UNITED STATES
SECURITIES AND EXCHANGE COMMISSION

WASHINGTON, D.C. 20549

FORM 8-K

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

Date of report (Date of earliest event reported): **January 9, 2023**

Xilio Therapeutics, Inc.

(Exact Name of Registrant as Specified in Charter)

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

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

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

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

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

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

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

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

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

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

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

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

Emerging growth company ☒

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

Item 7.01 Regulation FD Disclosure.

From time to time, Xilio Therapeutics, Inc. (the "Company") presents or distributes slide presentations to the investment community to provide updates and summaries of its business. The Company is posting a copy of its current corporate investor presentation to the "Investors & Media" portion of its website at https://ir.xiliotx.com. A copy of the presentation is furnished as Exhibit 99.1 to this Current Report on Form 8-K.

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

Item 9.01 Financial Statements and Exhibits.

(d) Exhibits.

The following exhibit relating to Item 7.01 of this Form 8-K shall be deemed to be furnished and not filed:

Exhibit No.	Description
99.1	Corporate investor presentation of Xilio Therapeutics, Inc. as of January 9, 2023
104	Cover Page Interactive Data File (embedded within the Inline XBRL document and incorporated as Exhibit 101)

SIGNATURES

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

XILIO THERAPEUTICS, INC.

Date: January 9, 2023

By: /s/ Chris Frankenfield
Chris Frankenfield
Chief Legal and Administrative Officer

Unleashing the Potential of Immuno-Oncology Therapies

January 9, 2023

Forward-Looking Statements

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: the initiation of patient enrollment in a Phase 2 clinical trial for XTX202 and reporting data from the Phase 1/2 clinical trial for XTX202; the initiation of patient enrollment in the planned Phase 1 clinical trial for XTX301 and reporting data from the Phase 1 clinical trial for XTX301; completing monotherapy dose-escalation for the Phase 1 clinical trial for XTX101 and reporting data from the Phase 1 clinical trial for XTX101; potential collaborations to advance XTX101; progressing Xilio's next research-stage program; the potential benefits of any of Xilio's current or future product candidates in treating patients; Xilio's ability to fund its operating expenses and capital expenditure requirements with its existing cash and cash equivalents; and Xilio's strategy, goals and anticipated financial performance, milestones, business plans and focus.

The words "aim," "may," "will," "could," "would," "should," "expect," "plan," "anticipate," "intend," "believe," "estimate," "predict," "project," "potential," "continue," "seek," "target" and similar expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words. Any forward-looking statements in this presentation are based on management's current expectations and beliefs and are subject to a number of important risks, uncertainties and other factors that may cause actual events or results to differ materially from those expressed or implied by any forward-looking statements contained in this presentation, including, without limitation, 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; and Xilio's advancement of multiple early-stage programs. There can be no assurance that interim or preliminary preclinical or clinical data or results will be predictive of future preclinical or clinical data or results, including, without limitation, the preliminary intra-tumoral pharmacodynamic data reported for two patients treated with XTX202 who had an optional on-treatment tumor biopsy and for whom a tumor biopsy analyses was available as of the date hereof; 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 current or future operating expenses and capital expenditure requirements; the impact of international trade policies on Xilio's business, including U.S. and China trade policies; and Xilio's ability to seek, establish and maintain a collaboration or partnership to develop XTX101 with a collaborator or partner.

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

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

This presentation contains trademarks, trade names and service marks of other companies, which are the property of their respective owners.

Xilio is a Clinical-Stage Company, Well-Positioned for Multiple Anticipated Milestones Across 3 Clinical Programs in 2023

- Focused pipeline prioritization
- Responsible financial discipline, success-gated investment
- Capital-efficient monotherapy clinical trial designs

XTX101: Completed enrollment in monotherapy dose-escalation cohort (Q4 2022)*

XTX202: Initiated enrollment in monotherapy expansion cohort (Q4 2022)

XTX301: IND cleared (November 2022)

XTX101: Report data from Phase 1 trial (Q2 2023)

XTX202: Initiate enrollment in Phase 2 (monotherapy) trial (1H 2023)

XTX301: Initiate enrollment in monotherapy dose-escalation (Q1 2023)

XTX202: Report preliminary anti-tumor activity and safety data from Phase 1/2 trial (Q3 2023)

XTX301: Report preliminary safety data from Phase 1 trial (Q4 2023)

Anticipate existing cash and cash equivalents will be sufficient to fund operating expenses and capital expenditure requirements into Q2 2024

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* Patient dosing and evaluation in Phase 1 monotherapy dose-escalation cohort is ongoing. Plan to explore opportunities for strategic collaborations to advance XTX101 and do not plan to initiate an anti-PD-1 combination cohort in the Phase 1 trial or initiate a Phase 2 trial without a development partner.

The Promise and Pitfalls of Immuno-Oncology Therapy

- **Immuno-oncology (IO) therapies have transformed the treatment landscape and long-term outlook for some patients with advanced cancer**
  - IO treatments are primarily available for “hot” tumors, while “warm” and “cold” tumors continue to make up the majority of annual cancer deaths
- **IO therapies engage the immune system to recognize and destroy tumor cells**
  - Potential to be curative
  - Potential to address wide range of tumor types
- **But treatment potential for some of the most exciting IO targets has been impeded by dose-limiting systemic toxicity**
  - Fatal multi-organ adverse events and peripheral side effects can occur with more potent IO agents
  - Often results in dose reductions, interruptions or discontinuations for many patients
  - Limits the ability to explore even more powerful targets or IO combinations that could have broad curative potential

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

We are here to pursue that promise for patients

2016	XLO	~100	3
Founded	NASDAQ	Employees	Clinical Stage Programs

xilio THERAPEUTICS

Pioneering Tumor-Activated Immuno-Oncology Therapies to Pursue Positive Outcomes for More Patients

Mission

Design and deliver tumor-activated immuno-oncology therapies that provide effective, tolerable and durable therapeutic options for patients with solid tumors

Vision

We envision a future where cancer is no longer a grim diagnosis because treatments exist that eliminate it at the source, and cures come without the severe systemic side effects of current-day IO therapies

Leveraging Our Deep Expertise to Build a Transformational Immuno-Oncology Company

- **Intentionally built** team with significant breadth and depth of biotech and big pharma experience including cytokines such as IL-12
- Team has collectively contributed to:
  - >15 IND applications
  - >25 NDAs, sNDAs or BLAs
  - 15 approved therapies
- Team has **direct experience** with pembrolizumab, dostarlimab, niraparib, docetaxel, trastuzumab, alpelisib and capmatinib

