential," "continue," "seek," "target" and similar expressions a 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 managen 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 any forward-looking statements contained in this presentation, including, without limitation, general market conditions, risks and uncertainties related to ongoing and planned research and developmen 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 attalics 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 candidate

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 Commic (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 ar obligation to update any forward-looking statements.

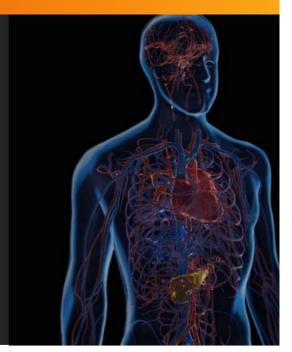
Certain information contained in this presentation relates to or is based on studies, publications, surveys and other data obtained from third-party sources and Xilio's own internal estimates and resear While Xilio believes these third-party studies, publications, surveys and other data to be reliable 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 intestimates 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.



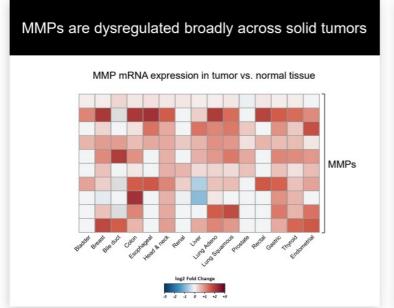
# Immuno-Oncology Therapy is the Key to Curative Potential, But Continues to Be Limited by Systemic Toxicity

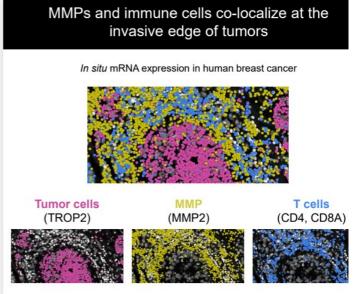
Xilio believes the next revolution in I-O therapy will harness the power of the body's immune system
by leveraging the dysregulated biology
of the tumor against itself





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



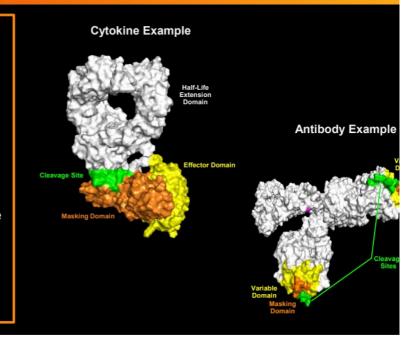




Left panel: Heatmap summarizing RNA expression changes of genes encoding for selected MMPs (bottom) in tumor vs. adjacent normal samples from multiple TCGA studies (x-axis). Color intensity tracks with log2-transformed fold changes (log2FC). Pre-processed TCGA data were obtained from UCSC Xena. Right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

## 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





# Advancing Pipeline of Clinical and Preclinical Tumor-Activated Molecules

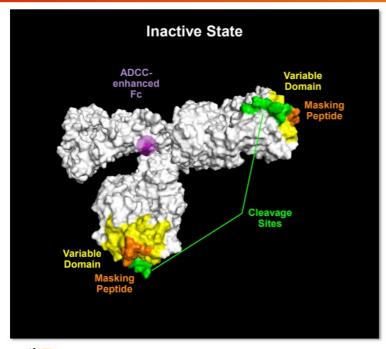
Program	Tumor Types	Mechanism of Action	Discovery	IND-Enabling	Phase 1	Phase 2	Phase 3	Partners
Vilastobart (XTX101) in combination with atezolizumab <sup>(1)</sup>	Metastatic MSS CRC	anti-CTLA-4 + PD-L1						Clinical colla with Ro (with co-fu
XTX301 <sup>(2)</sup>	Advanced Solid Tumors	IL-12						Exclusive license with
XTX501 (3)	Advanced Solid Tumors	PD-1/IL2 bispecific						
Additional research-stage programs	Undisclosed	Tumor-activated cell engagers						



