# Xilio Therapeutics Corporate Update Call

**March 28, 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: completing the Phase 1 combination dose escalation and selection of a recommended Phase 2 dose for XTX101 in combination with atezolizumab; initiating a Phase 2 trial to evaluate XTX101 in combination with atezolizumab in patients with MSS CRC; additional plans and anticipated milestones for XTX101, XTX202, XTX301 and Xilio's developmental candidates; Xilio's anticipated use of proceeds from the potential financing; the amount and use of proceeds expected from the transactions with Gilead Sciences, Inc. (Gilead); the timing and certainty of completion of the transactions with Gilead; expectations related to the cost, savings and timing of the strategic portfolio reprioritization and restructuring; the potential impact of the strategic portfolio reprioritization and restructuring on Xilio's operations and development timelines; Xilio's intent and ability to explore strategic opportunities to develop XTX202 in combination with other agents; the potential benefits of any of Xilio's current or future product candidates in treating patients as a monotherapy or combination therapy; the period in which Xilio expects to have cash to fund its operations; the potential for Xilio to leverage its research platform to develop bispecific and cell engager molecules; and Xilio's strategy, goals and anticipated financial performance, milestones, business plans and focus.

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# Today's Agenda

## Presenting On The Call Today

**René Russo, Pharm. D.**
PRESIDENT AND CHIEF EXECUTIVE OFFICER

**Chris Frankenfield**
CHIEF OPERATING OFFICER

**Uli Bialucha, Ph.D.**
CHIEF SCIENTIFIC OFFICER

## Agenda

**OPENING REMARKS**
René Russo, Pharm. D.

**XTX301 (IL-12) AND GILEAD PARTNERSHIP**
Chris Frankenfield

**XTX101 (ANTI-CTLA-4) OPPORTUNITY AND DEVELOPMENT PLAN**
René Russo, Pharm. D.

**XTX202 (IL-2) PHASE 2 DATA**
Uli Bialucha, Ph.D.

**NEW RESEARCH PROGRAMS**
Uli Bialucha, Ph.D.

**CLOSING REMARKS AND Q&A**
René Russo, Pharm. D.

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# Immuno-Oncology Therapy has Curative Potential

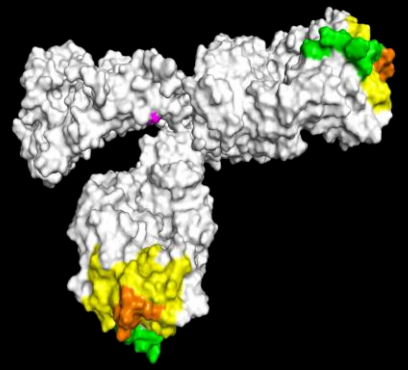
Treatment potential for some of the most promising immuno-oncology (IO) targets has been impeded by **dose-limiting systemic toxicity**

*Patient Portrayal*

**Xilio (*ex*-il-ee-oh)** believes the next revolution in IO cancer therapies will **trick tumors into activating their own treatments**, while simultaneously **sparing healthy tissues and cells**, by **leveraging dysregulated matrix metalloproteases (MMPs)**

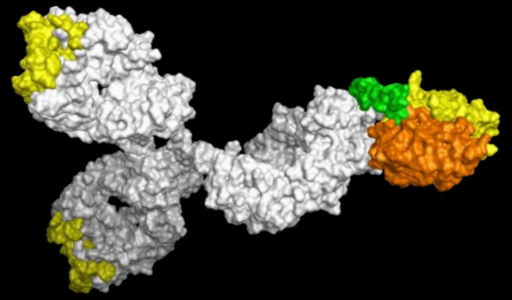
# Xilio is Advancing a Portfolio of Tumor-Activated Molecules Designed to Unleash the Full Potential of Immuno-Oncology Therapies

## Antibodies



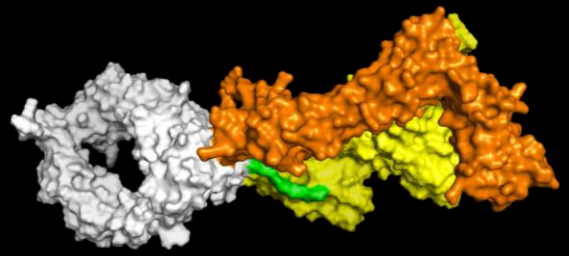
XTX101:
(Tumor-activated Fc-enhanced anti-CTLA-4 mAb)

## Bispecifics



XTX501:
(Tumor-activated PD1/IL2 bispecific)

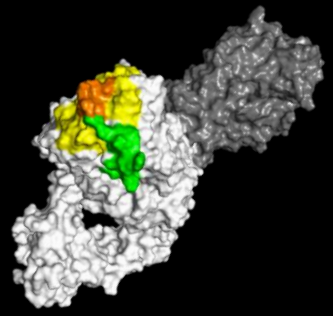
## Cytokines



XTX301:
(Tumor-activated IL-12)

XTX202:
(Tumor-activated βγIL-2)

## Cell Engagers



Tumor-activated cell engagers
(releasable half-life extension domain)

Tumor-activated effector-enhanced cell engagers

mAb: monoclonal antibody

# Prioritizing Clinical Development for XTX301 (IL-12) and XTX101 (anti-CTLA-4) with Focused Investments in Research Platform for Bispecific and Cell Engager Molecules

| Program | Tumor Types | Mechanism of Action | Discovery | IND-Enabling | Phase 1 | Phase 2 | Phase 3 | Partnerships |
|---|---|---|---|---|---|---|---|---|
| **XTX101 in combination with atezolizumab** [1] | Advanced MSS CRC | anti-CTLA-4 + PD-L1 | | | | | | **Clinical collaboration with Roche (with co-funding)** |
| **XTX301** [2] | Advanced Solid Tumors | IL-12 | | | | | | **Exclusive global license with Gilead** |
| **XTX202** [3] | Advanced RCC and Melanoma | IL-2βγ | | | | | | **Plan to explore strategic opportunities to develop in combinations** [3] |
| **XTX501** | Advanced Solid Tumors | PD-1/IL2 bispecific | | | | | | |
| **Additional research-stage programs** | Undisclosed | Tumor-activated cell engagers | | | | | | |

1. Evaluating XTX101 in combination with atezolizumab (Tecentriq®) in Phase 1 combination dose escalation trial and planned Phase 2 combination trial in MSS CRC.
2. Evaluating XTX301 in Phase 1 monotherapy dose escalation for the treatment of advanced solid tumors.
3. Plan to discontinue further investment in XTX202 as a monotherapy

MSS CRC: metastatic colorectal cancer; RCC: renal cell cancer

# XTX301 (IL-12) and Gilead Partnership

**Chris Frankenfield**

Chief Operating Officer

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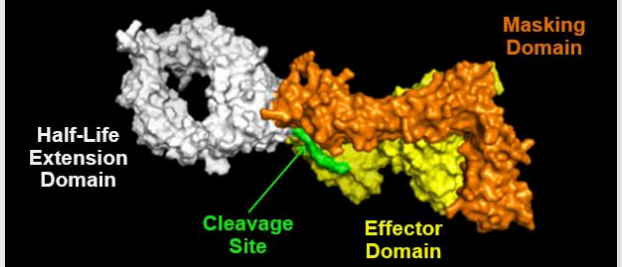
# XTX301: Designed to Overcome Limitations of Systemically Active IL-12

## XTX301:
Tumor-activated IL-12



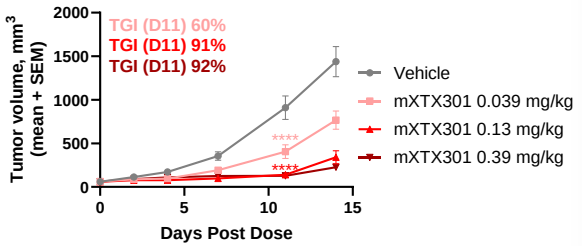

- Built using Xilio's validated masking platform and optimized for IL-12 mechanism
- Half-life extended in masked state, releases short half-life IL-12 once activated

## Efficient activation by human tumors demonstrated *ex vivo*

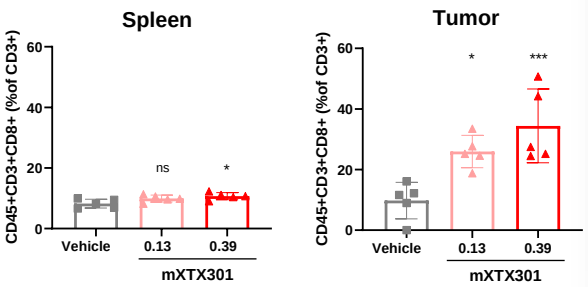
| Tumor Type | Confirmed High Activation Efficiency XTX301 (IL-12) |
|---|---|
| Colon | |
| Head & Neck | |
| Prostate | |
| RCC | |
| Lung | |
| Melanoma | |
| Plasma | |

## Robust anti-tumor activity and tumor-selective PD *in vivo* in preclinical model

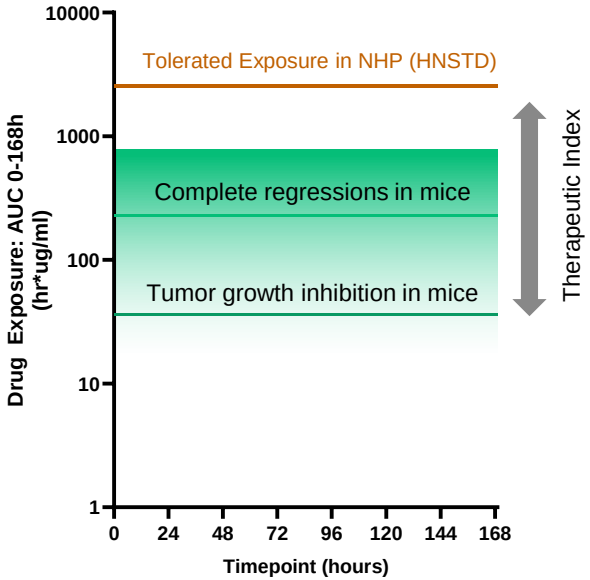
Dose-dependent anti-tumor activity




Tumor-selective increase in CD8 T cells




## Potential for broad therapeutic index supported by robust preclinical data




- Exposure in mice adjusted for 6x potency relative to human XTX301

**Second panel from left:** Activation of XTX301 assessed in human tumor samples ex vivo. **Third panel from left – Top:** MC38 model; single IV dose of mXTX301 or vehicle on Day 0. Tumor growth data shown as mean±SEM. Tumor volume data was assessed by a two-way Analysis of Variance (ANOVA) followed by Bonferroni post hoc test on Day 11 compared to vehicle treated animals. ****p<0.0001 for all mXTX301 treatment groups. **Third panel from left – Bottom:** MC38 model; single IV dose of mXTX301 or vehicle on Day 0. On day 4 post treatment percent CD8 positive T cells (out of CD45+/CD3+ gate) from spleens or tumors was assessed by flow cytometry. The results were analyzed by One-way ANOVA followed by Dunnett's multiple comparisons test (*P<0.05; **P<0.005) compared to vehicle (PBS) treated animals. **Right panel:** XTX301 exposures in NHP at the 2 mg/kg dose (HNSTD) over one week plotted over exposures of mXTX301 in mice at doses enabling tumor regression and tumor growth inhibition with 6x adjustment to account for potency difference between human XTX301 and mouse surrogate mXTX301. HNSTD: highest non-severely toxic dose; NHP: non-human primate; PD: pharmacodynamic; Q1W: once every week; TI: therapeutic index; TGI: tumor growth inhibition.

