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): **May 25, 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. The information contained on, or accessible through, the Company's website is not incorporated by reference into this Current Report on Form 8-K and should not be considered to be a part hereof. A copy of the presentation is furnished as Exhibit 99.1 to this Current Report on Form 8-K.

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

Item 8.01 Other Events.

On May 25, 2023, the Company issued a press release announcing preliminary monotherapy data from its ongoing Phase 1 clinical trial evaluating XTX101 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.

Cautionary Note Regarding Forward-Looking Statements

This Current Report on Form 8-K contains forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995, as amended, including, without limitation, statements regarding plans, statements regarding plans, timing and expectations related to timing and expectations related to: the ongoing Phase 1 monotherapy dose expansion cohort for XTX101; plans to continue to explore strategic opportunities to advance XTX101 with a partner beyond the current Phase 1 monotherapy cohorts; the potential safety and anti-tumor activity of any of the Company's current or future product candidates in treating patients, including without limitation XTX101; and the Company's strategy, goals and anticipated financial performance, milestones, business plans and focus. The words "aim," "may," "will," "could," "would," "should," "expect," "plan," "anticipate," "intend," "believe," "estimate," "predict," "project," "potential," "continue," "seek," "target" and similar expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words. Any forward-looking statements in this Current Report on Form 8-K are based on management's current expectations and beliefs and are subject to a number of important risks, uncertainties and other factors that may cause actual events or results to differ materially from those expressed or implied by any forward-looking statements contained in this Current Report on Form 8-K, including, without limitation, risks and uncertainties related to: ongoing and planned research and development activities, including initiating, conducting or completing preclinical studies and clinical trials and the timing and results of such preclinical studies or clinical trials; the delay of any current or planned preclinical studies or clinical trials or the development of the Company's current or future product candidates; the Company's ability to obtain and maintain sufficient preclinical and clinical supply of current or future product candidates; the Company's advancement of multiple early-stage programs; the Company's ability to replicate in future preclinical studies or clinical trials positive data results from earlier preclinical studies or clinical trials, such as the early anti-tumor data observed in a patient whose results were reported in the preliminary data from the Phase 1 clinical trial of XTX 101; the Company's ability to successfully demonstrate the safety and efficacy of its product candidates and gain approval of its product candidates on a timely basis, if at all; the potential for results from preclinical studies or clinical trials for the Company's product candidates not supporting further development of such product candidates; actions of regulatory agencies, which may affect the initiation, timing and progress of current or future clinical trials; the Company's ability to obtain, maintain and enforce patent and other intellectual property protection for current or future product candidates; the Company's ability to obtain and maintain sufficient cash resources to fund current or future operating expenses and capital expenditure requirements; the impact of international trade policies on the Company's business, including U.S. and China trade policies; and the Company'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 sections entitled "Risk Factor Summary" and "Risk Factors" in the Company's filings with the U.S. Securities and Exchange Commission ("SEC"), including the Company's Quarterly Report on Form 10-Q for the fiscal quarter ended March 31, 2023 and any other

filings that the Company has made or may make with the SEC in the future. Any forward-looking statements contained in this Current Report on Form 8-K represent the Company's views only as of the date hereof and should not be relied upon as representing its views as of any subsequent date. Except as required by law, the Company explicitly disclaims any obligation to update any forward-looking statements.

Item 9.01 Financial Statements and Exhibits.

(d) Exhibits.

Exhibit No.	Description
99.1	Corporate slide presentation of Xilio Therapeutics, Inc. dated May 25, 2023
99.2	Press release issued by Xilio Therapeutics, Inc. on May 25, 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: May 25, 2023

By: /s/ René Russo
René Russo
Chief Executive Officer

Unleashing the Potential of Immuno-Oncology Therapies

May 25, 2023

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: reporting data from the Phase 1 clinical trial for XTX101, Phase 1/2 clinical trial for XTX202 or Phase 1 clinical trial for XTX301; progressing Xilio's research pipeline programs; 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 existir 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 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 managem 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 implie any forward-looking statements contained in this presentation, including, without limitation, risks and uncertainties related to ongoing and planned research and development activities, including initiatir 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 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; or Xilio's advanceme 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, witho limitation, the preliminary intra-tumoral pharmacodynamic data reported for two patients treated with XTX202 who each had an optional on-treatment tumor biopsy; Xilio's ability to successfully demons 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, whic 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 ob 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; and the impact of international trade policies on Xilio's business, including U.S. and China trade policies.

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 Quarterly Report on Form 10-Q for the quarter ended March 31, 2023, as well as other subsequent 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 expli 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 researc While Xilio believes these third-party studies, publications, surveys and other data to be reliable as of the date of this presentation, Xilio has not independently verified, and makes no representation as the adequacy, fairness, accuracy or completeness of, any information obtained from third-party sources. In addition, no independent source has evaluated the reasonableness or accuracy of our intern 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.

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Deep Expertise to Build a Transformational Immuno-Oncology Company

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

Proven Track Record in Biotech and Pharma Developing Novel Therapies

- Collectively contributed to >25 NDAs, sNDAs and BLAs supporting 15 approved, marketed therapies
- Directly contributed to approved oncology therapies: pembrolizumab, dostarlimab, niraparib, docetaxel, trastuzumab, alpelisib and capmatinib

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BLA: biologics license application; NDA: new drug application; sNDA: supplemental new drug application

Immuno-Oncology Therapy has Curative Potential but is Often Limited by Systemic Toxicity

- Immuno-oncology (IO) therapies have **transformed the treatment landscape** and long-term outlook for some patients with advanced cancer
- Treatment potential for some of the most exciting IO targets has been impeded by **dose-limiting systemic toxicity**

Xilio (*ex*-il-ee-oh) believes th next revolution in IO cancer therapies will **trick tumors int activating their own treatmen** while simultaneously **sparing healthy tissues and cells**

The Critical Challenge: Maximizing Efficacy While Improving Tolerability

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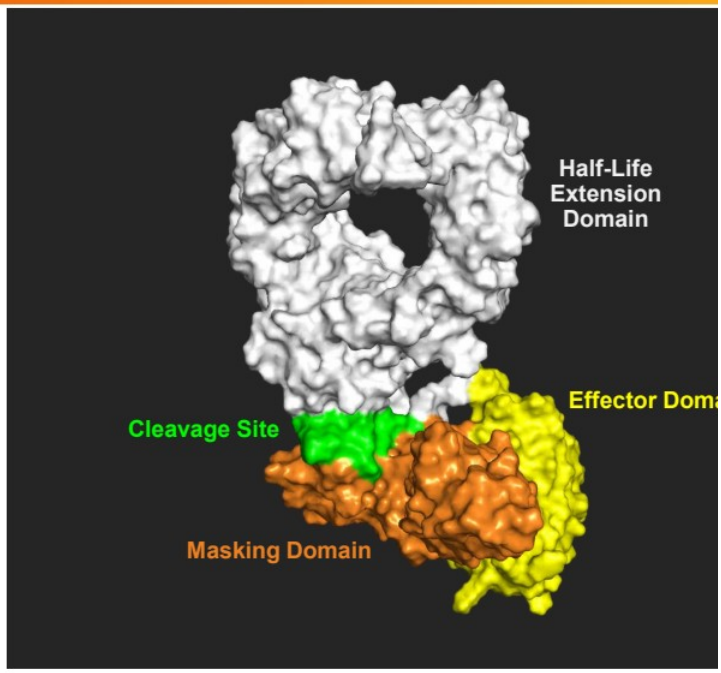
Xilio's Novel Tumor-Activated Molecules are Designed to Overcome the Limitations of Systemically Active Treatments

- **Harness and focus** the power of the immune system to fight cancer
- Novel design to **outsmart tumors** — using tumor growth activity against itself
  - Tumor proteases **activate a switch** in molecules to unleash active agent inside tumor microenvironment (TME)
- Each molecule **custom-designed** using our proprietary geographically precise solutions (GPS) platform **for tumor-selectivity** with a masking domain that is designed to prevent interaction with healthy tissue and cells
  - Molecules are activated by tumor's dysregulated matrix metalloproteases (MMPs)



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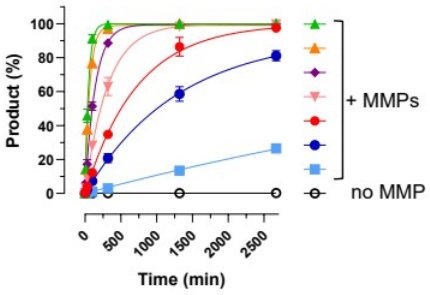
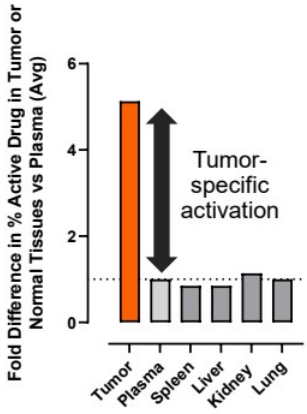
Xilio's Molecules are Designed to be Selectively Activated in the TME by MMPs

MMP-based activation *in vitro*

In vitro recombinant MMP kinetic cleavage assay



Tumor-specific activation *in vivo*



High activation efficiency across human solid tumors *ex vivo*

Demonstrated in >400 patient specimens

Tumor Type	Confirmed High Activation Efficiency (<24 hours) XTX101 (anti-CTLA-4)	XTX202 (IL-2)	XTX301 (IL-12)
Colon			
H&N			
Prostate			
RCC			
Lung			
Melanoma			
Plasma			

Left panel: Time-course of XTX301 activation by recombinant human 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 XTX101, XTX202 or XTX301 assessed in tumor biopsies ex vivo.