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



## 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 preclinic 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 <159 activated molecule in periphery
- Generally well-tolerated in Phase 1 monotherapy, consiste with tumor-activated design
- Confirmed PR observed with monotherapy in Phase 1 in a PD-L1 negative NSCLC patient, including resolution of innumerable liver metastases
- Confirmed PR observed with combination in Phase 1 in MI CRC patient, including full resolution of liver metastasis



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

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

## Phase 2 Combination Proof-of-Concept Trial

Metastatic MSS CRC patients with and without liver metastases

vilastobart at 100 mg Q6W + atezolizumab at 1200 mg Q3W

#### Currently Enrolling

# Anticipated Near-Term Phase 2 Data Milestones

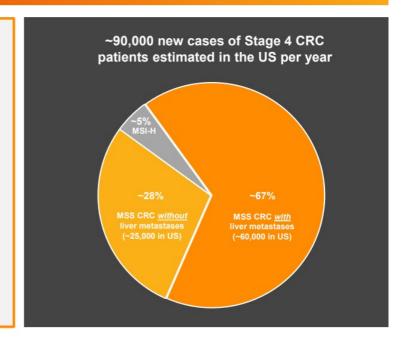
- Plan to report initial Phase 2 data (n = ≥20 total) in MSS CRC at ASCO GI in January 2025
- □ Plan to report additional Phase 2 data (n = ~40 total) i MSS CRC in mid 2025

X-ILIO

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 2<sup>nd</sup> 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 3<sup>rd</sup> 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 lateline 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



# 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

#### **Advanced solid tumors**

vilastobart at 75, 100 and 150 mg Q6W + atezolizumab at 1200 mg Q3W

Currently enrolling

### Phase 2 Combination Proof-of-Concept

Metastatic MSS CRC patients with and without liver metastases

vilastobart at 100 mg Q6W + atezolizumab at 1200 mg Q3W

Currently enrolling



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

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

1

Treatment discontinuation due to TRAE (2)

- 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.

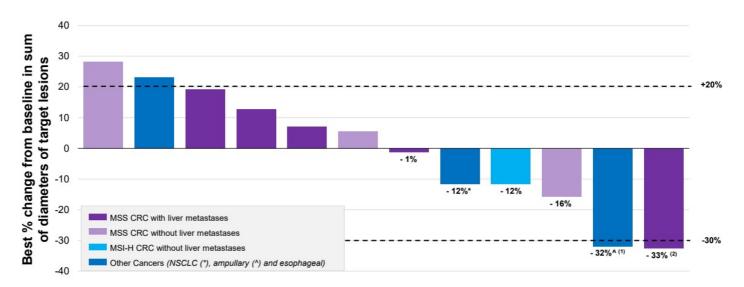
2. Reflects discontinuation of both vilastobart and atezolizumab.

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

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





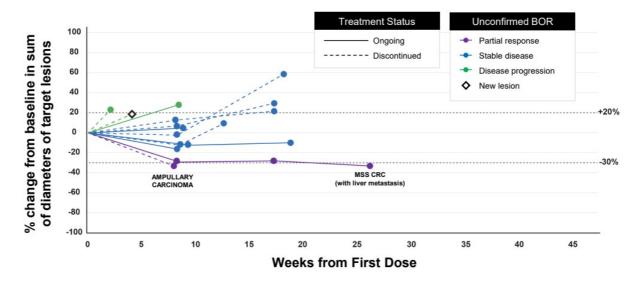
Data cutoff date: October 7, 2024. n=12 response-evaluable patients.