# Entered Into Transformational Partnership with Gilead, Designed to Explore Broad Potential of IL-12 Across Solid Tumors

**$43.5M**

**total upfront payments**

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

**Up to $604M**

**additional contingent payments:**

- **Includes up to $29M prior to transition fee for up to $11.5M in additional equity investments [1] and a development milestone**
- **$75M transition fee**
- **Up to $500M for additional development, regulatory and sales-based milestones after transition fee**

**Tiered royalties:**

**high single-digits to mid-teens**

*Gilead received an exclusive global license to develop and commercialize Xilio's tumor-activated IL-12 program, including XTX301*

- Xilio responsible for clinical development of XTX301 in ongoing Phase 1 trial through initial planned Phase 2 trial
- Following delivery by Xilio of specified clinical data package for XTX301, Gilead can elect to pay transition fee and transition development and commercialization to Gilead [2]

GILEAD
Creating Possible

xilio THERAPEUTICS

1. Subject to 19.9% ownership cap.
2. If Gilead elects not to transition responsibilities for development and commercialization, the agreement will automatically terminate.

# XTX301 Monotherapy Phase 1 Dose Escalation: No DLTs Observed Into DL3 (45 µg/kg, ~100x MTD for rhIL-12)

## *XTX301 Phase 1 Trial Design*

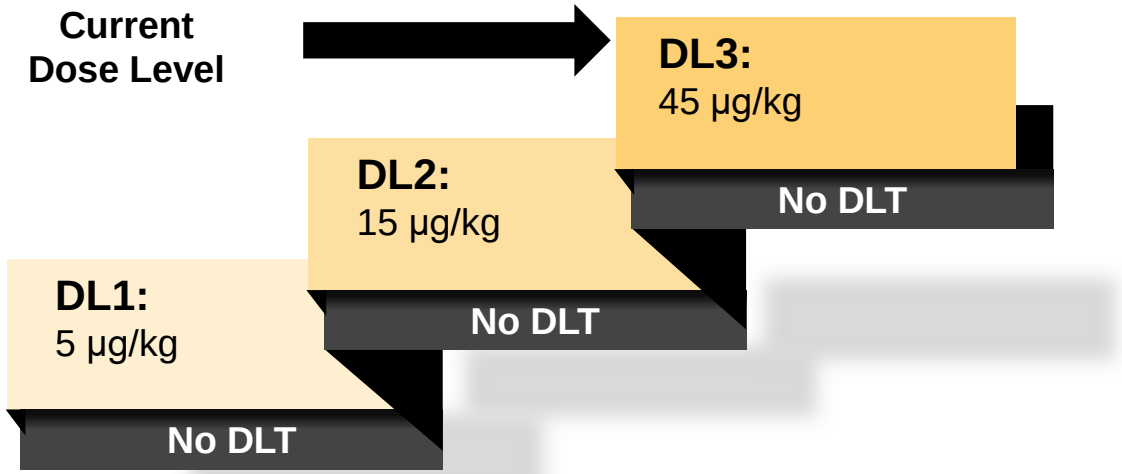
**Phase 1A**
**Monotherapy Dose Escalation**

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

**Phase 1B**
**Monotherapy PD Cohort**

- n = up to 40
- Selected solid tumors

## *XTX301 Phase 1 Dose Escalation Plan*




- XTX301 is administered in the outpatient setting
- DL3 (45 ug/kg) equivalent to ~100x MTD for rhIL-12
- Generally well-tolerated into DL3
- No DLTs reported through data cutoff date

**Q4**
2024

***Next Anticipated Milestone***

- Plan to report Phase 1 safety and PK/PD data



Data cutoff date: January 5, 2024, 9 patients
DL1: dose level 1; DL2: dose level 2; DL3: dose level 3; DLT: dose limiting toxicity; MTD: maximum tolerated dose; PK: pharmacokinetic; rHIL: recombinant human Interleukin 12

# XTX101 (anti-CTLA-4) Opportunity and Development Plan

**René Russo, Pharm. D.**

President and Chief Executive Officer

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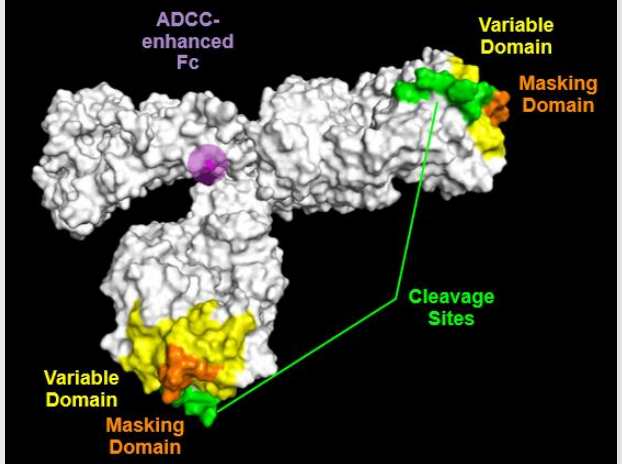
# XTX101: Tumor-Selective Activation and Anti-Tumor Activity Observed in Preclinical Studies and in Patients

## XTX101: Tumor-activated, high-affinity binding, Fc-enhanced anti-CTLA-4

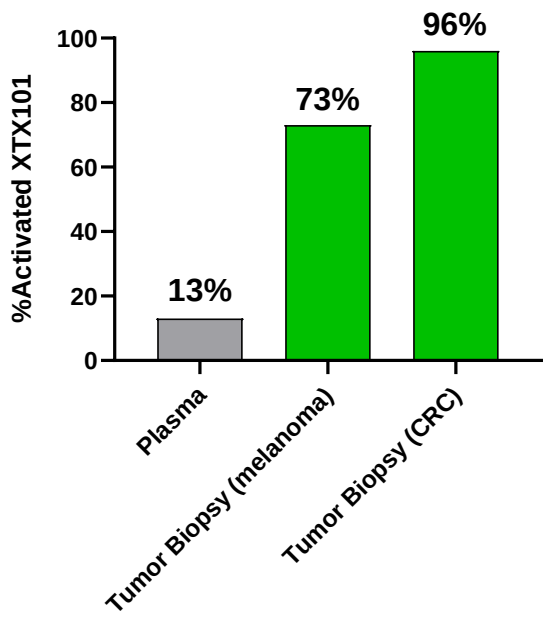



- Fc-enhanced for TREG depletion and optimal CD8 priming
- Picomolar affinity CTLA-4 blocking

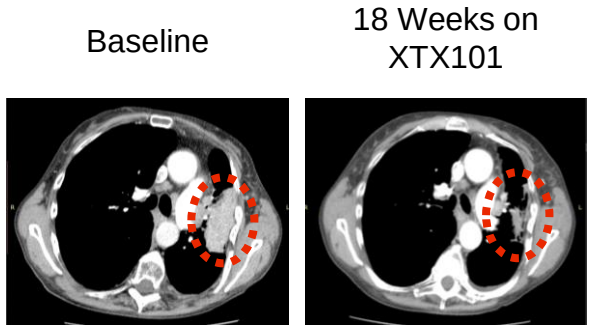
## Efficient activation by human tumors demonstrated *ex vivo*

| Tumor Type | Confirmed High Activation Efficiency |
|---|---|
| | XTX101 (aCTLA-4) |
| Colon | |
| Head & Neck | |
| Prostate | |
| RCC | |
| Lung | |
| Melanoma | |
| Plasma | |

## Tumor-selective activation observed in clinic




## Confirmed partial response without systemic immune activation




- Confirmed PR with 52% reduction in sum of target lesion diameters
- Resolution of liver metastases
- No evidence of systemic immune activation
- Only related AE: Grade 1 fatigue

**Second panel from left:** Activation of XTX101 assessed in human tumor samples ex vivo.
**Third panel from left**: Two patients treated with XTX101 in Part 1B for whom a tumor biopsy pharmacokinetic (PK) analysis was available as of September 11, 2023. Percent activated molecule in tumor was calculated using raw liquid chromatography / mass spectrometry data. Percent activated molecule in plasma represents the area under the curve (AUC) for Cycle 1.
**Fourth panel**: 66-year-old female patient with PD-L1-negative non-small cell lung cancer treated with XTX101 at 150 mg Q6W; baseline and 18-week on-treatment scan showing reduction in chest lesion. Patient discontinued treatment after week 36 due to an adverse event unrelated to treatment. Data cutoff date: November 13, 2023. Tumor response was assessed by RECIST version 1.1.
AE: adverse event; PR: partial response; Q6W: once every 6 weeks; TREG: regulatory T cells