Building a Pipeline of Novel Tumor-Activated Immuno-Oncology Therapies

Program	Initial Tumor Types	Mechanism of Action	Discovery	IND-Enabling	Phase 1	Phase 2	Phas
Antibody Program							
XTX101 [1]	Advanced Solid Tumors	Anti-CTLA-4					
Cytokine Programs							
XTX202 [2]	Advanced RCC and Melanoma	IL-2					
XTX301 [3]	Advanced Solid Tumors	IL-12					
Multifunctional Program							
Multifunctional	Advanced Solid Tumors	PD-1/IL-2					

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1. Initially plan to evaluate XTX101 as a monotherapy for the treatment of advanced solid tumors. Plan to explore opportunities for strategic collaborations to advance XTX101 with a partner beyond the current Phase 1 monotherapy cohorts (Part 1A / Part 1B), including in combination with a PD-(L)1 for the treatment of MSS CRC.
2. Initially plan to evaluate XTX202 as a monotherapy in patients with unresectable or metastatic melanoma and metastatic RCC prior to evaluating XTX202 in combination with an anti-PD-1/PD-L1 for the treatment of patients with non-small cell lung cancer (NSCLC) or potential expansion into additional cancer indications as a monotherapy or combination therapy.
3. Initially plan to evaluate XTX301 as a monotherapy for the treatment of advanced solid tumors.

CRC: colorectal cancer; MSS: microsatellite stable; PD: pharmacodynamic; PK: pharmacokinetic; RCC: renal cell carcinoma.


CTLA-4
Evolving Paradigm and Opportunity for
a Tumor-Activated Anti-CTLA-4
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Ipilimumab Data Demonstrated Transformative Potential of High Dose Anti-CTLA-4

High-Dose Ipilimumab Improved Efficacy, But Limited by Toxicity

3x

3-fold increase in therapeutic index has significant potential for transformational outcome

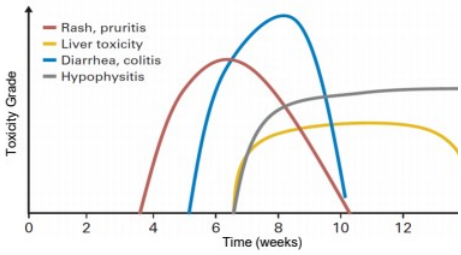
Improved efficacy seen with 10 mg/kg dose, but greater toxicity limits clinical use to 3 mg/kg dose

Ipilimumab dose further reduced in combination with PD-(L)1, typically to 1 mg/kg

Dose (mg/kg)	Median OS	Grade 3/4 irAEs	Discontinuations	Comments
3	**11.5 Months**	**14%**	**19%**	• Standard approved dose
10	**15.7 Months**	**30%**	**31%**	• Increased OS indicates greater efficacy • Increased irAEs indicate greater toxicity

Ipilimumab (10 mg/kg; USPI N=471)	
irAE	**All Grades**
Gastrointestinal	31% (up to 39% in Phase 2)
Endocrine	28%
Skin	25% (up to 47% in Phase 2)
Liver	15%
Infusion Related	3%

Average time to onset of AEs associa with Ipilimumab



Trial conducted by Bristol Myers Squibb.
Ascierto et al., J Immunother Cancer (2020); Larkin et al., N Engl J Med (2015); Wolchok et al., Lancet (2010); Hamid et al., J Transl Med (2011); Lebbe et al., J Clin Oncol (2019); Weber et al., J Clin Oncol (2012).
AE: adverse event; irAE: immune-related adverse event; OS: overall survival.

CTLA-4's Changing Paradigm: Fc Enhancement to Drive ADCC and High Dose Improves Outcomes

Fc enhancement to achieve TREG depletion

- Historically, IO agents have reported 0-5% response rates in MSS CRC (cold tumor): (1)
  - PD-1 monotherapy: ORR 0% (n=150)
  - Ipilimumab + nivolumab: ORR 5% (n=20)
- Phase 1 data for an Fc-enhanced anti-CTLA-4 in combination with a PD-1 in patients with MSS CRC: (2)
  - ORR: 23% (n=70)
  - Phase 1 safety data included any TRAE: Grade 3 (40%) and Grade 4 (3%)

High Dose CTLA-4 Improved Outcomes

- Single high dose (300 mg x1) administration of tremelimumab in combination with an anti-PD-L1 resulted in improved efficacy compared to multiple low doses (75 mg x4 Q4W) (3)

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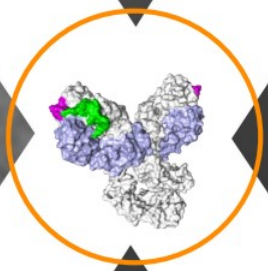
1. Bullock AJ, Grossman JE, Fakih MG, et al: ESMO World Congress on Gastrointestinal Cancer 2022. Abstract LBA-09. Presented June 29, 2022.
2. Phase 1 data reported by Agenus Inc. on January 21, 2023 at ASCO GI Symposium for botensilimab (AGEN1181) in combination with a balstilimab in MSS CRC patients previously treated with chemotherapy and/or with immunotherapy-resistant tumors.
3. Trials conducted by AstraZeneca Pharmaceuticals. Kelley et al., J. Clin. Oncol., 2021; Abou-Alfa et al., J. Clin. Oncol., 2022; Kudo M., Liver Cancer, 2022.

Illustration adapted from PDB entry 5TRU; original structure published: Ramagopal et al., Proc Natl Acad Sci 2017
ADCC: antibody-dependent cell-mediated cytotoxicity; ORR: objective response rate; TRAE: treatment-related adverse event; TREG: regulatory T cells; Q4W: once every four weeks.

XTX101

Tumor-Activated Anti-CTLA-4



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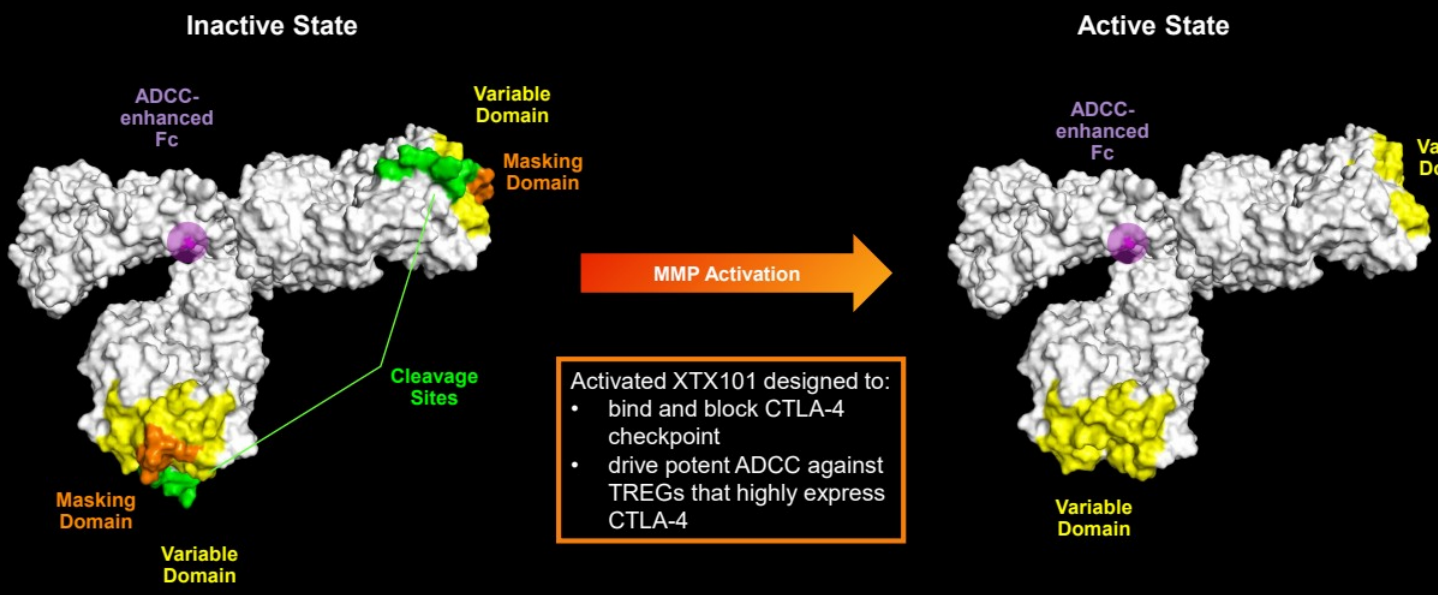
XTX101: Tumor-Activated, High Affinity Binding and Fc-Enhanced Anti-CTLA



Activated XTX101 designed to:

- bind and block CTLA-4 checkpoint
- drive potent ADCC against TREGs that highly express CTLA-4

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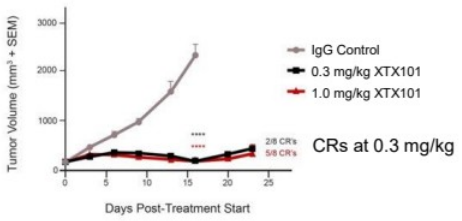
XTX101 Preclinical Profile Differentiated from Ipilimumab (10x potency, TRE depletion, safety) and AGEN1181 (safety)