1. PR (unconfirmed), patient withdrew consent prior to confirmatory scan.

2. PR confirmed after the data cutoff date.

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

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





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

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

## MSS CRC and Liver Metastasis

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

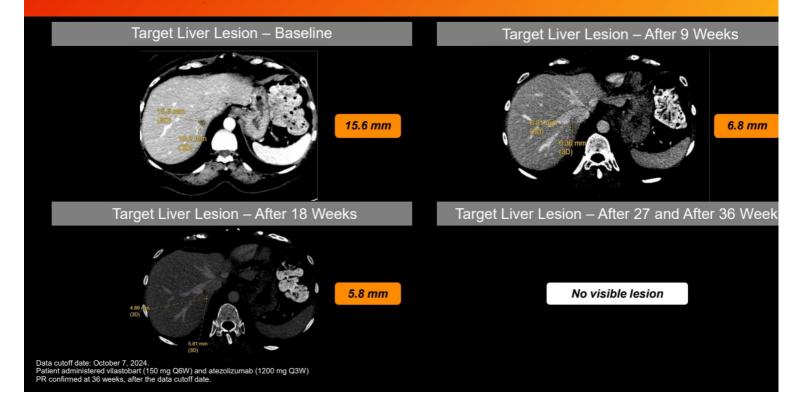
	Screening	1st follow-up (9 weeks)	2 <sup>nd</sup> follow-up (18 weeks)	3 <sup>rd</sup> follow-up (27 weeks)	4 <sup>th</sup> follo (36 we
					63.8
Change		- 28%	- 28%	- 33%	-35

Including full resolution of target lesion in the liver



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

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



# 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

	Scr	eening	8 weeks after C1D1
Sum of diameters	60	.5 mm	41.2 mm
Change			- 32%
Serum tumor marker	Screening	C1D1	6 weeks after C1D1
CA 19-9 (U/mL)	575.0	700.2	40.8



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

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

# Target Lesion At Screening

B 7 9mm
A 30 9mm

Target Lesion After 8 weeks

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

\* PR (unconfirmed) at week 8 (32% reduction in sum of diameters). Patient withdrew consent prior to confirmatory scan

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

#### Initial Phase 1C Data for Combination of Vilastobart and Atezolizumab

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

#### Anticipated Near-Term Phase 2 Data Milestones

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



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



# 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 INFy induction results in broad remodeling of the TME towards a more immune-permissive environment



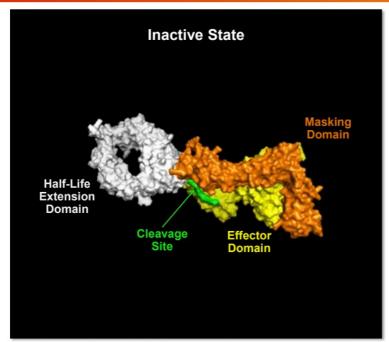
Demonstrated si agent objectiv responses in pati but poorly tolera (MTD <500 ng/kı repeat dosing



INFy 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.

INFy: interferon gamma; g/kg: nanograms/kilogram; NK: natural killer.

## XTX301: Tumor-Activated IL-12



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

- Activated XTX301 designed to have optimized short half-life IL-(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:<sup>(1)</sup>

  - Generally well-tolerated with no DLTs and no dose reductions observed to date
  - No Grade 4 or Grade 5 treatment-related AEs, with majority of treatment-related AEs Grade 1 or 2
- MTD not yet established and continuing to advance in Phase 1 dose escalation in partnership with Gilead



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

IFNy: interferon gamma

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

## \$55.0M

## total received to date

(\$30M cash upfront payment + \$25M in total equity investments)

# **Up to \$592.5M**

## additional contingent payments:

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

# **Tiered royalties:**

high single-digits to mid-teens

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

Gilead received an exclusive global license to devel 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 tr
- Following delivery by Xilio of specified clinical data package for XTX301, Gilead can elect to pay transition fee and transition development and commercialization Gilead (1)







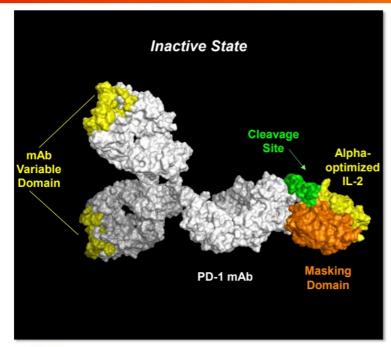
# XTX501 Has Potential to be Best-in-Class PD1/IL2 Bispecific

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

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



# XTX501: Tumor-Activated PD1/IL2 Bispecific



Demonstrated Synergistic Anti-Tumor Activity, Antibo 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 tolerabil in NHP

xiliō

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

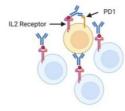
# XTX501 is Designed to Overcome Limitations of Non-Masked PD1/IL2 Bispecifics