René Russo, Pharm. D.
Chief Executive Officer, Director

Martin Huber, M.D.
President and Head of R&D

Uli Bialucha, Ph.D.
Chief Scientific Officer

Stacey Davis
Chief Business Officer

Chris Frankenfield
Chief Legal and Administrative Officer

Xilio's Core Expertise

Cytokines

Protease Biology

Protein Engineering

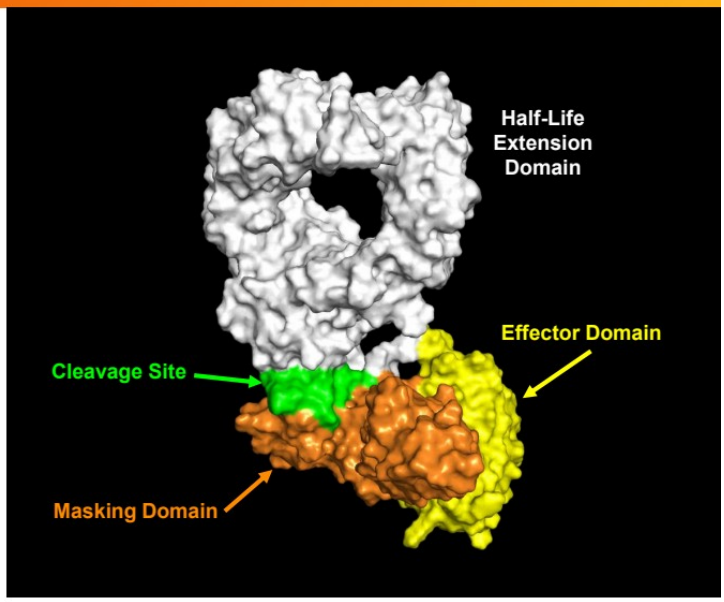
Clinical Development

Data Science

BLA: biologics license application; IND application: investigational new drug application; NDA: new drug application; sNDA: supplemental new drug application.

Xilio's Tumor-Activated Precision Immuno-Oncology

- We are passionate about **harnessing and focusing** the power of the immune system to treat cancer
- We have developed a novel approach designed to **outsmart tumors** by using the tumor's growth activities against itself
  - Tumor proteases **activate a switch** in our molecules, which unleashes the active agent once it is inside the tumor microenvironment
- Each of our molecules has a custom masking domain designed to prevent it from interacting with healthy tissues and cells
  - The mask is released by the tumor's **dysregulated matrix metalloproteinases (MMPs),** which are present but inhibited outside of the tumor microenvironment



Building a Transformative Immuno-Oncology Pipeline

Program	Disease Indication	Mechanism of Action	Discovery	IND-Enabling	Phase 1	Phase 2	Phase 3
Cytokine Programs							
XTX202[1]	Oncology	IL-2					
XTX301[2]	Oncology	IL-12					
Discovery Stage	Oncology	Tumor-Activated Cytokine					
Antibody Program							
XTX101[3]	Oncology	Anti-CTLA-4					

Plan to seek partnership for further investment

1. Plan to initially evaluate XTX202 as a monotherapy and as a combination therapy for the treatment of renal cell carcinoma (RCC) and melanoma prior to potential expansion into additional cancer indications. 2. Plan to initially evaluate XTX301 as a monotherapy for the treatment of advanced solid tumors. 3. Plan to explore opportunities for strategic collaborations to advance XTX101 and do not plan to initiate an anti-PD-1 combination cohort in the Phase 1 trial or initiate a Phase 2 trial without a partner.

Xilio Designed, Tumor Activated

Seeking to Develop a Transformational IO Approach

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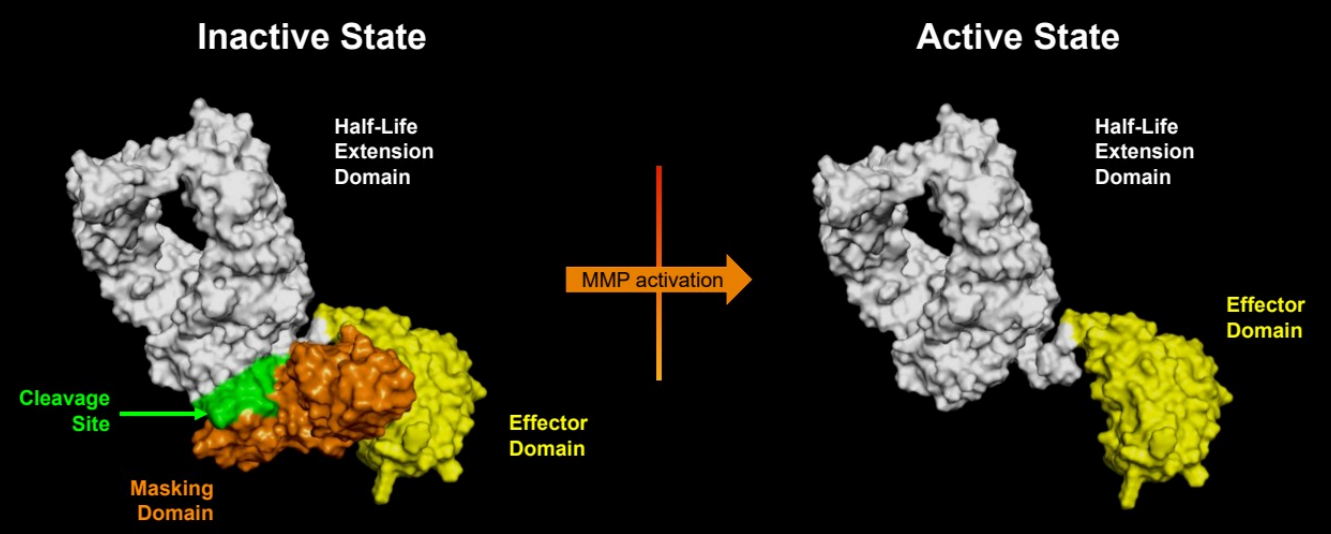
Xilio's Tumor-Activated Design Components – XTX202 (IL-2)



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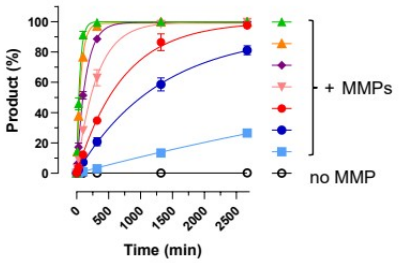
MMP: matrix metalloproteases

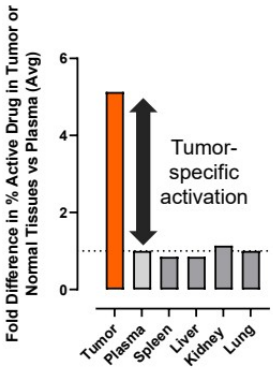
Xilio's Molecules are Activated by Dysregulated Tumor Proteases (MMPs)