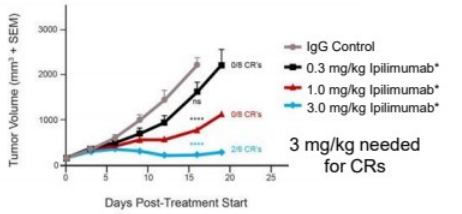
XTX101 is 10-fold more potent than ipilimumab[1] in *in vivo* studies

XTX101



CRs at 0.3 mg/kg

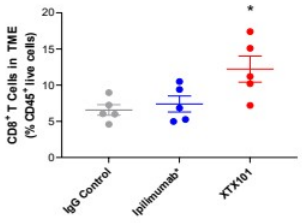
Ipilimumab[1]



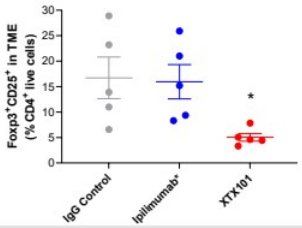
3 mg/kg needed for CRs

XTX101 increased intra-tumoral CD8 T cells and depleted TREGs, while ipilimumab[1] did not

Tumor CD8 T cells

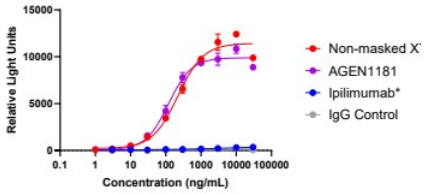


Tumor TREGs

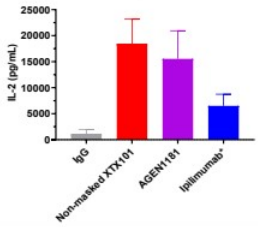


XTX101 exhibited enhanced AD and T cell activation vs ipilimum and in line with AGEN1181

ADCC activity

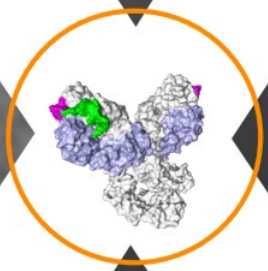


T cell activation (IL-2 secretion)



1. Ipilimumab analog comprising a monoclonal antibody of identical amino acid sequence to ipilimumab that was produced at Xilio for research purposes. CR: complete regression.
Left panel: MB49 cells were inoculated subcutaneously into C57BL/6-huCTLA-4 mice. When tumors reached approximately 150 mm3, mice received a single IV dose at the doses indicated in the figure. A two-way ANOVA with Bonferonni's multiple comparisons post-test was performed to determine the statistical significance of treatment vs. isotype on Day 16 (ns: not significant;*P<0.05; **P<0.01; ***P<0.001;****P<0.0001). **Middle panel:** MB49 cells were inoculated subcutaneously into C57BL/6-huCTLA4 mice. Mice were dosed 3 mg/kg single-dose i.v. A one-way ANOVA with Bonferroni's multiple comparisons post-test was performed to determine the statistical significance of treatment vs. isotype control IgG (*P<0.05).
Right panel: ADCC experiment utilized reporter gene assay with human FcγRIIIa F158 (low affinity) variant. T cell activation measured in SEB (Staphylococcal enterotoxin b superantigen) assay with test articles at 100 nM concentration.

Preliminary Phase 1 Clinical Trial Data for XTX101



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25 Patients Enrolled in Phase 1 Trial (Parts 1A and 1B) for XTX101 with a Wide Range of Advanced and Treatment Refractory Solid Tumors

XTX101 Phase 1 Trial Design

Enrollment Completed

Part 1A
Monotherapy Dose-Escalation
Advanced Solid Tumors
(n=20 dosed)

↓

Part 1B
Monotherapy Expansion PD [1]
(n=5 dosed)

Ongoing

Current dose level: 150 mg Q6W

Patient Characteristics	Total Dosed (N=25)
Demographics	
Age, median (range)	67 (49, 80)
Female	15 (60%)
ECOG PS 0	6 (24%)
ECOG PS 1	19 (76%)
Prior lines of anti-cancer treatment	Median 4 (1-12)
1	2 (8%)
2	4 (16%)
3	5 (20%)
4	6 (24%)
5	3 (12%)
6 and more	5 (20%)
Prior treatment with IO	
≥1	11 (44%)

Tumor Types	Total Dosed (N=25)
Colorectal	5
NSCLC	4
Pancreatic	3
Squamous cell skin	2
Breast	2
Uterine	2
Melanoma	1
Cervical	1
Prostate	1
Gastric	1
Fallopian tube cancer	1
Leiomyosarcoma	1
Merkel cell carcinoma	1

Treatment Status	Total (N=
Continuing on Treatment	3
Discontinued Treatment	2
Progressive Disease	1
Adverse Events	4
Investigator Decision	2
Consent Withdrawal (Hospice)	2
Death Due to Progressive Disease	1
Other	1

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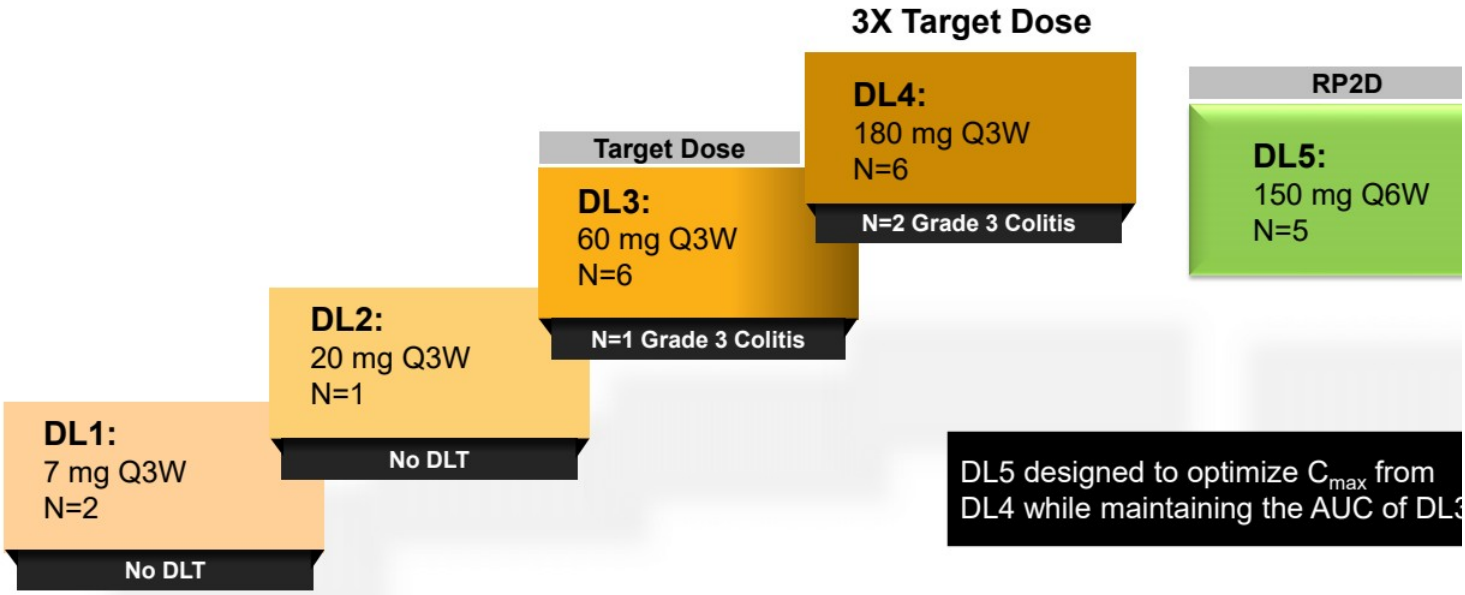
Data cutoff date: May 2, 2023
1. Eligible histology includes, but is not limited to, the following: melanoma, squamous cell skin cancer, NSCLC, head and neck squamous cell carcinoma, esophageal squamous cell carcinoma, RCC, urothelial carcinoma, MSS instability-high/mismatch repair deficient colorectal or endometrial cancer, cervical cancer, TNBC and mesothelioma.
ECOG PS: ECOG performance status; Q6W: once every six weeks; TNBC: triple-negative breast cancer

XTX101 Administered at 150 mg Q6W Identified as the RP2D in Part 1A



Data cutoff date: May 2, 2023
AUC: area under the curve; C_{max}: maximum concentration; DL: dose level; DLT: dose-limiting toxicity; Q3W: once every three weeks; RP2D: recommended Phase 2 dose.