#### Periphery



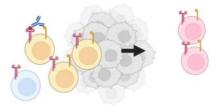
#### Non-masked PD1/IL2

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



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

#### Tumor

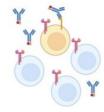


Lower concentration of unmasked PD1/IL2 in the TME reduces activation of tumor reactive PD1\* T cells (yellow), results in lower numbers of progeny functional effector T cells (pink) and reduces overall activity

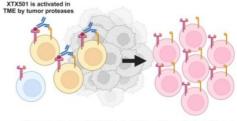


#### XTX501

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



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



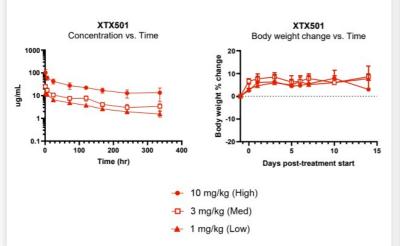
High concentration of XTX501 in the TME enables activation of tumorreactive PD1\*T cells, higher numbers of progeny functional effector T cells



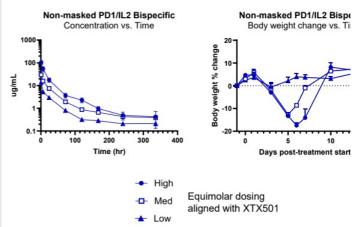
Figure generated using BioRender.com.

# Tumor-Activated Design of XTX501 Enabled Optimal PK and Tolerability

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



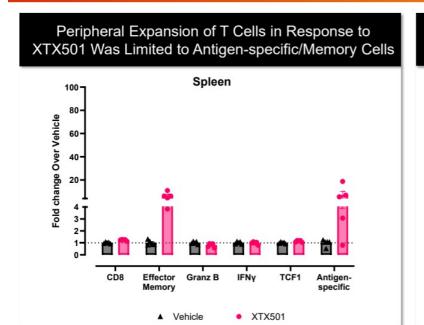
# Non-Masked PD1/IL2 Bispecific Was Rapidl Cleared and Poorly Tolerated



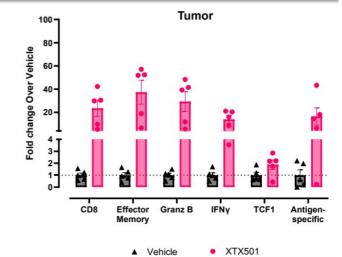


XTX501 exposure after a single 10, 3 or 1 mg/kg intravenous (i.v) injection in non-tumor bearing C57BL/6-hFcRn mice. Non-masked PD1/IL2 exposure after a single equal molar dose of 9.25, 2.75 or 0.92 mg/kg intravenous (i.v) injection in non-tumor bearing C57BL/6-hFcRn mice. Body weight data are displayed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

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



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

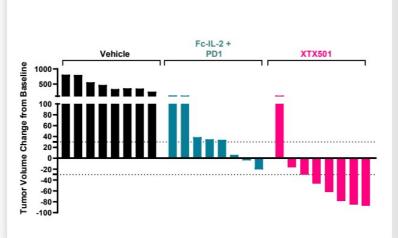




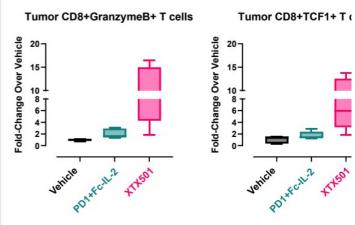
Female C57BL/6 hPD-1 mice (n=5 in each treatment group) were inoculated with 0.5x106 MC38 tumor cells subcutaneously in the right flank. On day 0, 3 mice received XTX501 bispecific or vehicle. The percentage of cells for each immune phenotype was calculated as percentage of live CD45+ cells and the ratio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