Xilio's optimized substrate sequences enable efficient activation of the molecule by MMPs

In vitro recombinant MMP kinetic cleavage assay



Xilio molecules demonstrated tumor-specific activation *in vivo*



Xilio molecules are readily activated by human tumors *ex vivo*

Tumor Type	Activation Efficiency	
	XTX202 (IL-2)	XTX301 (IL-12)
Colon		
H&N		
Prostate		
RCC		
Lung		
Melanoma		
Plasma		

Left panel: Time-course of XTX301 activation by recombinant human matrix metalloproteinases (MMPs).
Middle panel: Mice bearing MC38 syngeneic colorectal carcinoma tumors were dosed with mXTX301 (murine surrogate for XTX301), and the percent activated molecule was measured 72h post dose in tumor, plasma, spleen, liver, kidney and lung. Average % active molecule in plasma was set to 1 and fold difference in average % active drug in tumor or normal tissues vs plasma is shown.
Right panel: Activation of XTX202 or XTX301 assessed in tumor biopsies ex vivo.

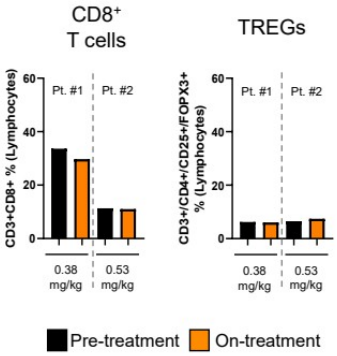
First Demonstration of Clinical Platform Validation and Tumor-Selective Activation in Patients

Preliminary Evidence of Intra-Tumoral Pharmacodynamic Effects Consistent with Known IL-2 Biology in Melanoma and RCC

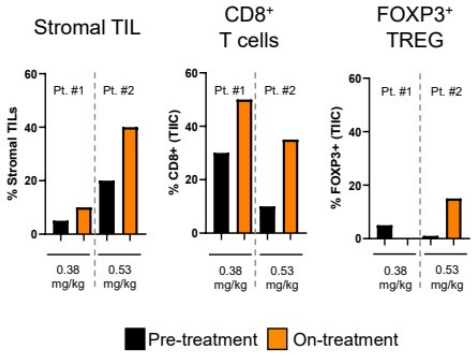
Patient Details (n=2)

- **Patient #1:** treated with XTX202 at 0.38 mg/kg, Q3W (dose level 2):
  - 51 year-old male with stage 4 melanoma
  - Heavily pre-treated, including prior IO
- **Patient #2:** treated with XTX202 at 0.53 mg/kg, Q3W (dose level 3):
  - 75 year-old male with stage 4 RCC
  - Heavily pre-treated, including prior IO
- Fresh biopsies at pre-treatment and on-treatment cycle 2, day 20 (patient #1) and cycle 2, day 14 (patient #2)
- No evidence of vascular leak syndrome

XTX202 treatment resulted in minimal pharmacodynamic changes in peripheral blood



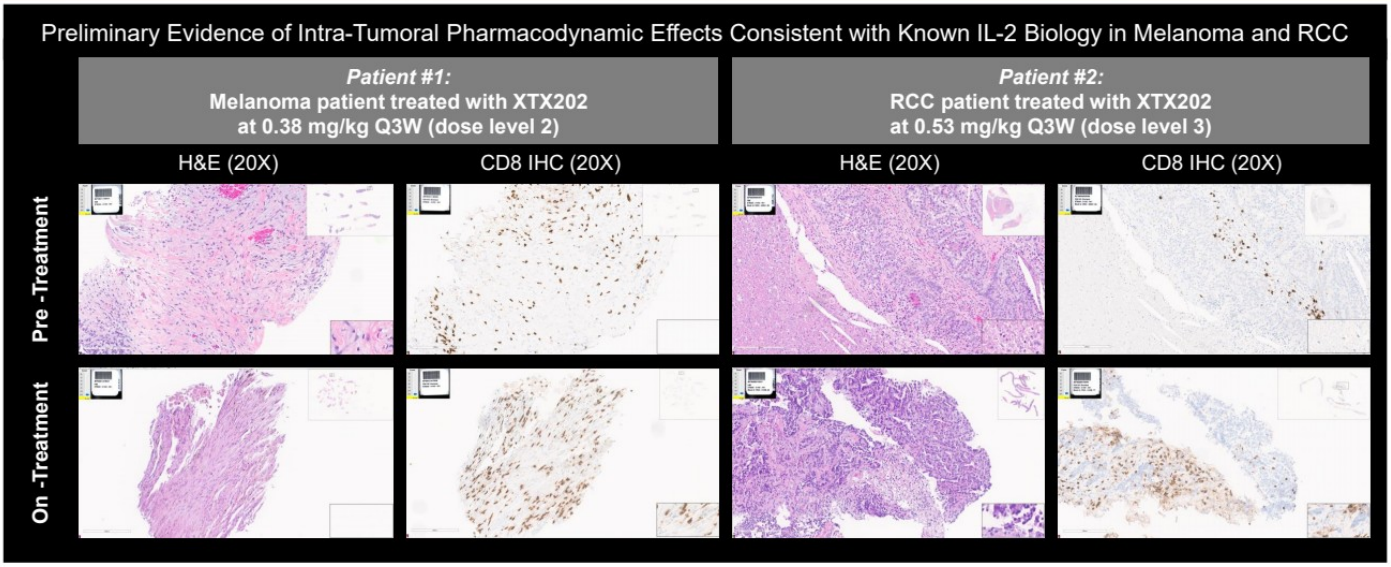
XTX202 treated tumors featured increased stromal TIL and robust increases in CD8+ T cells compared to pre-treatment



Patients had an optional on-treatment tumor biopsy and were the only two patients treated with XTX202 for whom a tumor biopsy analysis was available as of January 9, 2023.
Q3W: dosed every three weeks; TIIC: tumor infiltrating immune cell; TIL: tumor infiltrating lymphocyte; TKI: tyrosine kinase inhibitor; TREG: regulatory T cell.

First Demonstration of Clinical Platform Validation and Tumor-Selective Activation in Patients

Preliminary Evidence of Intra-Tumoral Pharmacodynamic Effects Consistent with Known IL-2 Biology in Melanoma and RCC

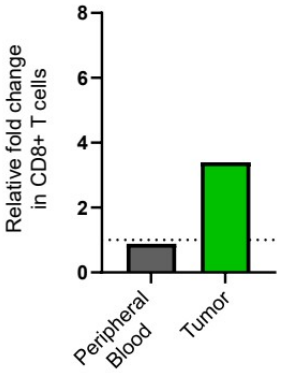


Patients had an optional on-treatment tumor biopsy and were the only two patients treated with XTX202 for whom a tumor biopsy analysis was available as of January 9, 2023.
H&E: hematoxylin-eosin; IHC: immunohistochemistry.