XTX101 Administered at 150 mg Q6W Dose Provided a 2-fold Higher C_{max} Compared to Ipilimumab at 10 mg/kg (Adjusted for 10x Higher Potency)

	Dose Level	Total $AUC_{0\text{-}504}$ (hr*ug/mL)	Cleaved $AUC_{0\text{-}504}$ (hr*ug/mL)	Total C_{max} (ug/mL)	Cleaved at C1D7 [2] (ug/mL)
Ipilimumab [1]	0.3 mg/kg	806		7.3	
	3 mg/kg	8114		76.1	
	10 mg/kg	26359		248.6	
XTX101	7 mg	478 ±312	25.9	3.21 ±2.1	0.16 ±0.11
	20 mg	666	80.7	5.16	0.22
	60 mg	2370 ±978	297 ±77	17.2 ±9.3	0.64 ±0.29
	150 mg	7390 ±1290	1020	51.4 ±5.4	2.49 ±0.42
	180 mg	6290 ±1280	712 ±245	45.2 ±13.2	1.84 ±0.78

C_{max} Comparison (Potency Adjusted)

248.6

514.0

XTX101 Percent Cleaved by $AUC_{0\text{-}504}$ (µg/ml±SD)

- All patients at all dose levels (7-180 mg, n=18): 11.5±2.3
- Patients at RP2D (150 mg, n=3): 11.8±0.8

1. FDA Center for Drug Evaluation and Research, Clinical Pharmacology and Biopharmaceutics Review of ipilimumab. https://www.accessdata.fda.gov/drugsatfda_docs/nda/2011/125377Orig1s000ClinPharmR.pdf. Accessed May 18, 2023.
2. Cleaved concentration calculated on cycle 1, day 7.

Results do not represent a head-to-head trial for ipilimumab and XTX101. Data reported as of December 22, 2022 for XTX101.

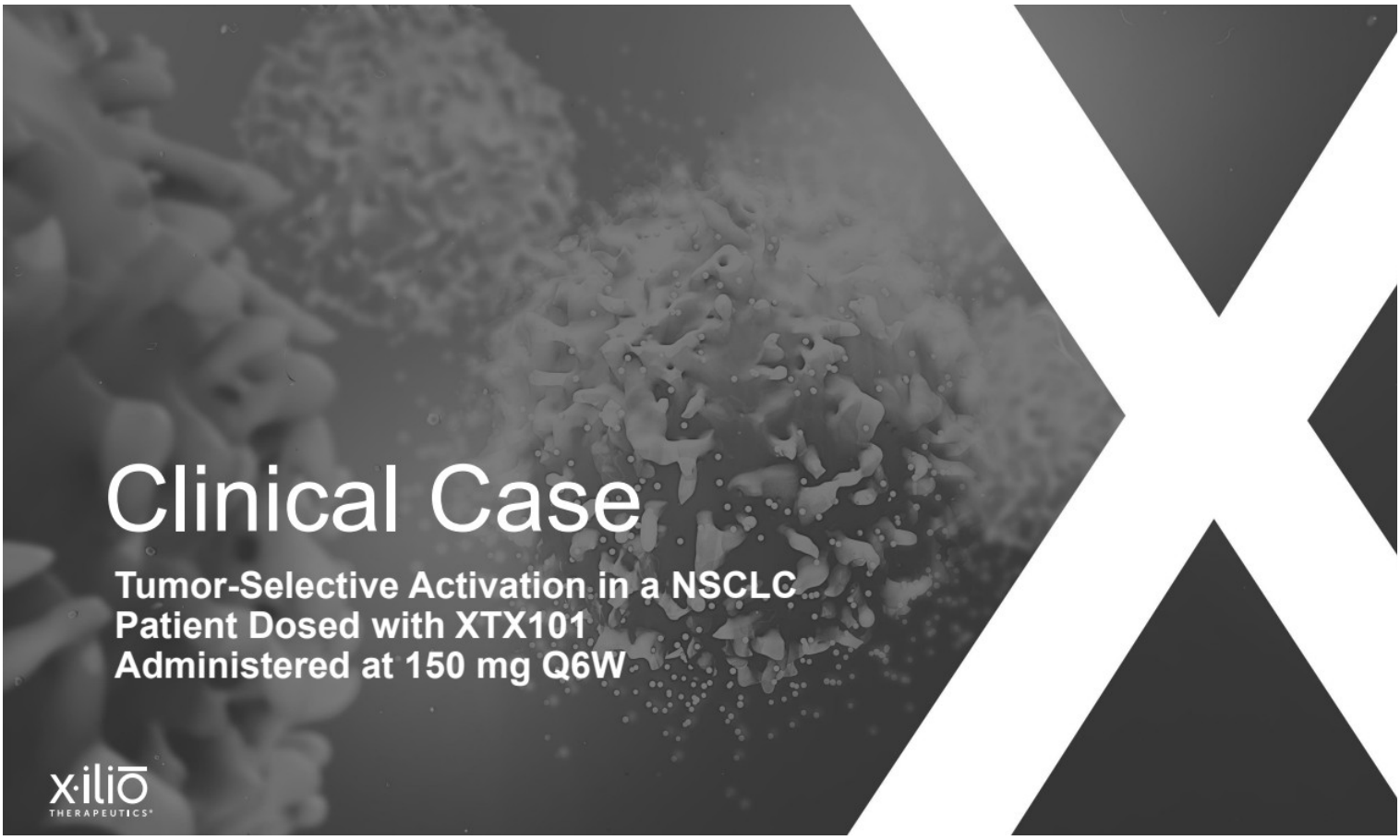
XTX101 Administered at 150 mg Q6W Identified as Optimal Dose / Schedule

No Grade 4 or 5 AEs observed at any dose level

AE Category / Term *All TRAEs with ≥10% incidence in any category*	All Patients at Q3W (7-180 mg) (n=18)		180 mg Q3W (n=6)		RP2D 150 mg Q6W (n=7)	
	Any	Grade 3	Any	Grade 3	Any	Grade 3
Diarrhea or Colitis	7 (39%)	4 (22%)	2 (33%)	2 (33%)	1 (14%)	1 (14%)
Diarrhea	*5 (28%)*	*1 (6.0)*	*2 (33%)*	*0*	*1 (14%)*	*1 (14%)*[1]
Colitis	*5 (28%)*	*4 (22.0)*	*2 (33%)*	*2 (33%)*	*0*	*0*
Nausea	3 (17%)	0	2 (33%)	0	0	0
Vomiting	3 (17%)	0	2 (33%)	0	0	0
Abdominal pain	2 (11%)	0	1 (17%)	0	0	0
Infusion related reaction [2]	5 (28%)	3 (17%)	3 (50%)	2 (33%)	0	0
Fatigue	1 (6%)	0	1 (17%)	0	1 (14%)	0
Pyrexia	1 (6%)	0	1 (17%)	0	0	0
Decreased appetite	1 (6%)	0	1 (17%)	0	1 (14%)	0
Urticaria	1 (6%)	0	1 (17%)	0	0	0
Dizziness	1 (6%)	0	1 (17%)	0	0	0
Dysgeusia	1 (6%)	0	1 (17%)	0	0	0
Dose reduction due to AE	2		2		1	
Treatment discontinuation due to TRAE [3]	4		3		0	

Data cutoff date: May 2, 2023. Data consists of 25 patients across all dose levels, including 20 patients dosed in Part 1A and 5 patients dosed in Part 1B.

1. Grade 3 diarrhea with onset 10 weeks after the start of therapy (after 2 doses), resolved within 5 days without steroid use, patient tolerated 2 additional XTX101 doses after dose reduction (to 75 mg Q6W) without any symptom recurrence
2. Infusion related reactions associated with antidrug antibodies (ADA).
3. All treatment discontinuations were due to TRAE for an infusion reaction.


Clinical Case
Tumor-Selective Activation in a NSCLC Patient Dosed with XTX101 Administered at 150 mg Q6W
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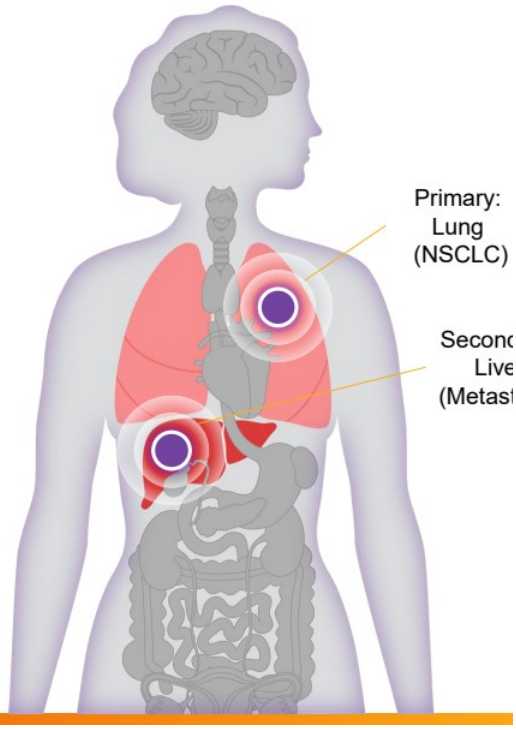
XTX101 Anti-Tumor Activity in a Patient with PD-L1 Negative NSCLC with Hepatic Metastases

- **Patient**: 66 year-old, female
- **Diagnosis**: Stage 4 NSCLC, PD-L1 negative
- **Previous Treatment**: 1 line of chemotherapy
  - 4 cycles of paclitaxel and carboplatin
  - Complete response (CR)
  - Progressed (four months after CR)
- **Enrolled in XTX101 trial**: Cycle 1 in November 2022
- **Dose Level**: 150 mg Q6W
- **Treatment to date:** 5 cycles of XTX101 administered (continuing on treatment)
- **Related AE**: Only Grade 1 fatigue