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

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



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

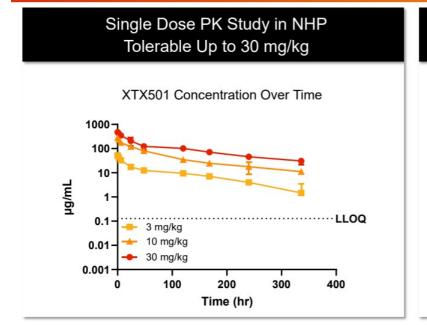




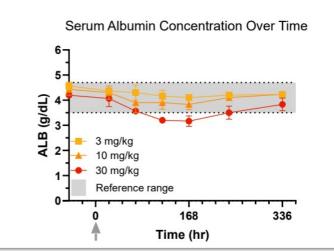
Left panel: Female C57BL/6 hPD-1 mice (n=8 in each treatment group) were inoculated with MB49 tumor cells. On day 0, 5 mice received vehicle or equimolar doses of anti-PD1 antibody (pembrolizumab) plus XTX202 (Masked βγIL-2), or XTX501. Tumor volume change on day 12 post treatment relative to baseline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

## XTX501 Demonstrated Favorable Tolerability in NHP



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





Female cynomolgus monkeys were given a single 30-minute intravenous infusion of XTX501 at 3, 10, and 30 mg/kg and samples were collected for PK and clinical pathology analysis. (A) PK analysis demonstrated dose-proportional exposure and linear elimination across all doses tested. (B) Albumin remained within normal ranges in animals receiving 3 and 10 mg/kg PD1/IL2 and was transiently decreased in animals receiving 30 mg/kg XTX501. There were no observed adverse clinical observations, and transaminase levels remained within normal ranges for all animals. Data generated with analogue of XTX501 with minimal variance in amino acid sequence.



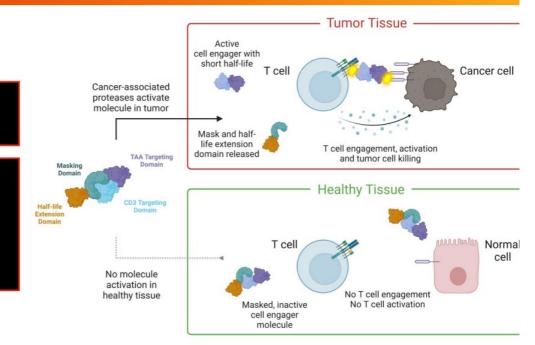
## ATACR Format Designed to Optimize Therapeutic Index of T Cell Engagers by Maximizing Tumor Exposure and Minimizing Healthy Tissue Binding

"ATACR":

<u>A</u>dvanced <u>T</u>umor-<u>A</u>ctivated <u>C</u>ell
<u>EngageR</u>

## Design Goals:

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





Illustrations generated using Biorender.com

# Xilio's Tumor-Activated SEECR Molecules are Designed to Deliver Potent T Cell Activation <u>and</u> Co-Stimulation Specifically to Tumors

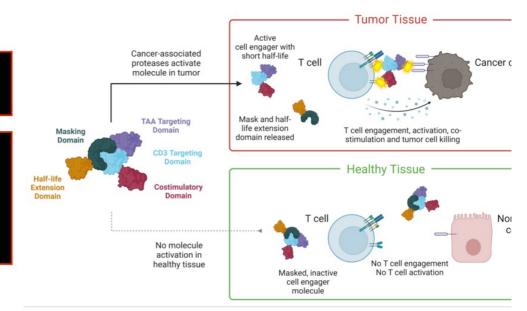
"SEECR":

<u>S</u>elective <u>E</u>ffector-<u>E</u>nhanced

<u>C</u>ell Engage<u>R</u>

## Design Goals:

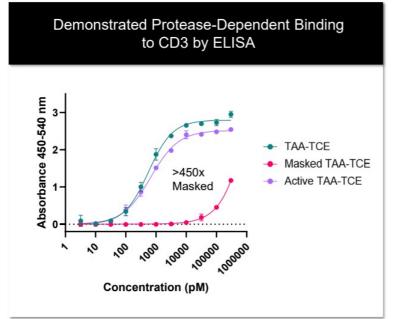
- Potent tumor-selective T cell engagement and co-stimulation
- Minimal peripheral activity and off-tumor cytotoxicity