Robust Increases in CD8+ T Cells Observed in Patient Tumors Following XTX202 Treatment

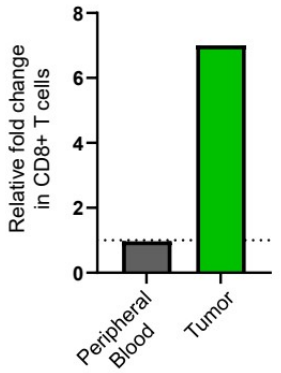
Patient #1:
Melanoma patient treated with XTX202 at 0.38 mg/kg Q3W (dose level 2)

Relative Fold-Change in CD8+ T cells Compared to Pre-Treatment



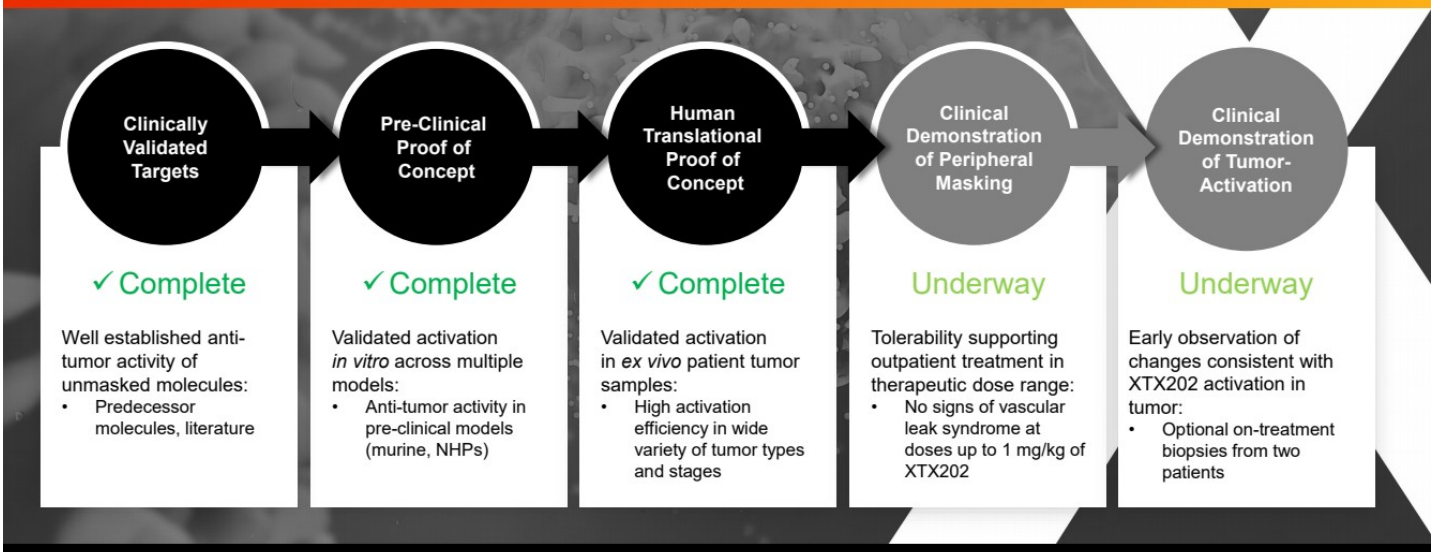
Patient #2:
RCC patient treated with XTX202 at 0.53 mg/kg Q3W (dose level 3)

Relative Fold-Change in CD8+ T cells Compared to Pre-Treatment



Patients had an optional on-treatment tumor biopsy and were the only two patients treated with XTX202 for whom a tumor biopsy analysis was available as of January 9, 2023.
CD8+ T cells assessed by FACS for peripheral blood and IHC for tumor. Relative fold-change in CD8+ cells in tumor takes into account increase in stromal TILs and CD8+ IHC (%TIL post-treatment x %cCD8+ post-treatment over (%TIL pre-treatment x %CD8+ pre-treatment).

Executing on Our Vision to Deliver Tumor-Activated Immuno-Oncology Therapies Created Through Our Unique and Efficient Design Process



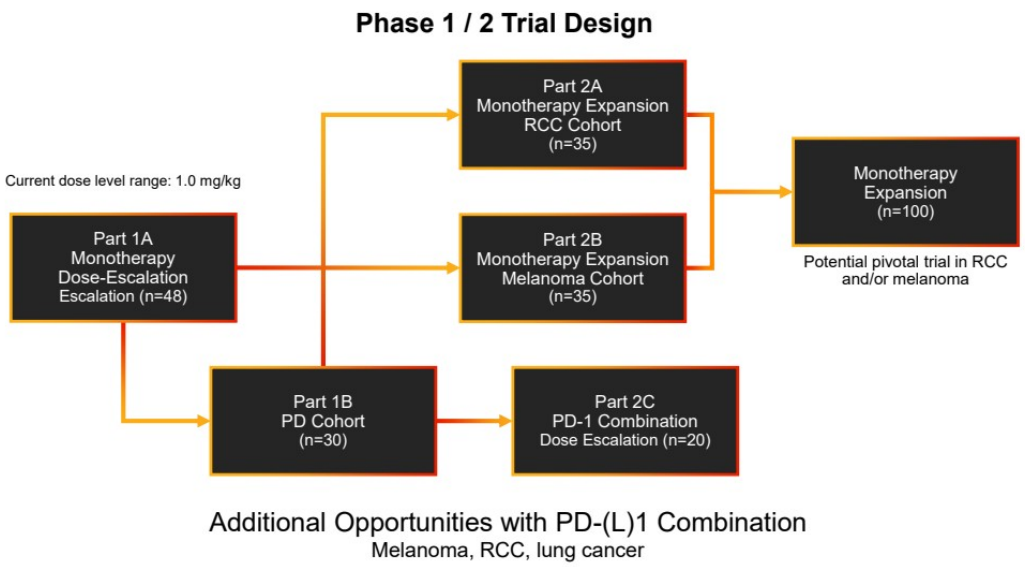
Xilio is positioned to demonstrate clinical platform validation in 2023

NHP: non-human primate.


XTX202
Tumor-Activated IL-2
x·ilio
THERAPEUTICS

XTX202 (IL-2) Phase 1/2 Trial Design Provides Efficient Path to Potential Monotherapy Proof-of-Concept

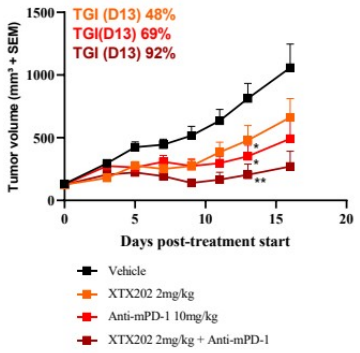
- Dosing patients at 1 mg/kg dose level, the target dose range for XTX202
- No signs of VLS or decreases in albumin (an early sign of VLS) observed
- Preliminary analyses indicated evidence of IL-2 specific biology including CD8+ effector T cells and NK cells increasing in peripheral circulation steadily over time*
- XTX202 treated tumors featured increased stromal TIL and robust increases in CD8+ T cells compared to pre-treatment
- MTD has not yet been determined, and enrollment in monotherapy dose-escalation is ongoing.