# Vast Majority of Metastatic Colorectal Cancer is MSS CRC with No Approved IO Treatment Options

**~85,000 patients with Stage 4 MSS CRC in the US alone have no IO options available to treat their disease**

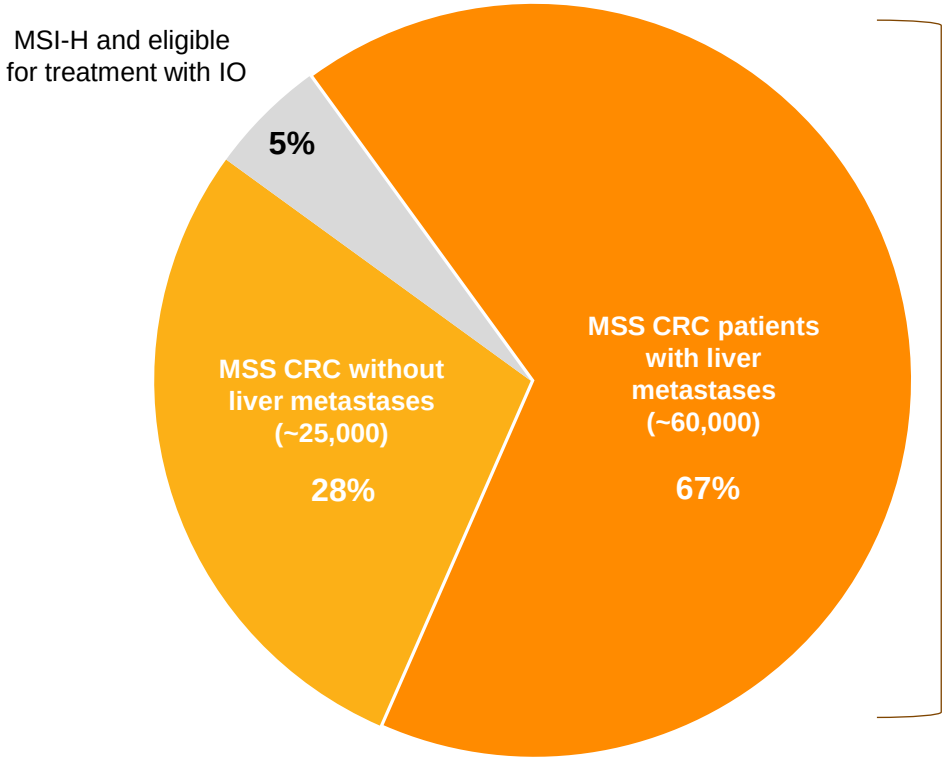
US patients projected to be diagnosed with CRC in 2023 (1) **~150,000**

~60% of patients will be diagnosed with Stage 4 disease (1) **~90,000**

~95% of Stage 4 disease is MSS CRC (2) **~85,000**

~70% of patients with Stage 4 disease develop liver metastases (3) **~60,000**

## US Stage 4 Patients




1. Siegel et al, Colorectal Cancer Statistics, (2023).
2. Ooki et al, Journal of Anus Rectum Colon, (2021).
3. Cerner Enviza, (2023).

MSI-H: microsatellite instability-high

# XTX101 Advancing Under Co-Funded Clinical Collaboration: Plan To Select RP2D for Combination in Q2 2024

***Stage 4 MSS CRC 2L+***

***Phase 1 Dose Escalation (Ongoing)***

**XTX101 + atezolizumab**
(n = ~12)

- All comers, advanced solid tumors
- Plan to evaluate two dose levels
- XTX101 starting dose: 75 mg Q6W

**Anticipated Milestones**

- ✓ FPI in Q4 2023
- ❑ Select RP2D in Q2 2024

***Phase 2 Proof-of-Concept (Planned)***

**XTX101 + atezolizumab**
(n= ~40)

MSS CRC with and without liver metastases

**Anticipated Milestones**

- ❑ FPI in Q3 2024
- ❑ Initial data (n = ~20) in Q4 2024
- ❑ Additional data (n = ~40) in Q1 2025

***Potential Pivotal Phase 2 Trial***

**XTX101 + atezolizumab**
(n=~200 patients:
~160 Phase 2 randomized patients +
~40 initial Phase 2 patients)

With and without liver metastases

- Potential for accelerated approval pathway
- Monotherapy cohorts (to demonstrate contribution of components) and/or standard-of-care comparator arm (if required) can have early stopping rules

**Q3 2024**

***Next Anticipated Milestone***

- Plan to initiate Phase 2 combination trial in MSS CRC



FPI: first patient dosed; 2L: second line.; RP2D: Recommended Phase 2 Dose

# XTX202 (IL-2) Phase 2 Data

**Uli Bialucha, Ph.D.**

Chief Scientific Officer

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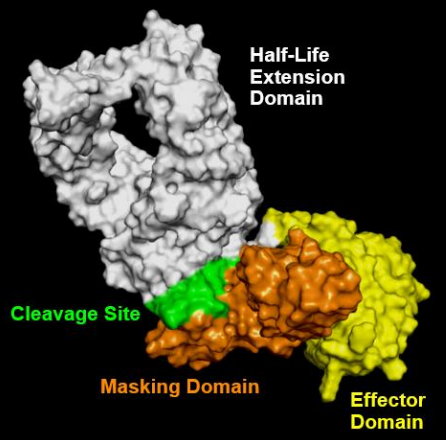
# XTX202: Evidence of Tumor-Selective Activation Validating Xilio Platform

## XTX202: Tumor-activated, IL-2βγ designed to overcome limitations of systemically active IL-2

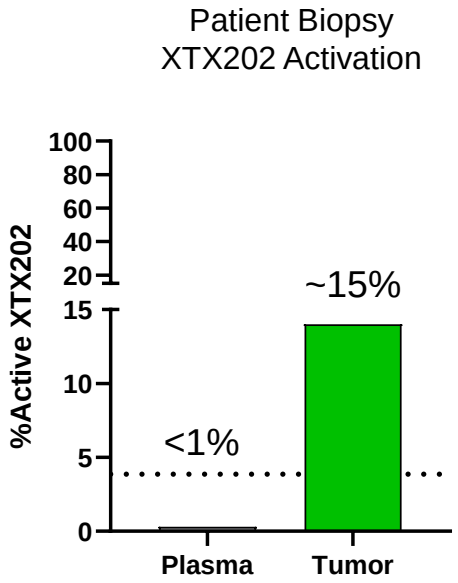



- Beta/gamma IL-2 for preferential activation of CD8+ T cells and NK
- Half-life extended with attenuated Fc for optimal tumor exposure

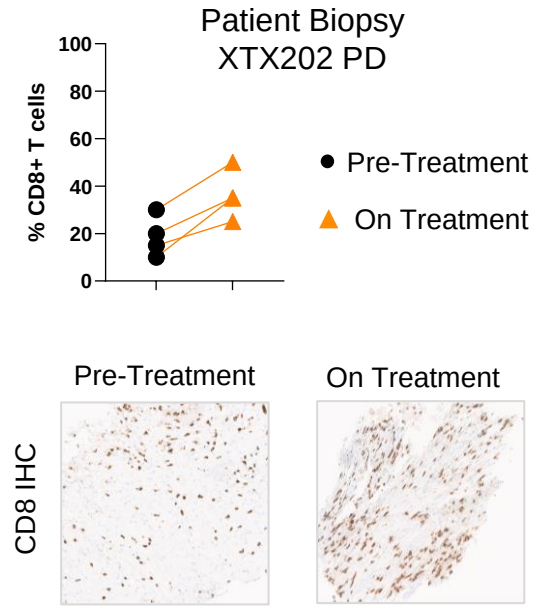
## Efficient activation by human tumors demonstrated *ex vivo*

| Tumor Type | Confirmed High Activation Efficiency XTX202 (IL-2) |
|---|---|
| Colon | |
| Head and Neck | |
| Prostate | |
| RCC | |
| Lung | |
| Melanoma | |
| Plasma | |

## Tumor-selective activation observed in clinic




## Tumor-selective pharmacology consistent with βγIL-2 design




**Second panel from left:** Activation of XTX202 assessed in human tumor samples ex vivo.
**Third panel from left**: Biopsy of 1 patient treated with XTX202 at 2.8 mg/kg dose level, which was the only biopsy available for XTX202 bioanalytical analysis. Percent activated XTX202 in tumor was calculated using raw liquid chromatography / mass spectrometry data. Tumor biopsy specimen was collected cycle 2, day 2. Percent activated molecule in plasma represents the average for area under the curve (AUC) for Cycle 1 for patients treated at 2.8 mg/kg dose level. **Right panel**: Intratumoral CD8+ T cell increases observed in four patient biopsies. Patients had an optional on-treatment tumor biopsy and were the only four patients treated with XTX202 for whom a tumor biopsy analysis was available as of August 1, 2023. Top: CD8+ T cells assessed by IHC. Bottom: Example of biopsy from melanoma patient treated with XTX202 at 0.38 mg/kg. CD8+ T cells assessed by Fluorescence-Activated Cell Sorting (FACS) for peripheral blood and Immunohistochemistry (IHC) for tumor. Change in CD8+ cells in tumor takes into account increase in stromal TILs and CD8+ IHC.
NK: natural killer

# XTX202: Phase 1/2 Trial Enrolled 95 Patients with Advanced Solid Tumors

***XTX202 Phase 1 Trial Design***

Phase 1A
Monotherapy Dose Escalation Advanced Solid Tumors

Phase 1B
Monotherapy PD Cohort "Hot Tumors"

***XTX202 Phase 2 Trial Design***

***Dose level 1: 1.4 mg/kg Q3W***

***Dose level 2: 4.0 mg/kg Q3W***

Phase 2A
Monotherapy Expansion RCC Cohort

Phase 2B
Monotherapy Expansion Melanoma Cohort

| | Phase 1 | Phase 2 |
|---|---|---|
| **Patient Characteristics** | **Total (N=58)** | **Total (N=37)** |
| **Demographics** | | |
| Age, median (range) | 68 (25, 82) | 63 (33, 80) |
| Female | 22 (38%) | 17 (46%) |
| ECOG PS 0 | 20 (35%) | 18 (49%) |
| ECOG PS 1+ | 38 (65%) | 19 (51%) |
| **Prior Lines of Anti-Cancer Treatment** | **Median 4 (1-13)** | **Median 3 (1-12)**** |
| 1 | 5 (9%) | 10 (27%) |
| 2 | 9 (16%) | 4 (11%) |
| 3 | 11 (19%) | 5 (14%) |
| 4 | 14 (24%) | 6 (16%) |
| 5 | 8 (14%) | 3 (8%) |
| ≥6 | 11 (19%) | 6 (16%) |
| **Prior Treatment with IO** | | |
| ≥1 | 41 (71%) | 33 (97%)** |
| **Time since initial diagnosis (months)** | **Median 29 (4-147)** | **Median 36 (2-198)** |

| | Phase 1 | Phase 2 |
|---|---|---|
| **Tumor Types** | **Total (N=58)*** | **Total (N=37)** |
| Colorectal | 8 | |
| NSCLC | 7 | |
| Melanoma | 7 | 20 |
| Sarcoma | 6 | |
| Pancreatic | 4 | |
| RCC | 6 | 17 |
| Prostate | 3 | |
| Endometrial | 2 | |
| Cervical | 1 | |
| Esophageal | 1 | |
| Ovarian | 1 | |
| Other | 13 | |

| | Phase 1 | Phase 2 |
|---|---|---|
| **Treatment Status** | **Total (N=58)** | **Total (N=37)** |
| **Continuing on Treatment** | **4** | **21** |
| **Discontinued Treatment** | **54** | **16** |
| Progressive Disease | 39 | 11 |
| Adverse Events | 2 | — |
| Consent Withdrawal | 2 | 1 |
| Death | 5 | — |
| Other | 6 | 4 |