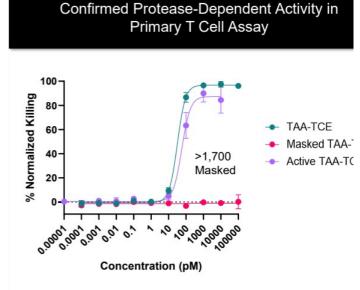




Illustrations generated using Biorender.com

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

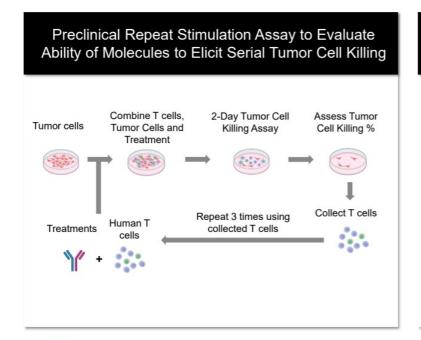


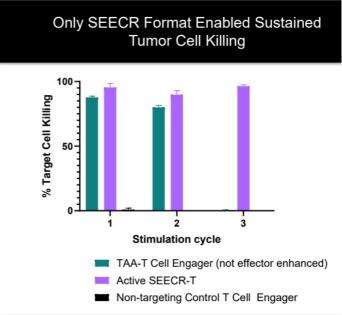




Left panel: Protease dependent CD3-binding demonstrated via TAA-TCEs bound to immobilized CD3 in an ELISA. Right panel: Protease-dependent tumor cell killing. Active TAA-TCEs led to killing in co-culture assay. A375 tumor cells were cultured overnight before addition of expanded T cells at a 5:1 E:T.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



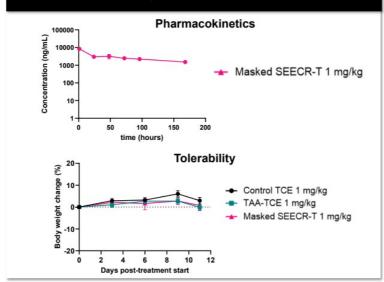




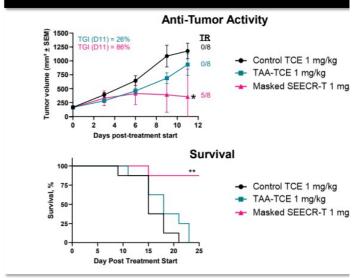
Human T cells were incubated over three consecutive rounds with indicated test articles and A431 cancer cells and percent tumor cell killing was assessed using a luminescence readout.

## 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), no 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: TAA-TCE and seed SEECR-T molecule (iv, 8 doses) significantly inhibited tumor growth, achieving 88% TGI on Day 11 (Data presented as mean a 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).



## 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 Therapi



## 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 \$44.7

Statement of	Operations

	Three Months End	Three Months Ended September 30	
	<b>2024</b> <sup>(1)</sup>	<b>2023</b> <sup>(1)</sup>	
License Revenue	\$2.3M	\$	
Research & Development Expenses	\$10.8M	\$11.	
General & Administrative Expenses	\$6.3M	\$6.3	
Net Loss	\$(14.0M)	\$(16.7	



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

#### Xilio Therapeutics to Present 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 at ASCO GI

Announces preliminary Phase 1 data for XTX301, a tumor-activated IL-12, demonstrating an improved tolerability profile over historical data for rhIL-12, with no dose-limiting toxicities

Completed additional private placement with Gilead for purchase of remaining equity investment in connection with XTX301 partnership

WALTHAM, Mass., December 19, 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 plans to present initial data from its ongoing Phase 2 trial for 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) at the ASCO Gastrointestinal (ASCO GI) Cancers Symposium in San Francisco, California from January 23-25, 2025. In addition, today the company announced preliminary data from Phase 1 dose escalation for XTX301, an investigational tumor-activated IL-12.