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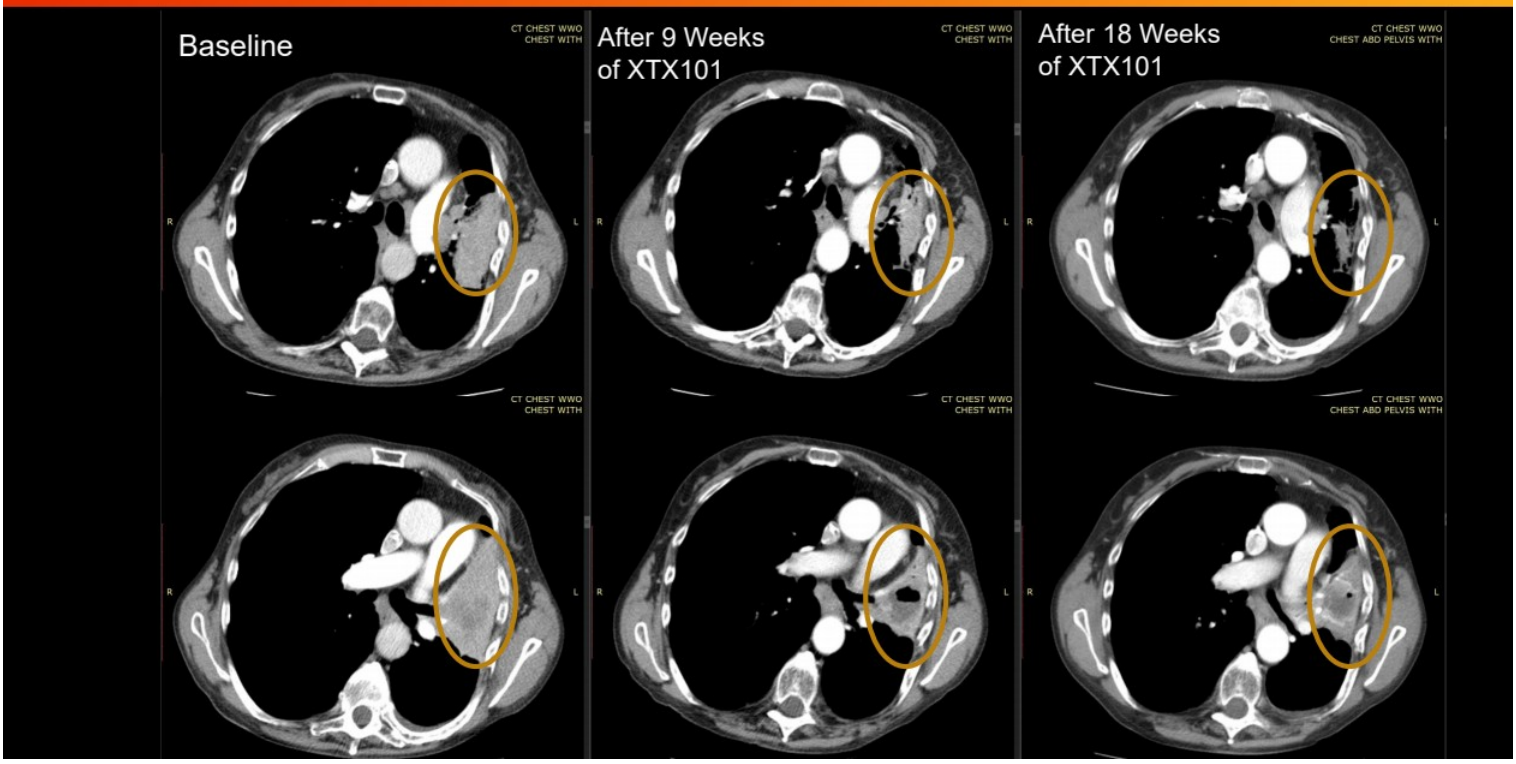
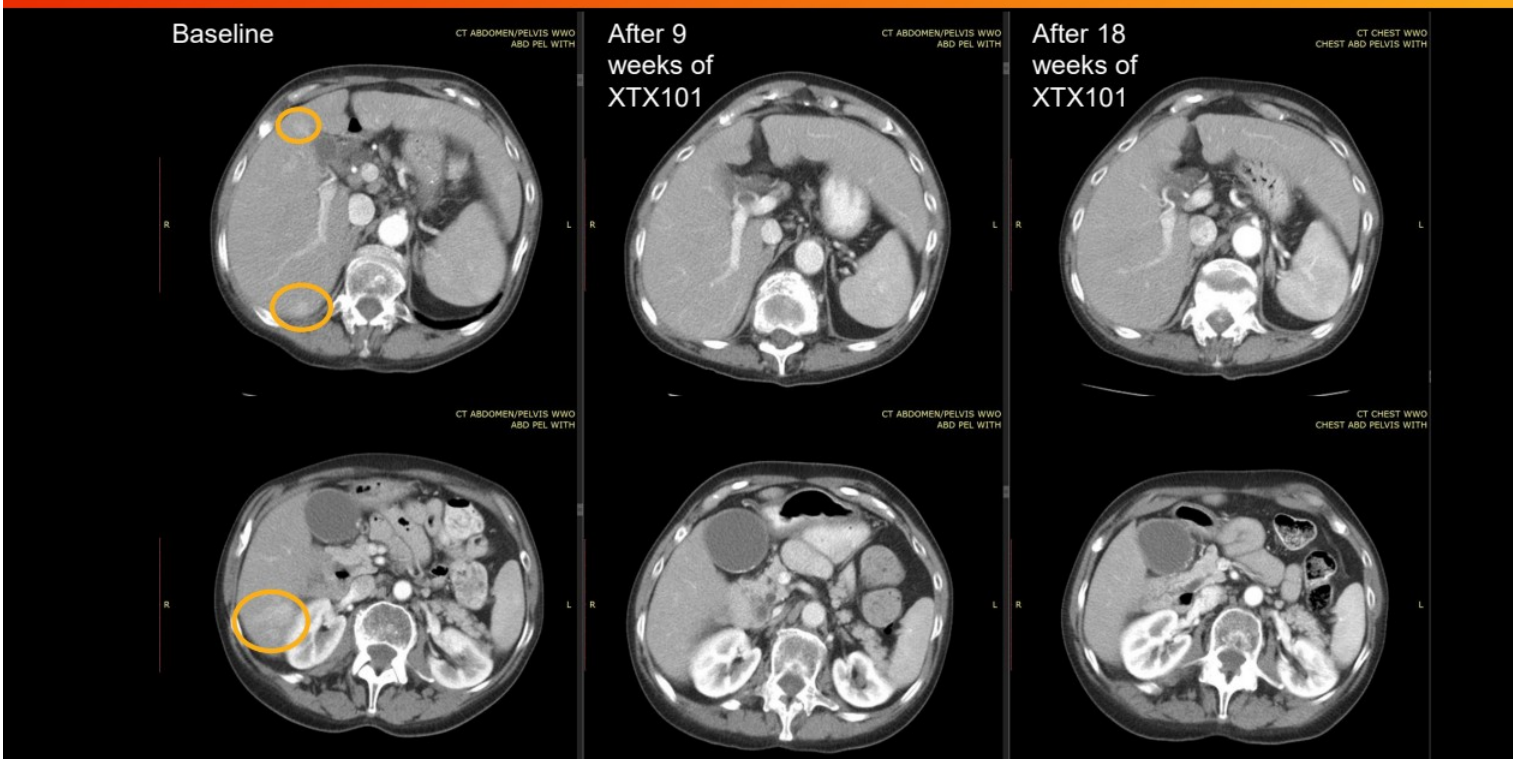
Data cutoff date: May 2, 2023

Primary Lung Lesion Decreased in Size and Developed Cavitation on XTX10 Monotherapy



Hepatic Metastases Resolved on XTX101 Monotherapy

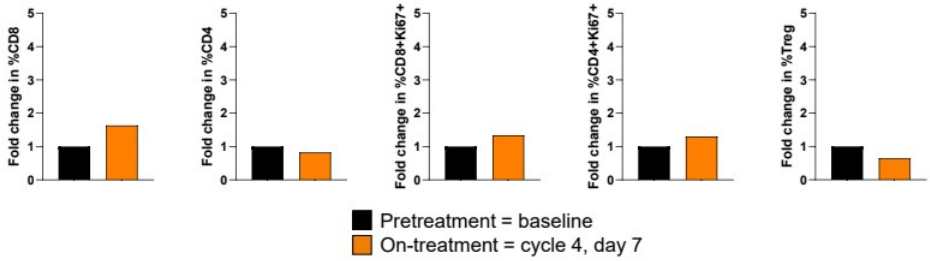


XTX101 Tumor-Selective Activity Demonstrated by Minimal Peripheral PD in the Patient with PD-L1 Negative NSCLC and a Confirmed PR

PR initially observed at Week 9, confirmed at Week 27 (per RECIST v1.1)

- Minimal changes in peripheral CD8, CD4 and TREG comparing pre- and on-treatment
- Lack of peripheral PD supportive of effective masking and tumor-selective activation

Fold Change from Baseline in Peripheral PD Markers of Anti-CTLA-4 activity



Data cutoff date: May 2, 2023. PR confirmed after the data cutoff date on May 17, 2023.
PR: partial response; RECIST: Response Evaluation Criteria in Solid Tumors

XTX101 Differentiated Clinical Profile Supports Continued Development in Combination With a PD-(L)1