**Phase 1**
- 58 patients enrolled with a wide range of advanced and IO-treatment refractory solid tumors
- 75% of patients had ≥3 prior lines of anti-cancer treatment
- 71% of patient had prior IO treatment

**Phase 2**
- 37 patients enrolled (17 RCC and 20 melanoma)
- 97% of patients had prior IO treatment

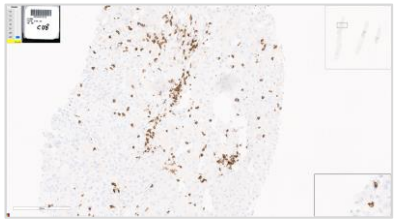
Data cutoff date: March 6, 2024.
* One patient at 2.8 mg/kg dose in Part 1A had 2 primary cancer diagnoses of pancreatic cancer and prostate cancer and is therefore included in both tumor types in the table.
** 3 patients had missing information on prior lines of therapy
IO: Immuno-oncology

# Tumor-Selective Increases in CD8+ Effector T Cells Observed with XTX202 in Heavily Pre-Treated Patients Across Dose Levels

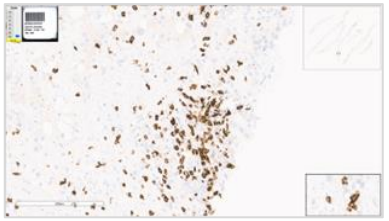
On-Treatment Tumor Biopsies vs Pre-Treatment Baseline Biopsies Collected at Enrollment

## 20% Increase in CD8+

Pre-Treatment



On-Treatment

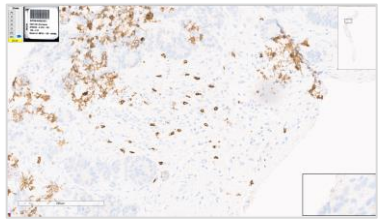


RCC patient treated with XTX202 at 1 mg/kg Q3W

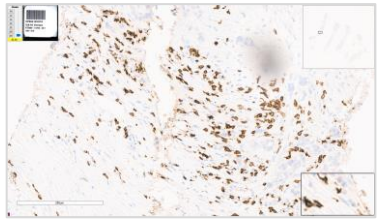
- 64M, Stage 4 RCC
- Initial diagnosis June 2016
- 5 prior lines of treatment
- Progressed on IO, multiple prior lines

## 120% Increase in CD8+

Pre-Treatment



On-Treatment

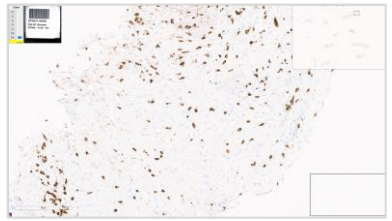


Rectal cancer patient treated with XTX202 at 2.8 mg/kg Q3W

- 58F, Stage 4 rectal cancer
- Initial diagnosis August 2021
- 4 prior lines of treatment
- Progressed on IO in 3L

## 230% Increase in CD8+

Pre-Treatment



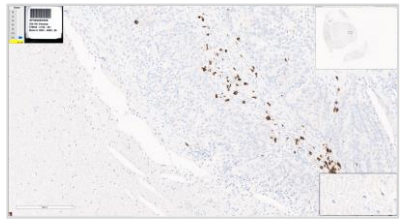
On-Treatment

Melanoma patient treated with XTX202 at 0.38 mg/kg Q3W

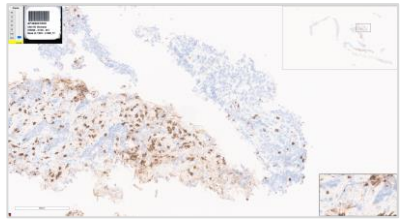
- 51M, Stage 4 melanoma
- Initial diagnosis November 2019
- 4 prior lines of treatment
- Progressed on IO in 2 prior lines

## 600% Increase in CD8+

Pre-Treatment



On Treatment



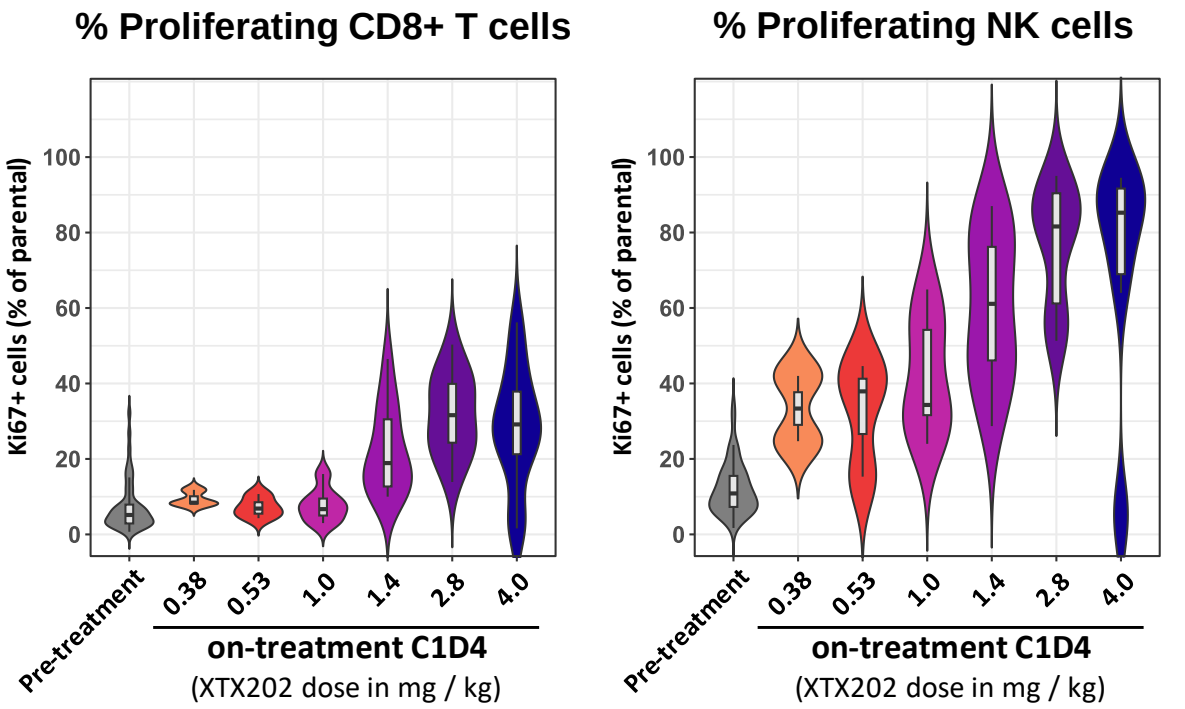
RCC patient treated with XTX202 at 0.53 mg/kg Q3W

- 75M, Stage 4 RCC
- Initial diagnosis May 2021
- 5 prior lines of treatment
- Progressed on IO in 1L

Patients had an optional on-treatment tumor biopsy and were the only four patients treated with XTX202 for whom a tumor biopsy analysis was available as of August 1, 2023. CD8+ T cells assessed by FACS for peripheral blood and IHC for tumor. Change in CD8+ cells in tumor takes into account increase in stromal TILs and CD8+ IHC.
1L: first line; 3L: third line.

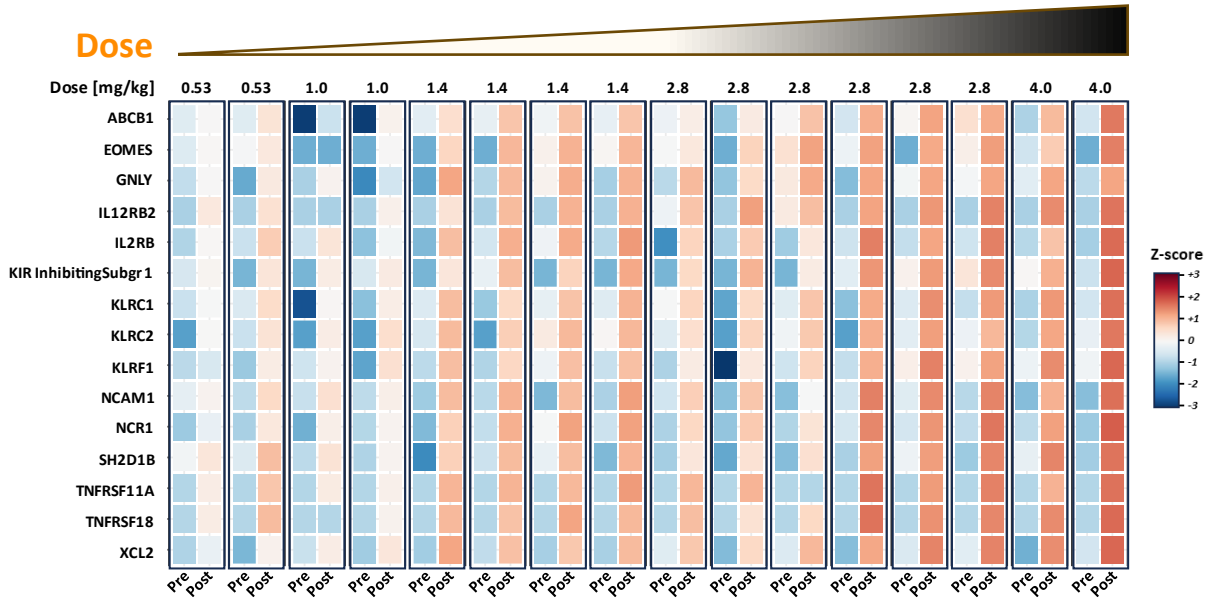
# XTX202 Demonstrated Dose-Dependent Pharmacology in CD8+ T and NK Cells Consistent with IL-2 Biology

## XTX202 Induced CD8+ T and NK Cell Proliferation in a Dose-Dependent Manner




## XTX202 Treatment Resulted in Dose-Dependent Upregulation of Key T and NK Cell Markers

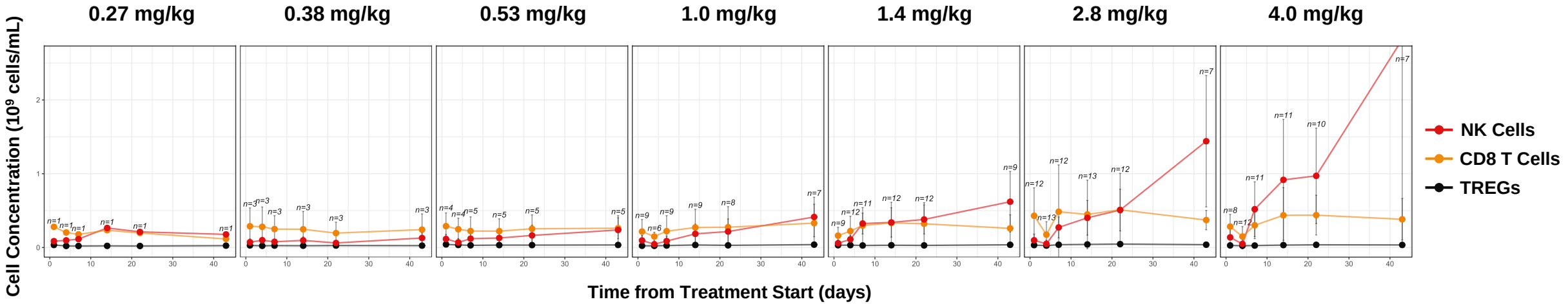
*N=12 paired samples shown (baseline and on-treatment at indicated doses)*