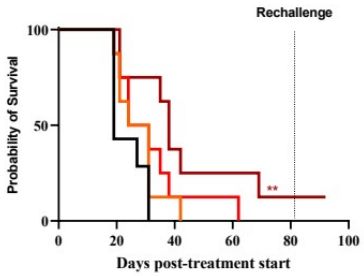
* Data reported as of November 7, 2022.
DLT: dose-limiting toxicity; MTD: maximum tolerated dose; NK: natural killer; PD: pharmacodynamic; RCC: renal cell carcinoma; TKI: tyrosine kinase inhibitor; VLS: vascular leak syndrome.

Enhancement of *In Vivo* Activity and Evidence of Memory Response for XTX202 (IL-2) in Combination with Anti-PD1

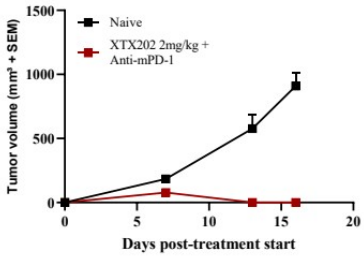
Enhanced *in vivo* activity with combination of XTX202 and anti-PD-1 mAb



XTX202 combination with anti-PD-1 induced complete responses in subset of animals



Complete responders rejected tumors upon rechallenge, indicating evidence of memory response

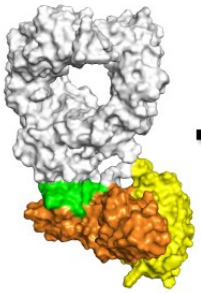


Data presented at Society for Immunotherapy of Cancer (SITC) in November 2022

Anti-tumor activity of XTX202 as a single agent and in combination with anti-mPD-1 was evaluated in hFcRn Tg32 transgenic mice bearing the murine MB49 bladder carcinoma model. The combination of XTX202 with anti-mPD-1 further improved anti-tumor activity with TGI 92% on Day 13 (Data presented as mean ±SEM, two-way ANOVA followed by post hoc Dunnett's test, *P < 0.05; **P < 0.005). The treatment with XTX202 alone or in combination with anti-mPD-1 improved animal survival from 19 days to 27.5 and 38 days, respectively (Geham-Breslow-Wilcoxon test, **P < 0.01). A mouse with complete regression of MB49 tumor after combination therapy with XTX202 and anti-mPD-1 was resistant to tumor rechallenge with autologous MB49 tumor implanted on the opposite flank.

Multiple Combination Opportunities Enabled by XTX202 (IL-2) Properties: Tumor-Activated, Well-Tolerated Preclinically, Clinically-Validated Target

IL-2
XTX202



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- Monoclonal antibodies (Checkpoint inhibitors[1]; ADCC-inducing mAbs[2])
- Other pro-inflammatory cytokines[3,4,5] (IL-12; IL-18)
- Cell therapies (CAR-T[6,7]; CAR-NK)
- Cancer vaccines[8,9]

Combination opportunities may be uniquely enabled by XTX202's novel proprietary design

1. Xilio data presented at SITC 2022. 2. Gola et al., Haematologica 2003. 3. Wigginton et al., J Natl Cancer Inst 1996. 4. Gollob et al., Journal of Clinical Oncology 2003. 5. Nielsen et al., Frontiers in Immunology, 2016. 6. Zhang et al., Sci Trans. Med., 2021. 7. Aspuria et al., Sci. Trans. Med., 2021. 8. Moynihan et al., Nature Medicine 2016. 9. Hernandez et al., Journal of Immunology, 2020.

XTX202 (IL-2) Key Takeaways

- IL-2 has significant therapeutic potential both as monotherapy and in combination
  - Monotherapy tumor types include: RCC, melanoma, lung cancer
  - Attractive combination partners include: mAbs (e.g., anti-PD-1), cytokines (e.g., IL-12), cell therapies, cancer vaccines
- Achieving therapeutic benefit from IL-2 requires high dose delivery in the tumor microenvironment
- XTX202 has achieved dose ranges in line with traditional high dose treatment with aldesleukin
  - XTX202 currently being dosed at 1 mg/kg, the target dose range for XTX202
  - Preliminary analyses demonstrated evidence of IL-2 specific biology, including CD8+ effector T cells and NK cells increasing in peripheral circulation over time for patients consistent with data observed in preclinical studies*
  - No signs of VLS or decreases in albumin (an early sign of VLS) have been observed
  - Intra-tumoral PD data for two patients provide preliminary evidence that the patients' tumors featured increased stromal TIL and robust increases in CD8+ T cells compared to pre-treatment**
- Adaptive Phase 1/2 trial design with multiple clinical milestones anticipated in 2023
  - Initiated patient enrollment in a monotherapy expansion cohort of Phase 1 clinical trial in Q4 2022
  - Anticipate initiating patient enrollment in Phase 2 monotherapy trial in 1H 2023
  - Anticipate reporting preliminary anti-tumor activity and safety data from Phase 1/2 trial in Q3 2023

TREG: regulatory T cells.
* Data reported as of November 7, 2022.
** Patients had an optional on-treatment tumor biopsy and were the only two patients treated with XTX202 for whom a tumor biopsy analysis was available as of January 9, 2023.


XTX301
Tumor-Activated IL-12
x·ilio
THERAPEUTICS

The Potential of IL-12 as a Therapeutic Agent

- IL-12 has ground-breaking potential as a potent IO therapeutic agent
- Poor tolerability has limited its clinical progress for decades
- No currently approved IL-12 agents

IL-12 Has Highly Compelling Biology for IO Applications

Exquisitely potent stimulator of NK and T cell cytotoxicity and INFγ production

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

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

Demonstrated single agent objective responses in patients, but poorly tolerated (MTD <500 nanograms/kg on repeat dosing)

INFγ: interferon gamma; MTD: maximum tolerated dose; NK: natural killer; TME: tumor microenvironment.
INFγ is a pleiotropic molecule with associated antiproliferative, pro-apoptotic and antitumor mechanisms. Th1-type cytokines tend to produce the proinflammatory responses responsible for killing intracellular parasites and for perpetuating autoimmune responses.