- RP2D defined at 150 mg Q6W with differentiated safety profile
  - N=1 reversible Grade 3 GI toxicity after 2 doses at RP2D
  - No immune-related endocrine or skin toxicity
  - No infusion reactions
- Preliminary PK analyses demonstrated dose-proportional drug exposure and limited acti (unmasked) molecule in the periphery
- 150 mg dose provided a 2-fold higher C_{max} (adjusted for 10x higher potency) compared t ipilimumab 10 mg/kg
- Monotherapy confirmed partial response in a patient with PD-L1 negative NSCLC report at 150 mg Q6W with resolution of hepatic metastases [1]
  - Tumor-selective activation for XTX101 demonstrated by minimal peripheral PD in this patient

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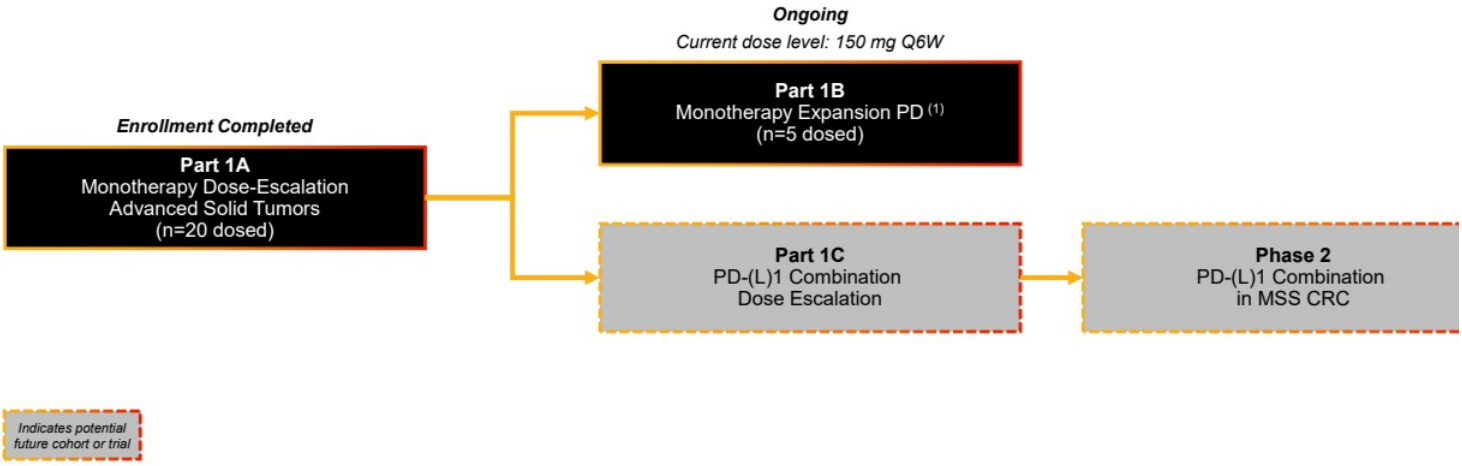
Data cutoff date: May 2, 2023. PR confirmed after the data cutoff date on May 17, 2023.
1. Tumor response was assessed by RECIST version 1.1.

Clinical Development Plan for XTX101



Plan to explore opportunities for strategic collaborations to advance XTX101 with a partner beyond the current Phase 1 monotherapy cohorts (Part 1A / Part 1B), including in combination with a PD-(L)1 for the treatment of MSS CRC

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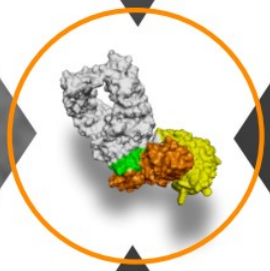
Data cutoff date: May 2, 2023

1. Eligible histology includes, but is not limited to, the following: melanoma, squamous cell skin cancer, NSCLC, head and neck squamous cell carcinoma, esophageal squamous cell carcinoma, RCC, urothelial carcinoma, MSS instability-high/mismatch repair deficient colorectal or endometrial cancer, cervical cancer, TNBC and mesothelioma.

XTX202

Tumor-Activated, Beta-Gamma IL-2



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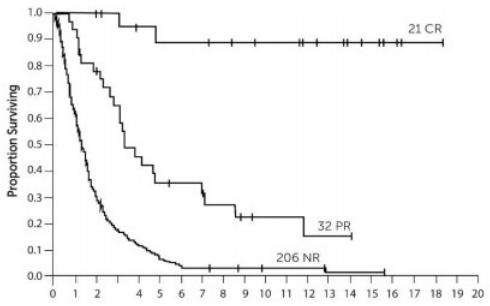
High-Dose IL-2 has Curative Potential but is Limited by High Systemic Toxici

High-dose IL-2 resulted in PFS >10 years, mostly in patients who achieved a CR



High-Dose IL-2

- Deep and durable responses
- CRs in Melanoma and RCC
- High systemic toxicity

Low-Dose IL-2

- Tolerable but immunosuppressive

The critical challenge in the development of IL-2 therapies to **maximize efficacy** while **improving patient tolerabilit**

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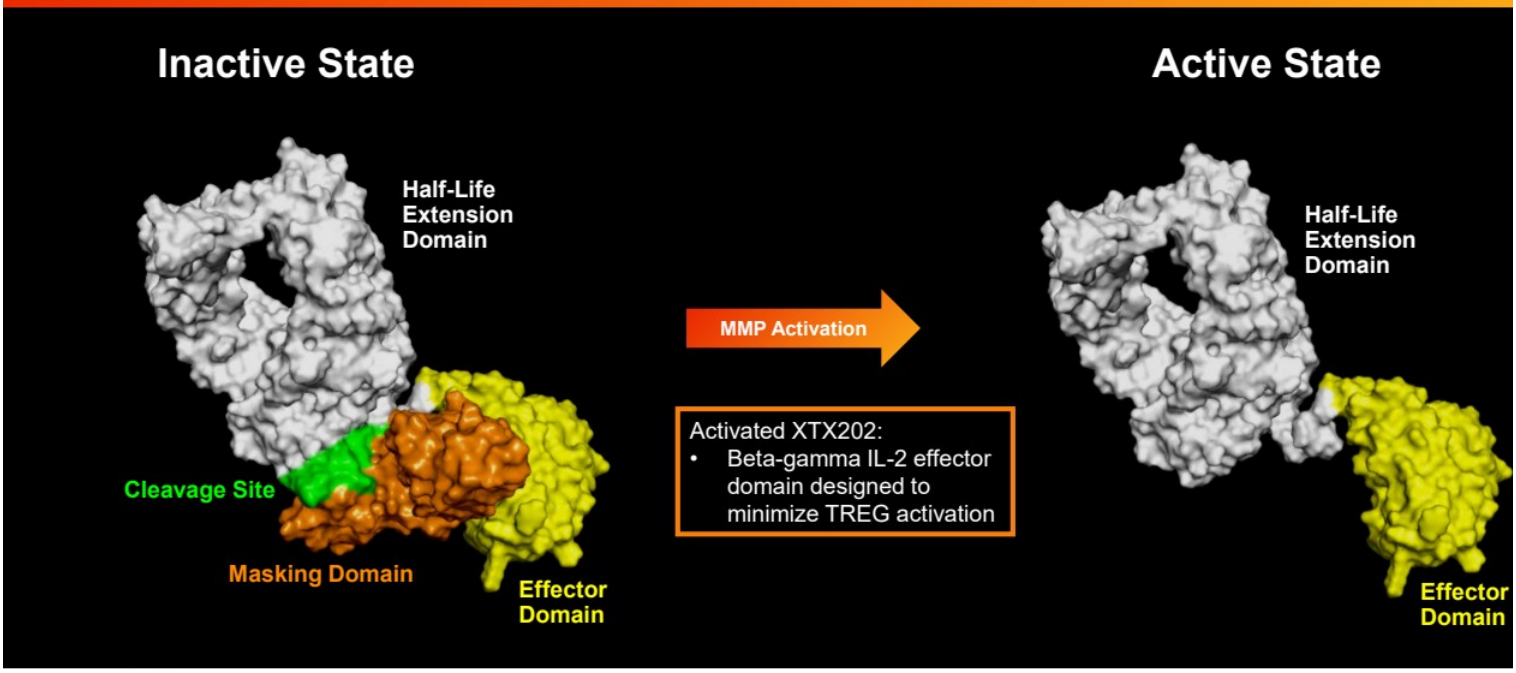
Data represents all patients that received high dose IL-2 (no control group).
NR: no response; PFS: progression free survival.