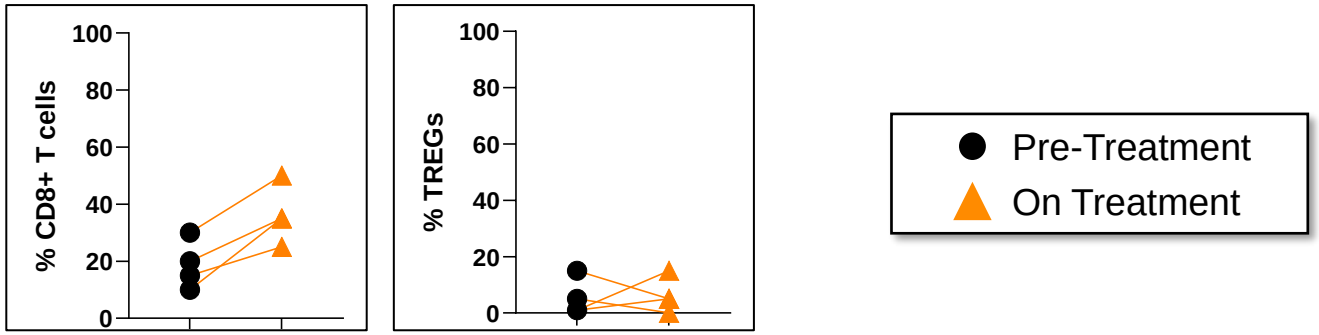

**Left panel:** %Ki67+ cell populations determined by flow cytometry of peripheral blood mononuclear cells at pre-dose and at cycle 1, day 4 (C1D4). Data cutoff date: January 24, 2024
**Right panel:** Heatmap showing standardized expression (z-score-transformed log2-nanoString signal) of top differentially expressed genes (y-axis), separated pre vs. post treatment across all paired XTX202 samples. Data cutoff date: January 24, 2024

# XTX202 Demonstrated Stimulation of CD8+ T and NK Cells Without Expansion of TREGs

## No Peripheral TREG Stimulation at Any Dose Level Consistent with Beta Gamma Biased Design Intent




## Intratumoral CD8+ T Cell Increase Without Concomitant TREG Expansion



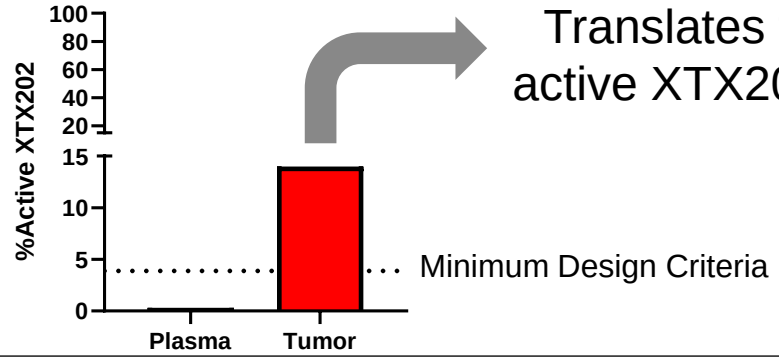

**Top:** Absolute Lymphocytes Count. Spaghetti graph showing the average concentration of different cell types in the periphery (y-axis, concentration expressed in $10^9$ cells / L) at different timepoints (x-axis) for each treatment dose group (columns). Colors indicate cell types. Points and error bars indicate average +/- sd. The sample size is annotated for each group and timepoint. Data cutoff date: January 24, 2024
**Bottom:** Patients had an optional on-treatment tumor biopsy and were the only four patients treated with XTX202 for whom a tumor biopsy analysis was available as of August 1, 2023. CD8+ T cells and TREGs assessed by IHC.

# XTX202 On-Treatment Biopsy Demonstrated Tumor-Selective Activation

**Data suggest minimum of ≥2.8 mg/kg monotherapy doses approaching optimal range to activate CD8+ effector T cells and NK cells in the tumor**

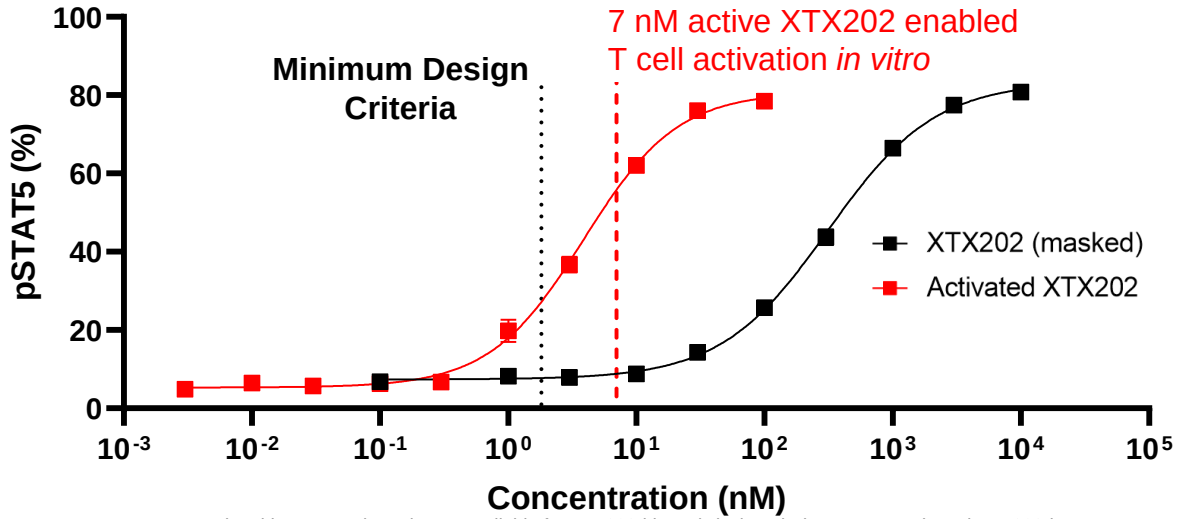
## CLINICAL DATA

- Patient with leiomyosarcoma treated with XTX202 at 2.8 mg/kg Q3W, tumor specimen collected cycle 2, day 2 (C2D2)
- >40-fold increase of active XTX202 in tumor relative to plasma for patients at 2.8 mg/kg dose level
- Well above minimum design criteria and consistent with range that enabled T cell and NK cell stimulation in preclinical models

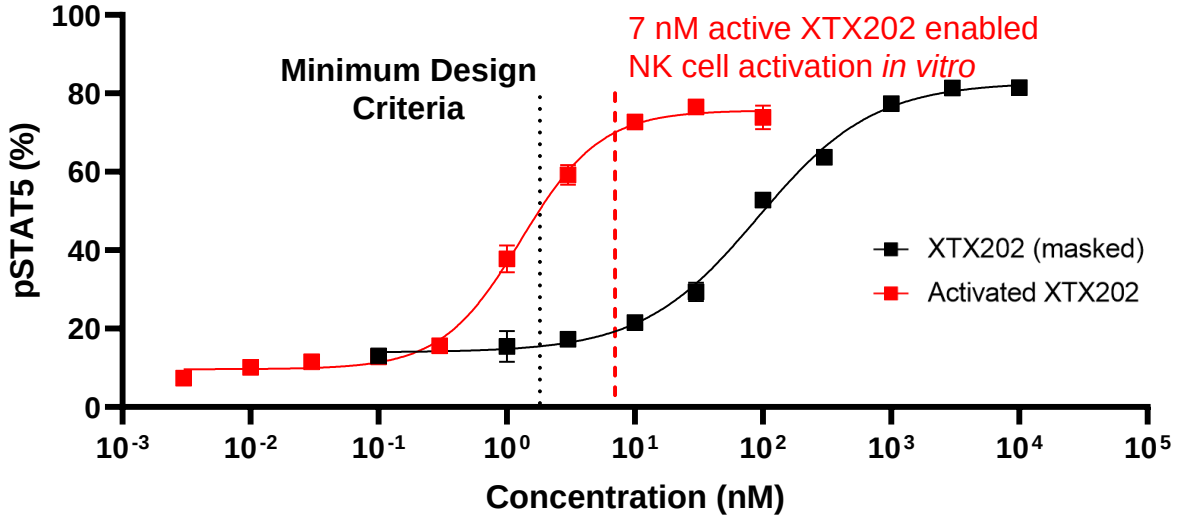



## PRECLINICAL DATA

### CD8+ T cells




### NK cells

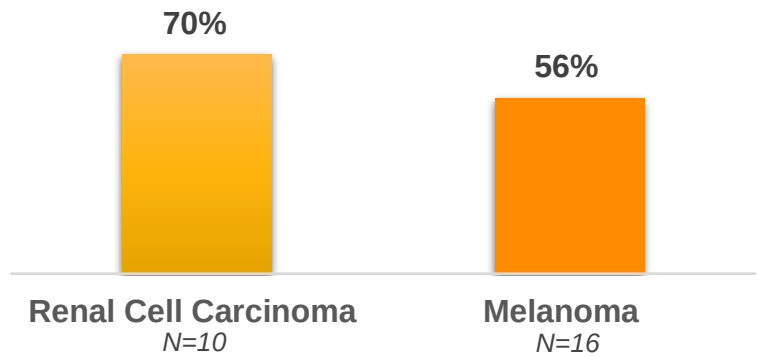



**Top:** Patient biopsy was the only one available for XTX202 bioanalytical analysis. Percent activated XTX202 in tumor was calculated using raw liquid chromatography / mass spectrometry data. Tumor biopsy specimen was collected C2D2. Percent activated molecule in plasma represents the average for area under the curve (AUC) for Cycle 1 for patients treated at 2.8 mg/kg dose level.
**Bottom:** Primary human PBMC were treated with a dose-titration of activated XTX202 (unmasked, red) or XTX202 (masked, black) and pSTAT5 positivity was assessed by FACS. The concentration of active XTX202 detected in the human biopsy (7 nM) is overlayed as a red vertical dotted line.
nM: nanomolar