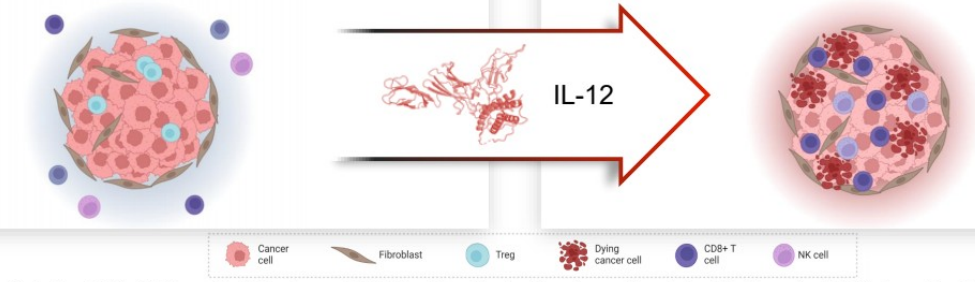
IL-12 Can Remodel Cold Tumor Microenvironment Towards a Pro-Inflammatory (Hot) State that Favors Anti-Tumor Immunity

Cold Tumor

- Lack of CD8 T and NK cells within tumor
- Presence of immune suppressive cells (TREGs, MDSCs)
- Poor response to checkpoint inhibitors

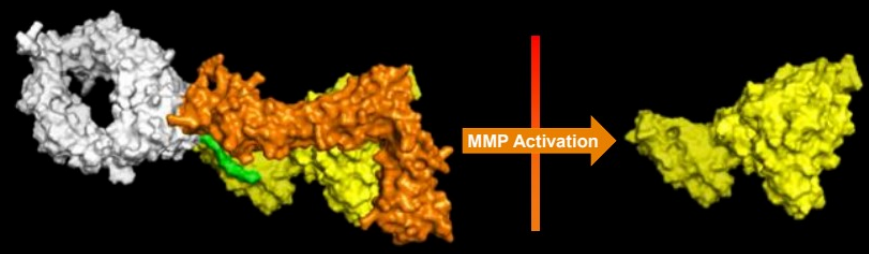
Hot Tumor

- CD8 T and NK cells are abundant in tumor
- Pro-inflammatory microenvironment
- Improved prognosis and effective killing of tumor cells with immunotherapy treatment



Adapted from "Cold vs Hot Tumors", by BioRender.com, 2022. Retrieved from https://app.biorender.com/biorender-templates Barraondo et al., Clin. Cancer Res., 2018. Nguyen et al., Front. Immunol., 2020.

XTX301 – Tumor-Activated IL-12



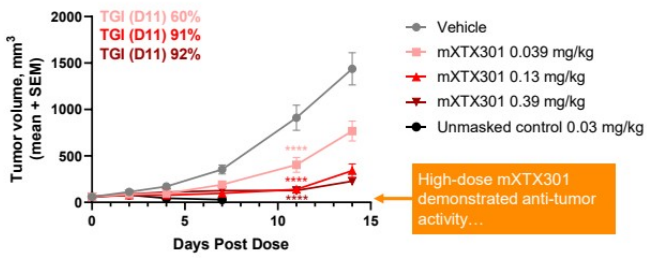
Designed to Outsmart Tumors

XTX301 custom mask designed to address unique challenges presented by the complex heterodimer structure of IL-12

Half-Life Extension Domain | Cleavage Site | Masking Domain | Effector Domain

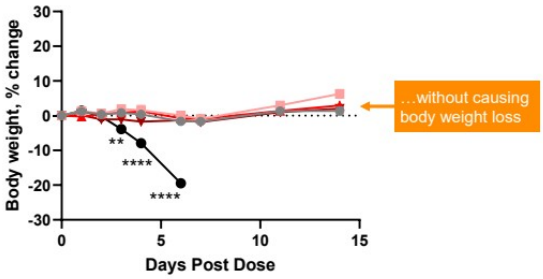
mXTX301 (Murine Surrogate) Demonstrated Dose-Dependent Anti-Tumor Activity Without Body Weight Loss *In Vivo*

Tumor Growth



- mXTX301 demonstrated dose-dependent anti-tumor activity in MC38 murine model at all tested doses
- Dosing with mXTX301 at 0.13 and 0.39 mg/kg resulted in complete tumor regression in individual mice

Body Weight



- mXTX301 was well-tolerated in MC38 murine model with no significant body weight loss at all tested doses
- Unmasked control (mXTX302) not tolerated at 0.03 mg/kg dose; 75% (9/12) mice were euthanized by Day 11 due to body weight loss

Data presented at New York Academy of Sciences' Frontiers in Cancer Immunotherapy in May 2022

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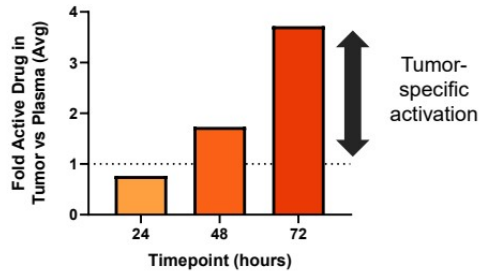
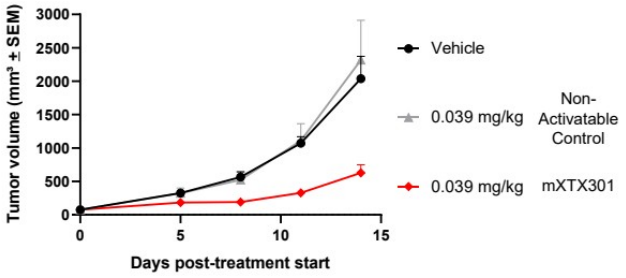
TGI: tumor growth inhibition.
MC38 model: s.c. 0.5x106 cells; single IV dose of mXTX301 and mXTX302 on Day 0. Tumor growth data shown as mean±SEM. Tumor volume data was assessed by a two-way ANOVA followed by Bonferroni post hoc test on Day 11 compared to vehicle treated animals. ****p<0.0001 for all mXTX301 treatment groups. Body weight data are shown as mean ±SEM. A two-way ANOVA followed by Bonferroni post hoc test compared to vehicle treated animals was performed **p<0.005, ****p<0.0001.

mXTX301 (Murine Surrogate) was Preferentially Activated in Tumors vs. Plasma *In Vivo*

mXTX301 demonstrated tumor-specific activation *in vivo*



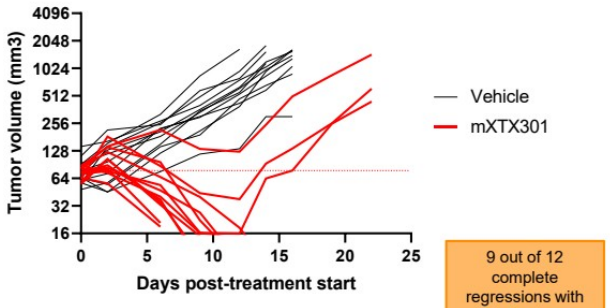
mXTX301 treatment resulted in cleavage-dependent enhancement in activity vs. non-activatable control