"We are encouraged by the early evidence of responses in patients with cold tumors, including MSS colorectal cancer, reported for the combination of vilastobart and atezolizumab in Phase 1C dose escalation earlier this year, and we look forward to sharing initial Phase 2 data for the combination in MSS CRC at ASCO GI in January," said Katarina Luptakova, M.D., chief medical officer of Xilio. "In addition, the preliminary Phase 1 data we reported today for XTX301, our tumoractivated IL-12, highlight its promising clinical profile, including no dose-limiting toxicities reported to date and consistent interferon gamma signaling observed throughout treatment cycles.'

### ASCO GI Presentation Details for Vilastobart (anti-CTLA-4)

Xilio will present initial data from its ongoing Phase 2 trial for vilastobart (XTX101), a tumor-activated, Fc-enhanced, high affinity binding anti-CTLA-4, in combination with atezolizumab (Tecentriq®) in patients with metastatic MSS CRC:

- Title: Phase 1/2 study of XTX101, a tumor-activated, Fc-enhanced anti-CTLA-4 monoclonal antibody, in combination with atezolizumab in patients with advanced solid tumors and in MSS CRC
- Abstract Number: 206
- Presentation Date: Saturday, January 25, 2025
- Poster Session C: Cancers of the Colon, Rectum, and Anus Time: 7:00 AM-7:55 AM PST
- Location: Moscone West, San Francisco, CA

In November 2024, Xilio presented encouraging initial data from the ongoing Phase 1C dose escalation trial for the combination of vilastobart and atezolizumab in patients with advanced solid tumors. For more information, read the press release here.

## Preliminary Data from Ongoing Phase 1 Trial for XTX301 (IL-12)

As of the data cutoff date of November 25, 2024, 34 patients with advanced solid tumors had been treated with XTX301 at doses ranging from 5 µg/kg to 60 µg/kg administered once every three weeks (Q3W) or

once every six weeks (Q6W). Patients were generally heavily pre-treated, and approximately 68% of patients received three or more prior lines of anti-cancer therapy.

A maximum tolerated dose has not yet been established. 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.

In addition, preliminary results as of the data cutoff date showed:

- Sustained interferon gamma (IFNx) signaling without evidence of tachyphylaxis throughout treatment cycles. Tachyphylaxis has historically limited other IL-12 agents.
- Evidence of dose-dependent pharmacology with T cell, natural killer (NK) cell and NKT cell proliferation.
- Consistent with the tumor-activated design of XTX301, no measurable activated XTX301 was detected in peripheral circulation across all dose levels and schedules.
- Across all dose levels and schedules, no Grade 4 or Grade 5 treatment-related adverse events (AEs) were reported by investigators and no patients experienced a dose limiting toxicity or a dose reduction due to a treatment-related AE.
   In addition, across all dose levels and schedules, the majority of treatment-related AEs were Grade 1 or 2 and most commonly consisted of flu-like
- In addition, across all dose levels and schedules, the majority of treatment-related AEs were Grade 1 or 2 and most commonly consisted of flu-like symptoms, cytokine release syndrome, increased aspartate aminotransferase (AST) and alanine aminotransferase (ALT) and decreased blood cell counts.

#### Additional Private Placement with Gilead

On December 18, 2024, Xilio issued and sold an aggregate of approximately \$8.2 million in common stock and prefunded warrants to Gilead Sciences, Inc. (Gilead) in an additional private placement pursuant to the stock purchase agreement Xilio entered into with Gilead in March 2024. Upon the closing of the additional private placement, Xilio has issued and sold an aggregate of \$25.0 million in common stock and prefunded warrants to Gilead, representing the maximum aggregate investment under the March 2024 stock purchase agreement. After giving effect to the proceeds from the additional private placement with Gilead together with Xilio's existing cash and cash equivalents, Xilio now anticipates that its existing cash and cash equivalents will be sufficient to fund its operating expenses and capital expenditure requirements into the third 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.).

### 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 to present initial data from the ongoing Phase 2 trial for vilastobart in combination with atezolizumab in patients with advanced MSS CRC; expectations regarding the clinical profile of XTX301; the period in which Xilio expects to have cash to fund its operations; and Xilio's strategy, goals, business plans and focus. The words "aim," "may," "will," "could," "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; interim or preliminary 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 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**

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