# XTX202 is Combination Ready with Dose Dependent Anti-Tumor Activity Across a Broad Range of Tumor Types and a DCR Rate > 50% at 4 mg/kg

| Dose Level [1] (mg/kg) | # Patients Treated (Phase 1 & 2) | # EOT Without Response Assessment | # Ongoing Before 1st Response Assessment | # Response Evaluable | # SD for 9+ Weeks as BOR | DCR (% of evaluable) |
|---|---|---|---|---|---|---|
| **<1.4** | 16 | 2 | 0 | 14 | 2 | 14% |
| **1.4** | 22 | 1 | 0 | 21 | 8 | 38% |
| **2.8** | 13 | 6 | 0 | 7 | 3 | 43% |
| **4** | 44 | 5 | 8 | 31 | 16 | 52% |
| **All** | **95** | **14** | **8** | **73** | **29** | **40%** |

## Phase 2 DCR in Evaluable Patients by Tumor Type



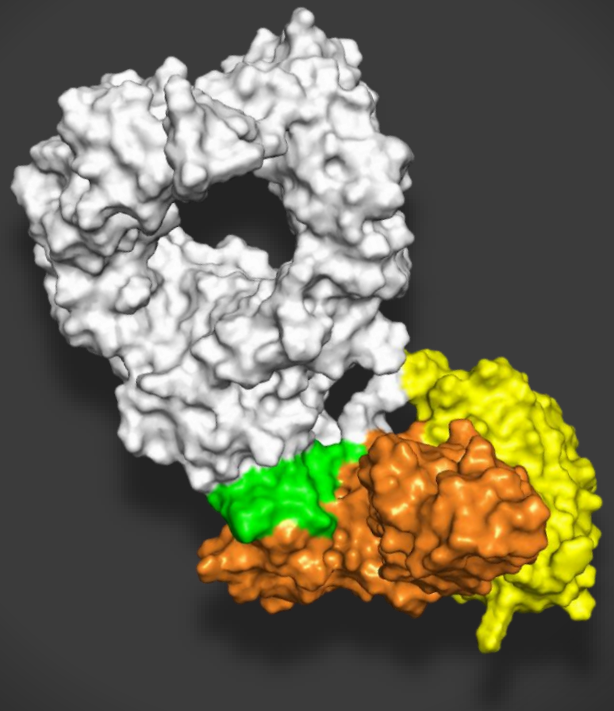

- 37 patients treated in Phase 2 at dose level of 1.4 mg/kg or 4 mg/kg
- Best overall response reported by investigators is stable disease (SD)
- Generally well-tolerated with safety profile consistent with previously report data[2]

**Best response: long-term stable disease (> 18 months) in Stage IV MSS CRC patient with liver metastases**

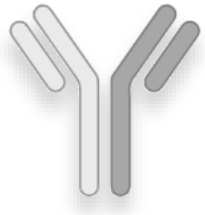
Data cutoff date: March 6, 2024.
1. All dose levels are Q3W outpatient administration. Patients are categorized based on their highest administered dose.
2. Initial Phase 1/2 data reported in November 2023 at Society for Immunotherapy of Cancer (SITC) 38th Annual Meeting.
EOT: end of treatment; SD: stable disease; BOR: best overall response; DCR: disease control rate (defined as SD or PR at 9+ weeks)

# Combination with IL-2 Required for Many Modalities to Pursue Maximum Potential and XTX202 Well-Suited for Broad Applications

XTX202's novel design has potential to enable wide range of combination modalities

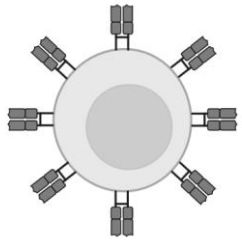


XTX202 (IL-2)



## Cell Engagers

- Increased quantity and quality of effector cells induced by XTX202 benefits T cell engagers, as well as NK engagers
- Demonstrated combination benefit preclinically (internal data on file)

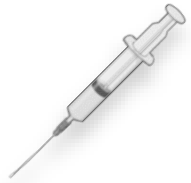


## Cell Therapies

- TIL-based therapies require co-administration with IL-2 to engraft and expand T cells
- IL-2 co-administration limited by poor aldesleukin tolerability[1]

## Checkpoint Inhibitors

- Preclinical data supportive of IL-2 combination with checkpoint inhibitors including CTLA-4[2,3]



## Cancer Vaccines

- IL-2 addition key to vaccination regimen enabled eradication of large tumors in preclinical studies[4]


1.Chesney and Lewis, JITC, 2022
2. Broucek et al., JITC, 2013
3. Caudana et al., Cancer Immunology Research, 2019
4. Moynihan et al., Nature Medicine, 2016

# New Research Programs

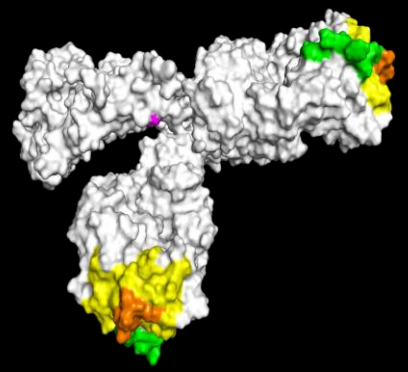
**Uli Bialucha, Ph.D.**

Chief Scientific Officer

x·ilio THERAPEUTICS®

# Leveraging Validated Platform Technology for Antibodies and Cytokines to Develop a New Generation of Tumor-Activated Bispecifics and Cell Engagers

## Antibodies



XTX101:
(Tumor-activated Fc-enhanced anti-CTLA-4 mAb)

## Bispecifics

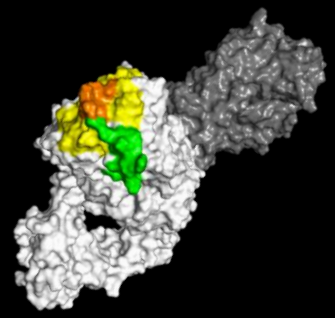
XTX501:
(Tumor-activated PD1/IL2 Bispecific)

## Cytokines

XTX301:
(Tumor-activated IL-12)

XTX202:
(Tumor-activated βγIL-2)

## Cell Engagers



Tumor-activated Cell Engagers
(releasable half-life extension domain)

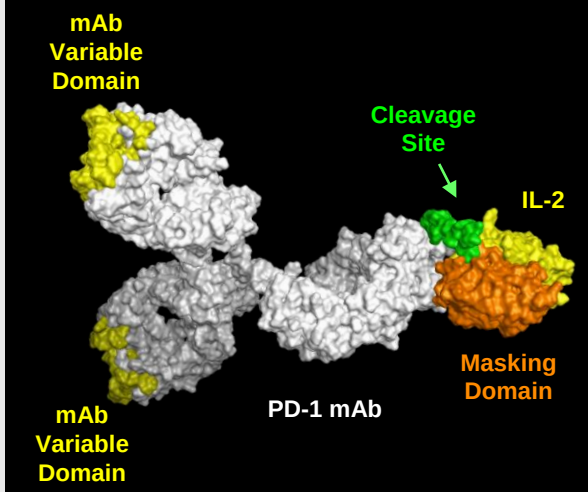
Tumor-activated Effector-Enhanced Cell Engagers



mAb: monoclonal antibody

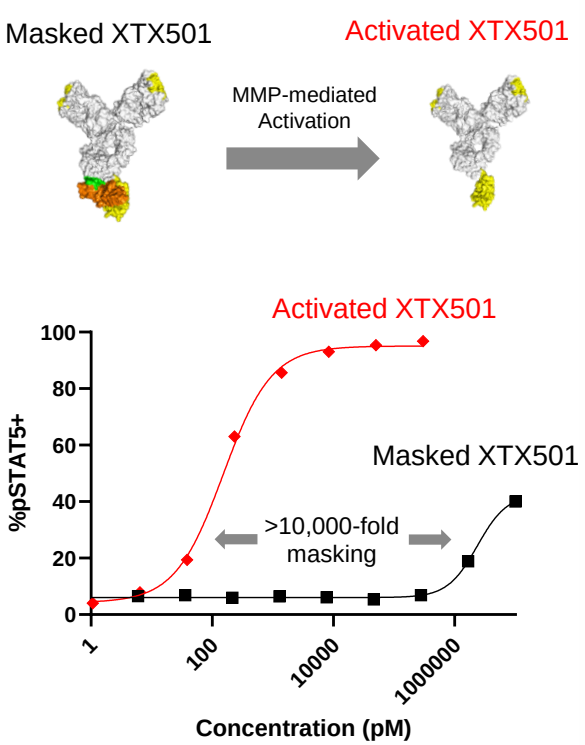
# XTX501: Tumor-activated PD1/IL2 Bispecific Demonstrated Synergistic Anti-Tumor Activity, Antibody-Like PK and Favorable Tolerability in NHP

## XTX501: Tumor-activated, PD1/IL2 bispecific

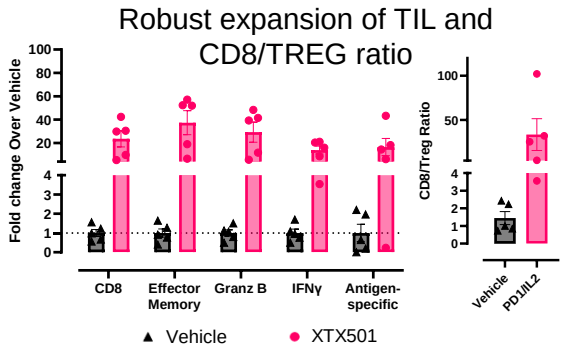


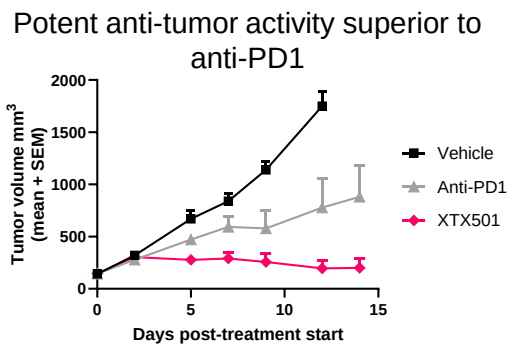

- Affinity-tuned, VHH-based mask
- Alpha-optimized IL-2
- Non-masked PD1 in Fc-silenced heterodimeric IgG1 backbone
- XTX501 designed to direct IL-2 to PD1+ T cells