Left panel: Mice bearing MC38 syngeneic colorectal carcinoma tumors were dosed with mXTX301 (murine surrogate for XTX301), and the percent activated drug was measured over time in tumors and plasma.
Right panel: Mice bearing MC38 syngeneic colorectal carcinoma tumors were dosed once with mXTX301 or a non-activatable control and tumor growth was monitored over time.

mXTX301 Induced Memory Responses in Murine Model Enabling Tumor Rejection Upon Rechallenge of Complete Responders

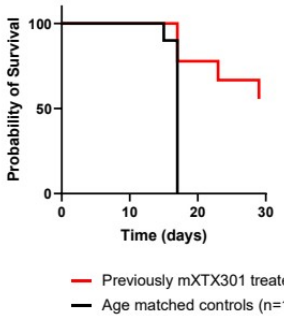
mXTX301 treatment resulted in complete regressions in 9 out of 12 mice



9 out of 12 complete regressions with single dose mXTX301

Majority of mXTX301 complete responders rejected tumors upon rechallenge

Fresh tumor cells implanted into control animals or complete responders

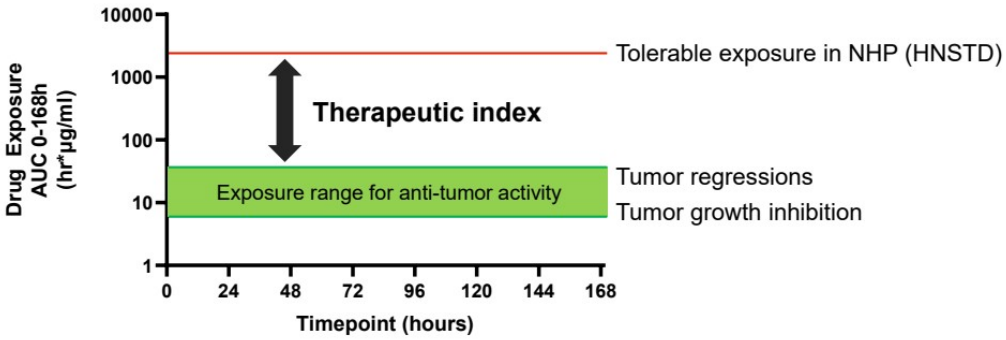


Evidence of memory response

Left panel: Mice bearing MC38 syngeneic colorectal carcinoma tumors were dosed with mXTX301 (murine surrogate for XTX301) or vehicle, and tumor growth was followed over time.
Right panel: Mice having shown complete responses to mXTX301 were rechallenged with MC38 tumor cells on day 34 post initial treatment, while treatment-naïve, age-matched control animals were concurrently implanted with the same amount of MC38 tumor cells. Survival data are plotted over time; study was terminated once all animals on the control arm reached tumor size limits.

XTX301 (IL-12) Preclinical Data Support Potential for Broad Therapeutic Index

- XTX301 was tolerated at doses up to 2.0 mg/kg Q1W x4 in NHP (HNSTD)
- mXTX301 induced tumor regressions in murine model following a **single dose** of 0.13 mg/kg



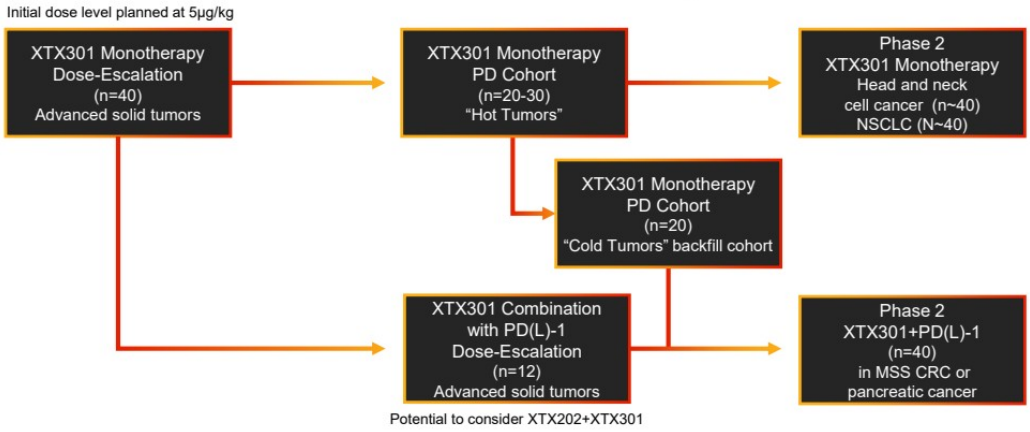
Compound	In vivo model	Dose (mg/kg)	$AUC_{0\text{-}168}$ (hr*µg/mL)	Estimated Therapeutic Index (AUC_{Safety} / $AUC_{Activity}$)
mXTX301	**Anti-tumor activity** (murine)	0.13	37.8	**66**
XTX301	**Safety** (NHP)	2.0	2510	

HNSTD: highest non-severely toxic dose; NHP: non-human primates; Q1W: once every week.

XTX301 (IL-12) Trial Designed to Enable Multiple Monotherapy and Combination Opportunities for Expansion in Both Hot and Cold Solid Tumors

- IND cleared in November 2022
- Anticipate initiating enrollment in monotherapy dose-escalation in planned Phase 1 trial in Q1 2023
- Initial dose level planned at 5µg/kg
- Anticipate reporting preliminary safety data from Phase 1 trial in Q4 2023

Planned Phase 1 / 2 Trial Design



Multiple Opportunities with Monotherapy and Combination Strategies

NSCLC, head & neck, melanoma, TNBC, MSI high CRC, Prostate, Ovarian, Pancreas, Colorectal MSS

CRC: colorectal cancer; NSCLC: non-small cell lung cancer; TNBC; triple negative breast cancer.
µg: micrograms.