XTX202: Tumor-Activated, Beta-Gamma IL-2 Designed to Overcome the Limitations of Systemically Active Molecules



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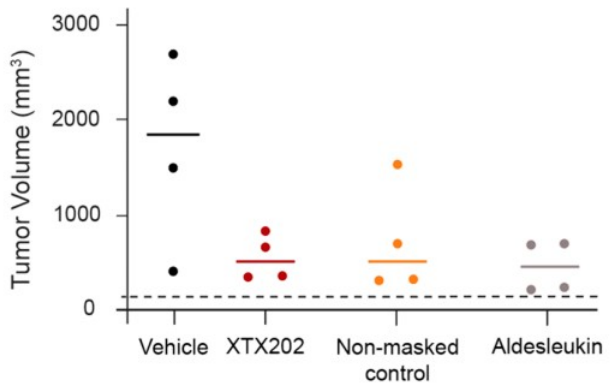
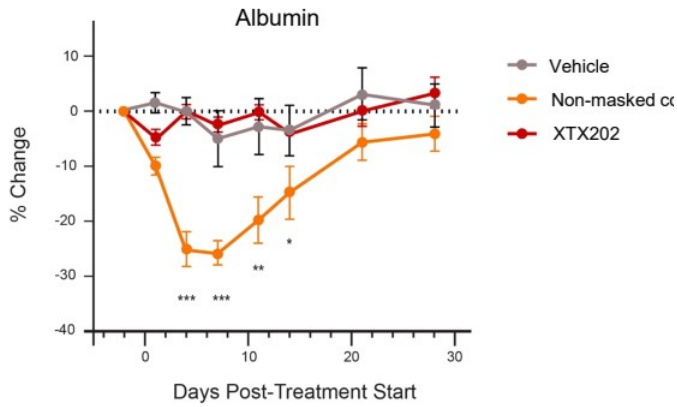
XTX202 Demonstrated Improved Therapeutic Index *In Vivo* Compared to Aldesleukin and Non-Masked Control

Tumor Growth Inhibition at Day 5



Well-tolerated in NHP with no signs of VLS

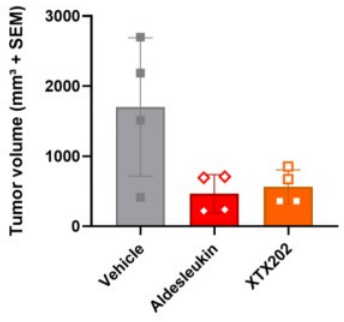


Left panel: XTX202 dose at 2 mg/kg every other day; non-masked control dose at 0.4 mg/kg every other day; aldesleukin dose at 3 mg/kg twice daily. Data presented by O'Neill et al., ASCO 2021.
Right panel: NHPs administered a single intravenous infusion: non-masked control at 0.73 mg/kg and a masked analog of XTX202 (single amino acid change from XTX202) at equimolar dose of 1.0 mg/kg. A repeated measurement two-way ANOVA with Bonferroni's multiple comparison correction was performed to determine the statistical significance of treatment versus vehicle (*P<0.05; **P<0.01; ***P<0.001; ****P<0.0001).
NHP: non-human primate; VLS: vascular leak syndrome.

XTX202 Demonstrated TIL Expansion (CD8+ Effector T Cells and NK) and Anti-Tumor Activity Without Significant TREG Stimulation *In Vivo*

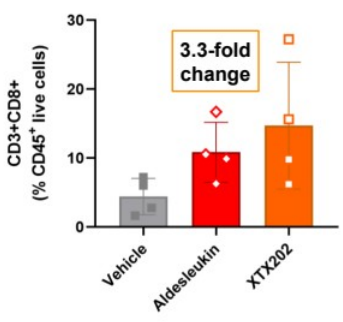
XTX202 and aldesleukin featured comparable anti-tumor activity

Tumor Volume (mm^3) Day 5



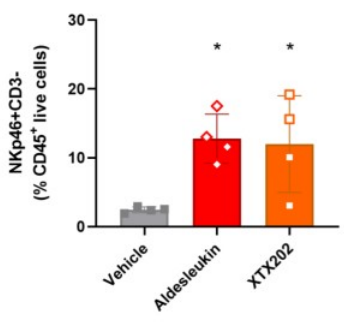
XTX202 and aldesleukin treatment increased CD8+ T cells in tumors

Tumor CD8+ T Cells



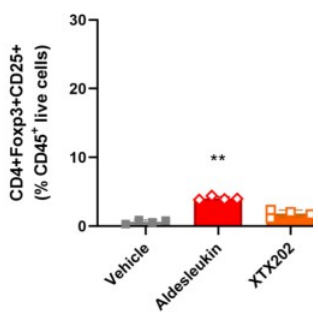
XTX202 and aldesleukin treatment increased NK cells in tumors

Tumor NK Cells



Aldesleukin increased TREGs in tumors while XTX202 had minimal effec

Tumor Regulatory T Cells



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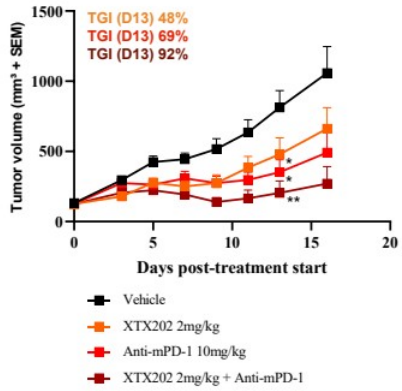
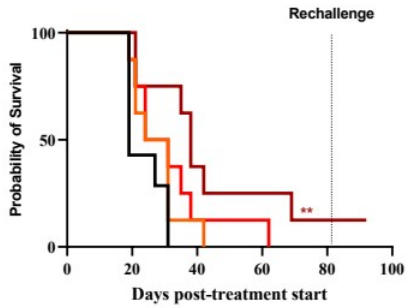
MC38 tumor-bearing mice were treated with either vehicle, aldesleukin (3 mg/kg BID) or XTX202 10mg/kg QDx5. Tumor volume was recorded at day 5 post first dose and tumor infiltrating immune cells were phenotyped and enumerated using flow cytometry. One-way ANOVA was performed to determine statistical significance. *p<0.05; **p<0.001.
NK: natural killer; TIL: tumor infiltrating lymphocytes.

Enhancement of *In Vivo* Activity and Evidence of Memory Response for XTX202 in Combination with Anti-PD-1

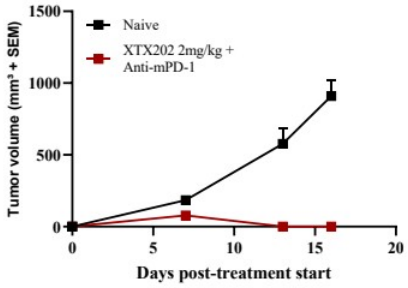
Enhanced *in vivo* activity observed with combination of XTX202 and anti-PD-1 mAb



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



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



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

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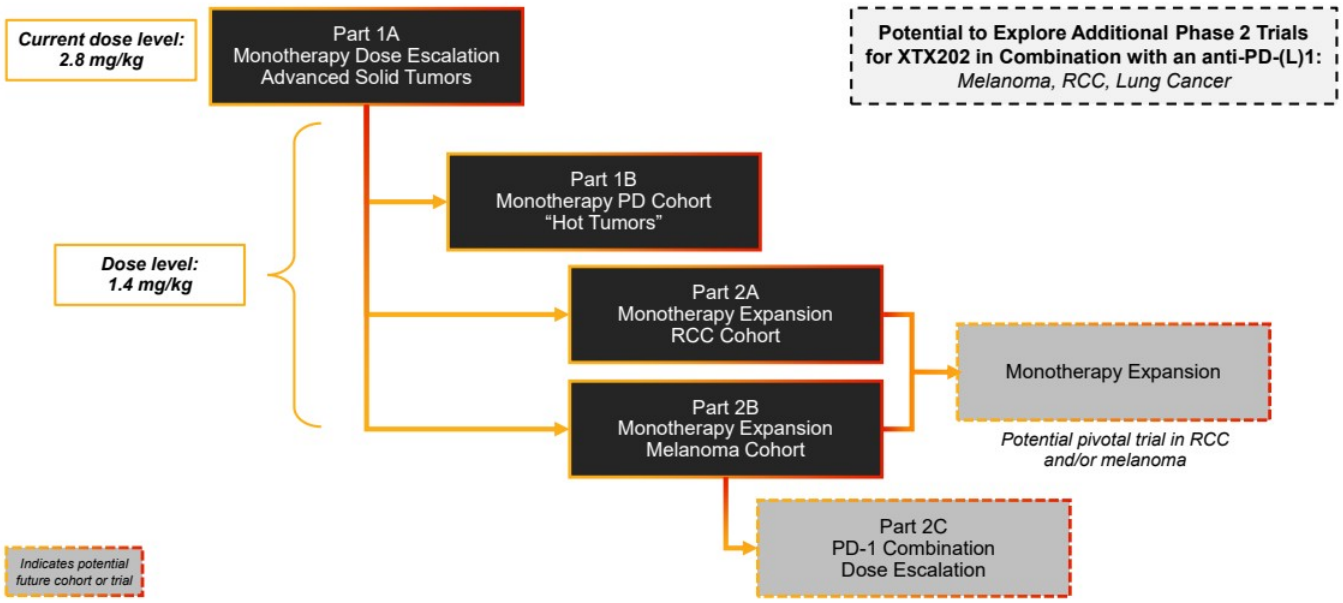
Anti-tumor activity of XTX202 as a single agent and in combination with anti-mPD-1 was evaluated in hFcRn Tg32 transgenic mice bearing the murine MB49 bladder carcinoma model. The combination of XTX202 with anti-mPD-1 further improved anti-tumor activity with TGI 92% on Day 13 (Data presented as mean ±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.
mAb: monoclonal antibody; TGI: tumor growth inhibition.