## Effective masking in vitro

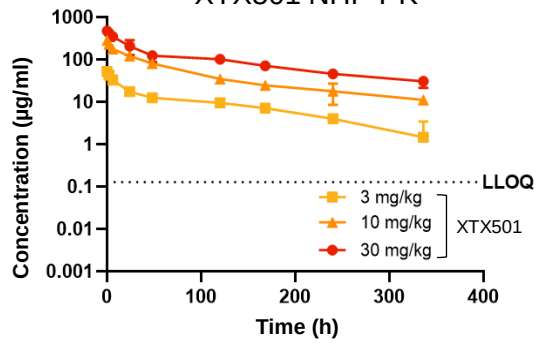


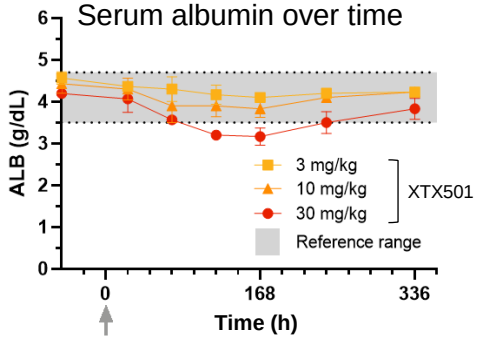

## Potent in vivo pharmacology as monotherapy




## Antibody-like half-life and tolerability in NHP

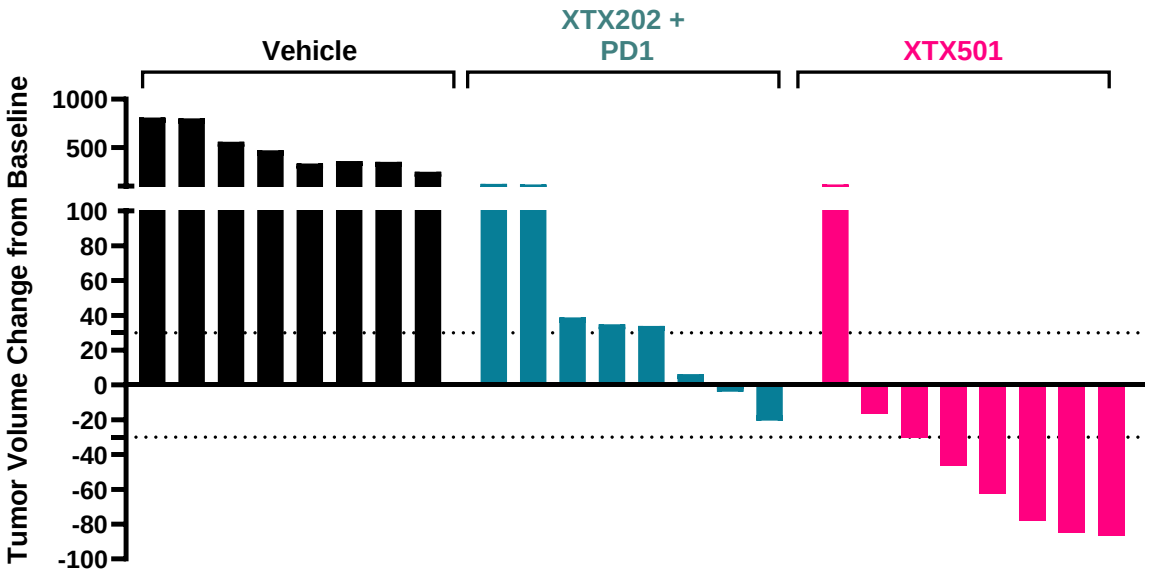


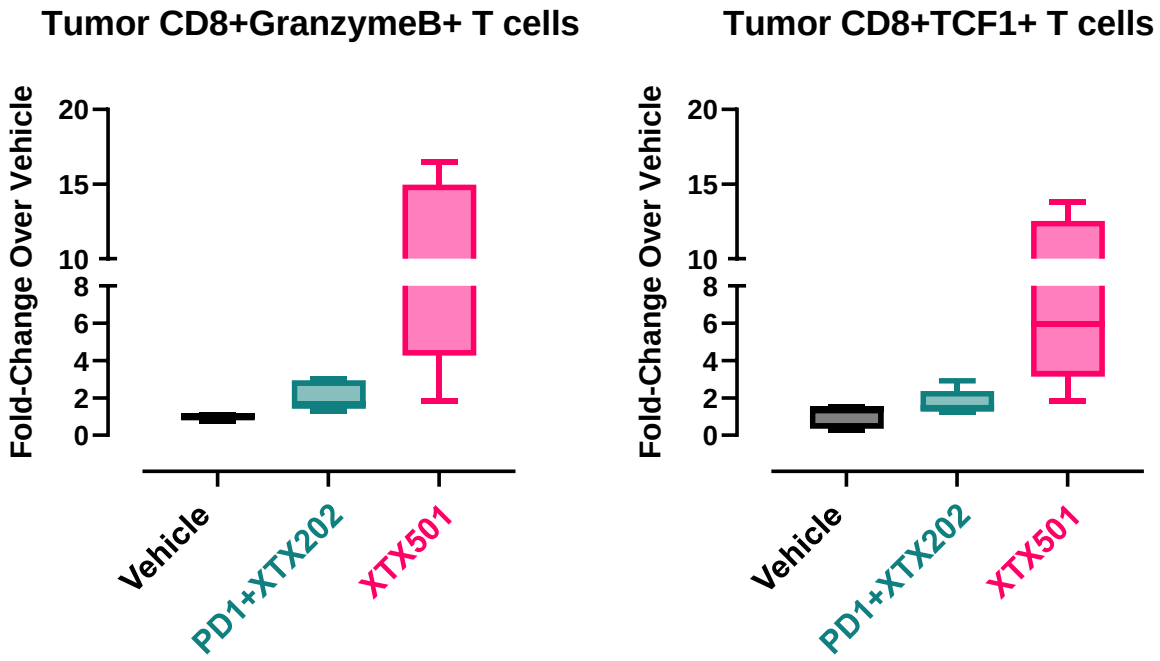

**Left panel:** Structural model of XTX501 (PD1/IL2 bispecific). **Second panel from left**: Preactivated PBMCs were incubated with varying concentrations of XTX501 or MMP-activated XTX501 for 12 minutes followed by evaluation for STAT5 phosphorylation. **Third panel from left, top:** Female C57BL/6 hPD-1 mice (n=5 in each treatment group) were inoculated with MC38 tumor cells. On day 0, 3 mice received 7.5 mg/kg of XTX501 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). **Third panel from left, bottom:** In the same mouse model as above, in anti-tumor activity of XTX501 at 7.5 mg/kg Q3Dx2 was compared to vehicle or equimolar doses of PD1 antibody. **Right panel top:** Concentration over time profile (PK) for XTX501 following single dose administration in non-human primate (NHP). **Right panel bottom:** Serum albumin measurements over time following single dose administration of XTX501 in NHP. VHH: Variable Heavy domain of Heavy chain. Data generated with analog of XTX501 with minimal variance in amino acid sequence.

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

## Robust Preclinical Monotherapy Activity Beyond XTX202 + PD1 Combination




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



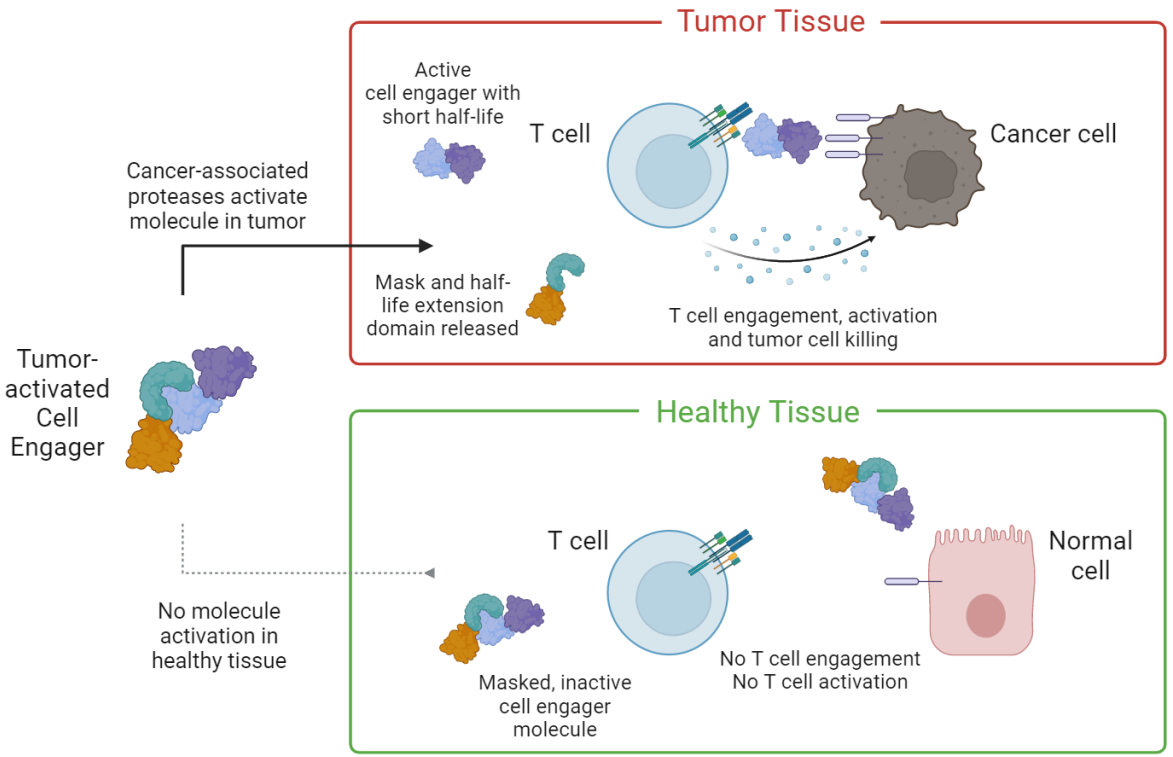

**Left panel:** Female C57BL/6 hPD-1 mice (n=8 in each treatment group) were inoculated with MB49 tumor cells. On day 0, 5 mice received vehicle or equimolar doses of anti-PD1 antibody (pembrolizumab) plus XTX202 (Masked βγIL-2), or XTX501. Tumor volume change on day 12 post treatment relative to baseline is shown as a waterfall plot. **Right panel:** Female C57BL/6 hPD-1 mice (n=5 in each treatment group) ) were inoculated with MB49 tumor cells. On day 0, 5 mice received vehicle or equimolar doses of anti-PD1 antibody (pembrolizumab) plus XTX202 (Masked βγIL-2), or XTX501. Tumors were harvested on day 7 post initial treatment and tumor infiltrating lymphocytes were phenotyped using flow cytometry. Fold-over mean vehicle is shown for the treatment arms for CD8+/GranzymeB positive and CD8+/TCF1+ T cells. Data generated with analog of XTX501 with minimal variance in amino acid sequence.