XTX301 (IL-12) Key Takeaways

- IL-12 has significant therapeutic potential across both “hot” and “cold” tumor types
  - “Hot” tumors include lung, bladder, head & neck, kidney, liver, melanoma, MSI high CRC
  - “Cold” tumors include prostate, ovarian, breast, pancreatic, brain, MSS CRC
- No approved IL-12 agents to date due to fatal dose limiting toxicities
- Believe XTX301 is first systemically-delivered, tumor-activated IL-12 cleared for clinical development
  - XTX301 tumor-activation designed to overcome dose limiting toxicities of existing IL-12 agents
  - IND cleared in November 2022; anticipate initiating enrollment in monotherapy dose-escalation in planned Phase 1 trial in advanced solid tumors in Q1 2023
  - Preclinical data showed anti-tumor activity in both “hot” and “cold” tumor models, often with a single dose
- Adaptive design for planned Phase 1/2 trial with preliminary safety data anticipated in Q4 2023
  - Patients will receive treatment with XTX301 in the outpatient setting
  - Initial dose level planned at 5µg/kg (10x MTD for recombinant human IL-12 of 0.5 µg/kg IV)
  - Trial design incorporates both “hot” and “cold” tumor cohorts


XTX101
Tumor-Activated aCTLA-4
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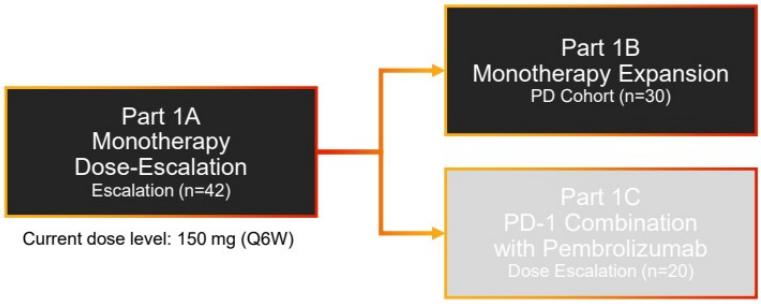
XTX101 (aCTLA4) Phase 1 Trial

- Announced encouraging preliminary Part 1A data in August 2022
- Preliminary PK analyses demonstrated dose-proportional drug exposure, with limited active (unmasked) XTX101 in peripheral circulation consistent with PK data observed in preclinical studies*
- Completed enrollment in Part 1A in Q4 2022
- Enrollment in Part 1B ongoing
- Seeking partnership prior to advancing Part 1C / Phase 2

Phase 1 Trial Design



Current dose level: 150 mg (Q6W)

Additional Opportunities with PD-(L)1 Combination
Melanoma, renal cell carcinoma, MSS colorectal cancer

PK: pharmacokinetic; Q6W: once every six weeks.
* Data reported as of November 7, 2022.
Clinical trial collaboration and supply agreement established with Merck in May 2021 to evaluate XTX101 in combination with KEYTRUDA® (pembrolizumab).

XTX101 Anti-CTLA-4 Key Takeaways

- Next generation anti-CTLA-4 molecules seek to improve upon the efficacy and tolerability of existing molecules, such as ipilimumab
- XTX101 is an Fc-enhanced, tumor-activated, anti-CTLA-4 currently being studied in a Phase 1 clinical trial for advanced solid tumors
- Phase 1 monotherapy dose escalation patients currently receiving XTX101 at 150 mg (Q6W)
  - Completed enrollment in monotherapy dose-escalation (Part 1A) in Q4 2022
  - Enrollment in monotherapy dose expansion (Part 1B) is ongoing
  - Anticipate reporting preliminary data from Phase 1 trial in Q2 2023
- Preliminary PK analyses demonstrated dose-proportional drug exposure, with limited active (unmasked) XTX101 in peripheral circulation consistent with PK data observed in preclinical studies*
- Plan to continue to explore opportunities for strategic collaborations to advance XTX101
  - Seeking partnership prior to initiating Part 1C cohort (anti-PD-1 combination) or Phase 2 trial

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* Data reported as of November 7, 2022.

Looking Ahead

Xilio's Tumor-Activated Platform Opportunities are Broad

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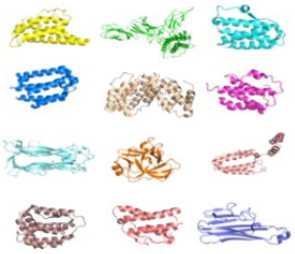
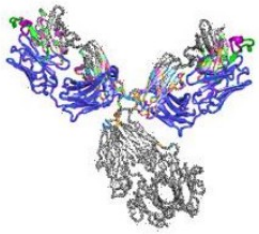
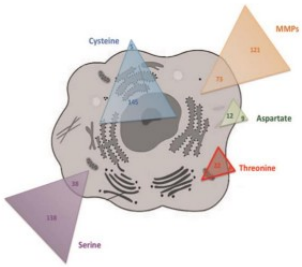
Looking Ahead: Potential to Deliver Highly Potent, Locally-Activated Immunotherapies Beyond Cancer

Masked Cytokines	Masked Antibodies	Pro- and Anti-Inflammatory Processes	Proteases in Diseases of Immune Dysregulation
		IL-2 IL-12 IL-15 IL-17 IL-23 IL-22 GM-CSF IL-18 TNF-a IL-1 IL-7 IL-6 INF-y  IL-2 IL-4 IL-5 IL-9 IL-10 IL-13 IL-25 IL-27 IL-35 TGF-B LIF	

Actively pursuing the next generation of tumor-activated platform capabilities

Third Quarter 2022 Financial Results

Balance Sheet	September 30, 2022*	December 31, 2021
Cash and Cash Equivalents	$139.1M	$198.1M

Statement of Operations	Three Months Ended September 30,	
	2022*	2021*
Research & Development Expenses	$13.0M	$10.5M
General & Administrative Expenses	$7.2M	$5.5M
Net Loss	$(19.8M)	$(16.3M)

Anticipate existing cash and cash equivalents will be sufficient to fund operating expenses and capital expenditure requirements into Q2 2024

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* Unaudited

Xilio is a Clinical-Stage Company, Well-Positioned for Multiple Anticipated Milestones Across 3 Clinical Programs in 2023

- Focused pipeline prioritization
- Responsible financial discipline, success-gated investment
- Capital-efficient monotherapy clinical trial designs

XTX101: Completed enrollment in monotherapy dose-escalation cohort (Q4 2022)*

XTX202: Initiated enrollment in monotherapy expansion cohort (Q4 2022)

XTX301: IND cleared (November 2022)

XTX101: Report data from Phase 1 trial (Q2 2023)

XTX202: Initiate enrollment in Phase 2 (monotherapy) trial (1H 2023)

XTX301: Initiate enrollment in monotherapy dose-escalation (Q1 2023)

XTX202: Report preliminary anti-tumor activity and safety data from Phase 1/2 trial (Q3 2023)

XTX301: Report preliminary safety data from Phase 1 trial (Q4 2023)

Anticipate existing cash and cash equivalents will be sufficient to fund operating expenses and capital expenditure requirements into Q2 2024

* Patient dosing and evaluation in Phase 1 monotherapy dose-escalation cohort is ongoing. Plan to explore opportunities for strategic collaborations to advance XTX101 and do not plan to initiate an anti-PD-1 combination cohort in the Phase 1 trial or initiate a Phase 2 trial without a development partner.

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

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