# Xilio Cell Engager Programs

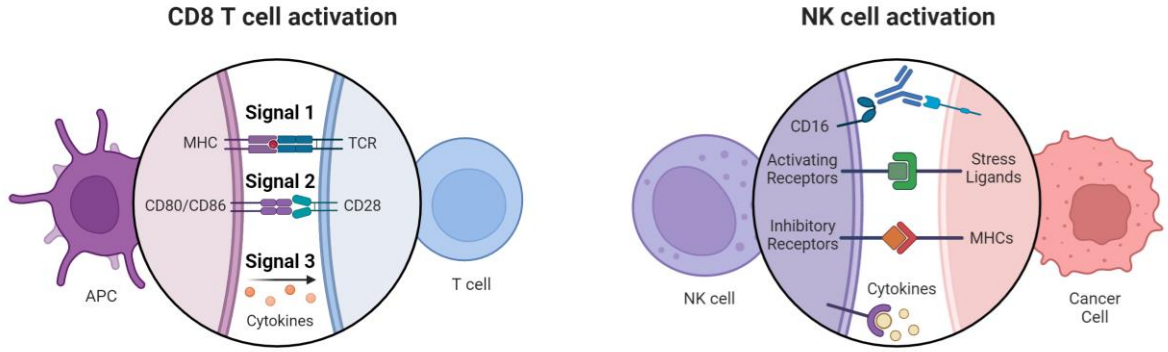
xilio THERAPEUTICS®

# Xilio is Developing Two Formats of Tumor-Activated Cell Engagers Built on our Validated Masking Approach and Conditional Half-life Optimization

## Advanced Tumor-Activated Cell EngageRs (ATACRs)




## Selective Effector-Enhanced Cell EngageRs (SEECRs)

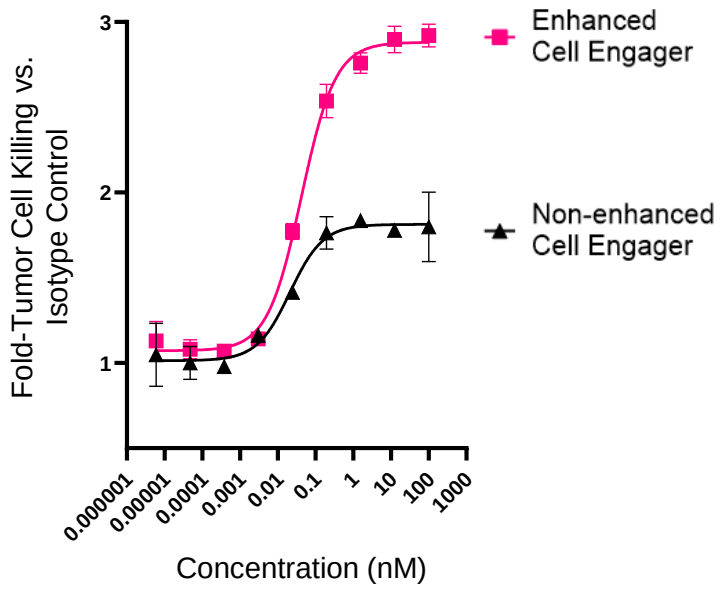



- Designed to provide multiple stimulatory signals in a tumor-selective manner
- Uniquely enabled by Xilio's masking approach, keeping individual components masked until activated in the tumor microenvironment

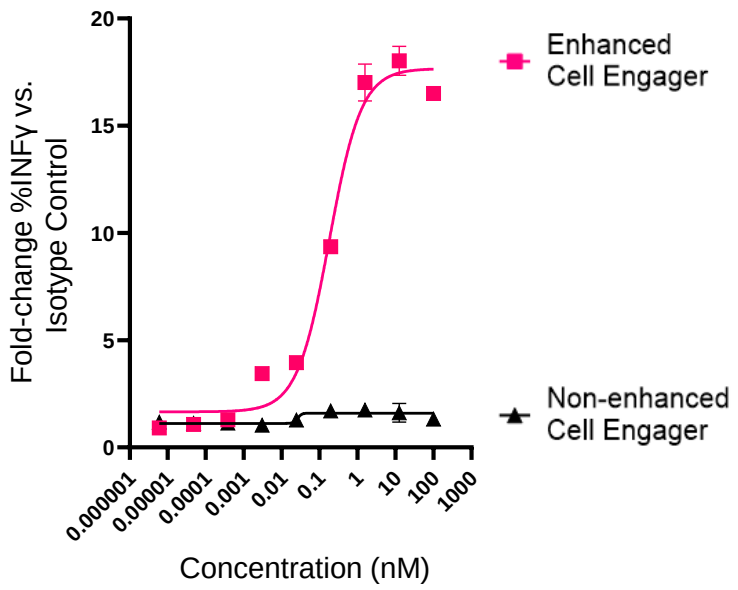
Illustrations generated using Biorender.com

# SEECR Format Demonstrated Enhanced Functionality Compared to Established Cell Engager Format

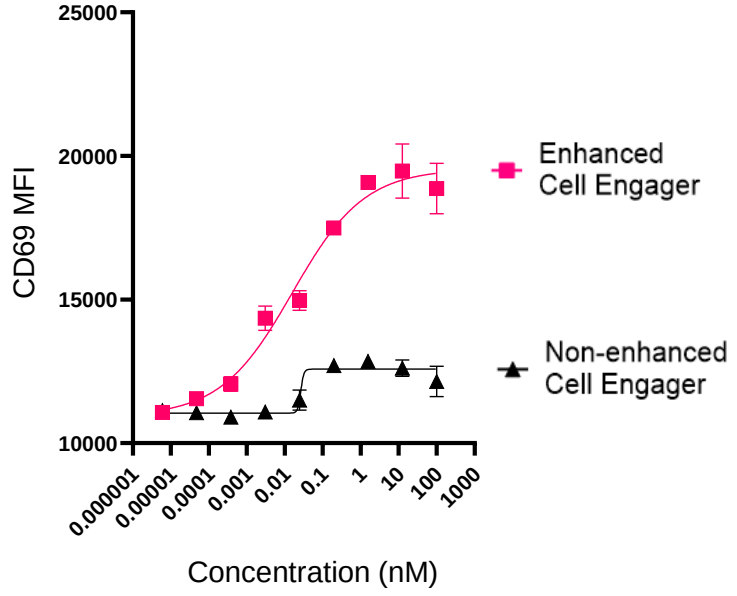
## Enhanced Tumor Cell Killing




## Potent IFNγ Induction




## Increased Expression of CD69 Activation Marker



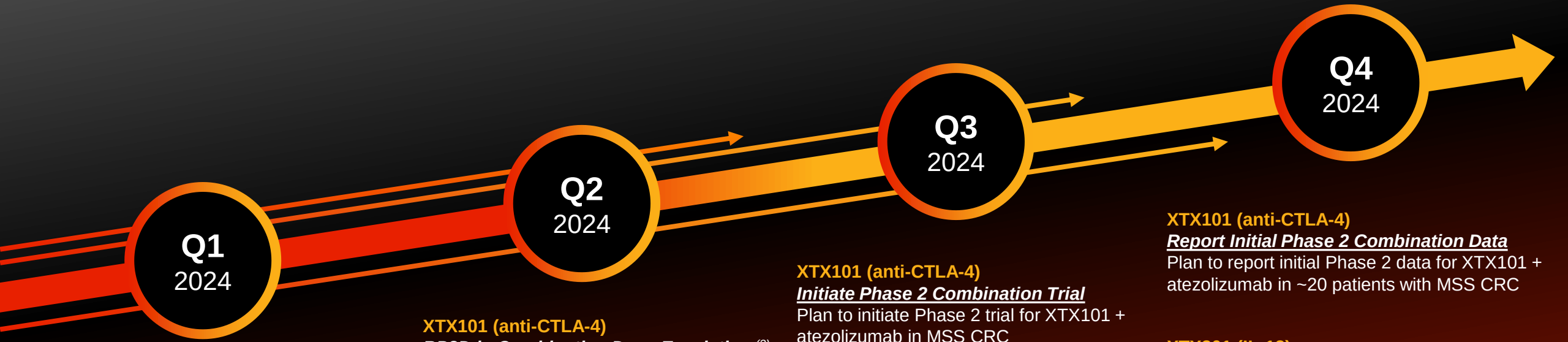

Co-culture assay using human primary immune cells and luciferized A375 cancer cells. Tumor cell killing was assessed by luciferase readout. Interferon gamma (IFNγ) readout and CD69 mean fluorescence intensity (MFI) were determined by flow cytometry.

# Closing Remarks and Q&A

**René Russo, Pharm. D.**

President and Chief Executive Officer

# Positioned for Multiple Anticipated Key Clinical Milestones in 2H 2024
## *Anticipate Cash Runway Into Q2 2025**




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

**XTX202 (IL-2)**
***Reported Additional Phase 2 Data*** (1)
Plan to explore strategic opportunities to continue to develop XTX202 in combination with other agents

**XTX101 (anti-CTLA-4)**
***RP2D in Combination Dose Escalation*** (2)
Plan to select RP2D for XTX101 + atezolizumab

**XTX501 (PD-1/IL2 bispecific)**
***Preclinical poster presentation at AACR***

**XTX101 (anti-CTLA-4)**
***Initiate Phase 2 Combination Trial***
Plan to initiate Phase 2 trial for XTX101 + atezolizumab in MSS CRC

**XTX101 (anti-CTLA-4)**
***Report Initial Phase 2 Combination Data***
Plan to report initial Phase 2 data for XTX101 + atezolizumab in ~20 patients with MSS CRC

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

1. In March 2024, announced plans to discontinue further investment in XTX202 as a monotherapy.
2. Evaluating XTX101 in combination with atezolizumab (Tecentriq®) under co-funded clinical collaboration with Roche in Phase 1 combination dose escalation trial and planned Phase 2 combination trial in MSS CRC.

* As of December 31, 2023, cash and cash equivalents were $44.7 million. This cash estimate is a preliminary estimate and is based on information available to management as of the date hereof, and these estimates could change. Anticipated cash runway includes cash and cash equivalents as of December 31, 2023, together with upfront payment under license agreement with Gilead, proceeds from initial equity investment by Gilead, anticipated net proceeds from the private placement and after giving effect to one-time costs and anticipated future cost savings associated with the strategic portfolio reprioritization and workforce reduction and repayment of outstanding loan balance under PacWest loan agreement in the first quarter of 2024.