Clinical Development Plan for XTX202



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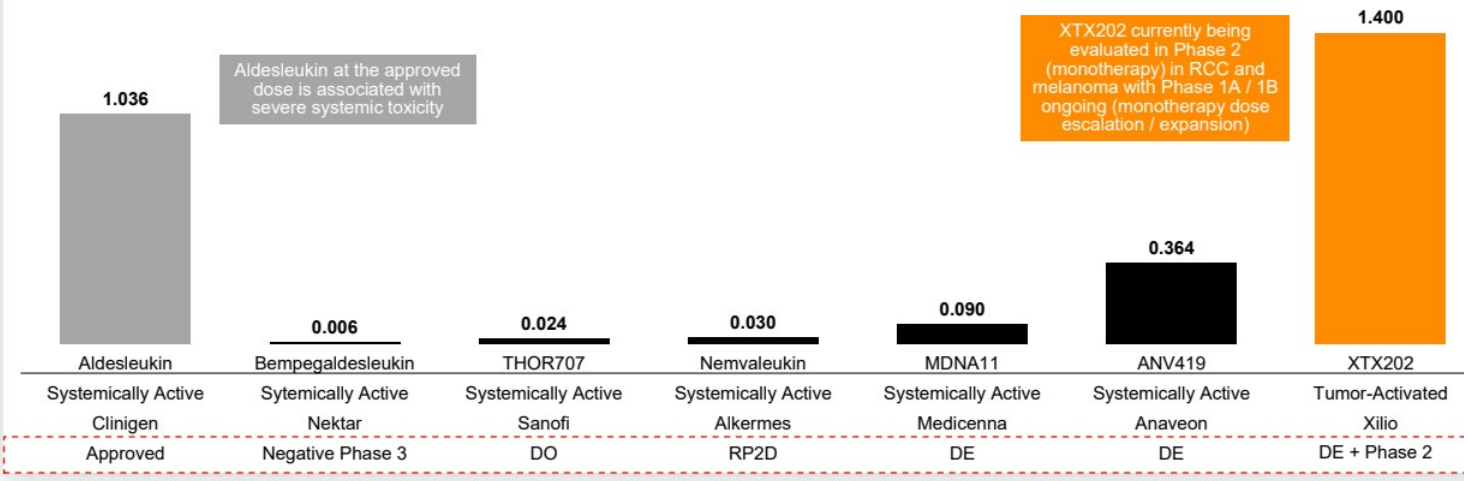
XTX202 Has Achieved Dose Levels Beyond High-Dose IL-2

High-Dose IL-2 and IL-2 Clinical Molecules
(doses in mg/kg)

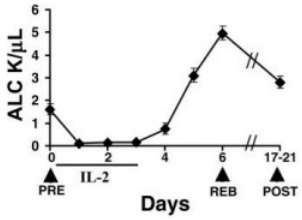


Aldesleukin dose if full indicated administration completed (0.037mg/kg*14 over 5 days + 9 days rest + 0.037 mg/kg*14 over 5 days). In preclinical studies, XTX202 at a total dose of 20 mg/kg had similar activity for tumor growth inhibition and PD to aldesleukin at a total dose of 24 mg/kg.
DO: dose optimization; DE: dose escalation.

No Peripheral Lymphocytosis Observed with XTX202 in Patients at the 1 mg/kg Dose Level

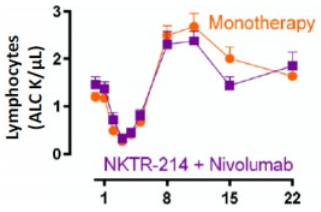
Aldesleukin [1]
hr IL-2
First Generation

Dose: 3 daily doses of high-dose IL-2 (720K IU/kg for 9 doses)



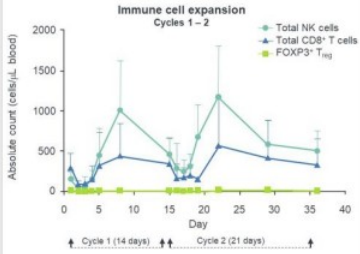
Bempegaldesleukin [2]
NKTR-214
Second Generation

Dose: 0.006 mg/kg



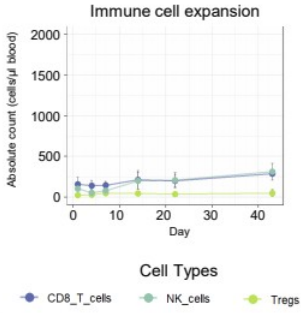
Nemvaleukin Alfa [3]
ALKS-4230
Second Generation

Dose: 0.006 mg/kg (RP2D)
IV x 5D Q3W



Tumor-Activated XTX202
Third Generation

Dose: 1 mg/kg Q3W



XTX202: Decrease in ALC count observed on day 2; magnitude of increase in ALC on day 7 lower than what has been reported for aldesleukin and b

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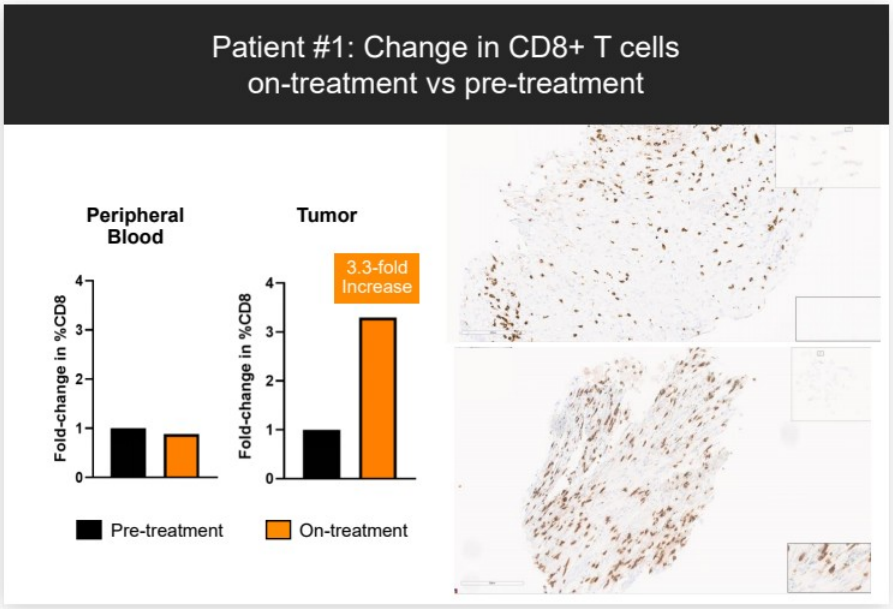
1. Mojgan Ahmadzadeh, Steven A. Rosenberg 2006 DOI: 10.1182/blood-2005-06-2399. 2. ASCO 2017, Abstract #2545. 3. ASCO 2022, Abstract # 2500. Results do not represent a head-to-head trial for 3rd party products and XTX101.
Peripheral lymphocytosis is a PD marker of IL-2 biology.
hr: human recombinant; ALC: absolute lymphocyte count

XTX202 Clinical Patient Data: Tumor-Selective Increases in CD8+ Effector T Cells Observed in Melanoma Patient Tumor Sample at Dose Level 2



Patient #1 (Dose Level 2

- 51 year-old male patient with melanoma
- Treated with XTX202 at 0.38 mg/kg Q3W in Part 1A
- Prior treatment included IO and other systemic agents
- No signs or symptoms of VLS
- Biopsy obtained prior to treatment and prior to cycle 3 (6 weeks after cycle 1, day 1)

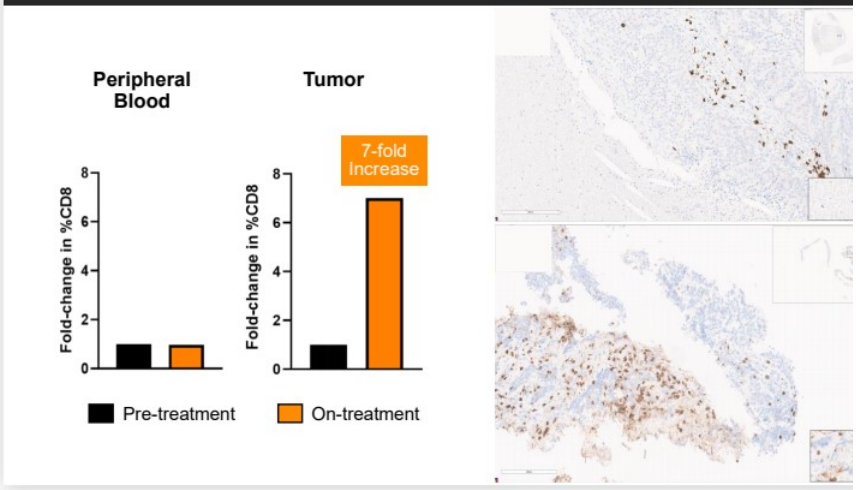
Patient had an optional on-treatment tumor biopsy and was one of the only two patients treated with XTX202 for whom a tumor biopsy analysis was available as of March 1, 2023. CD8+ T cells assessed by flow cytometry for peripheral blood and IHC for tumor. Relative fold-change in %CD8+ cells in tumor takes into account increase in stromal TILs and CD8+ count by IHC.
IHC: immunohistochemistry

XTX202 Clinical Patient Data: Tumor-Selective Increases in CD8+ Effector T Cells Observed in RCC Patient Tumor Sample at Dose Level 3

Patient #2 (Dose Level 3)

- 75 year-old male patient with RCC
- Treated with XTX202 at 0.53 mg/kg Q3W in Part 1A
- Prior treatment included IO and other systemic agents
- No signs or symptoms of VLS
- Biopsy obtained prior to treatment and on cycle 2 day 20 (5 weeks after cycle 1, day 1)

Patient #2: Change in CD8+ Effector T cells post-treatment vs pre-treatment

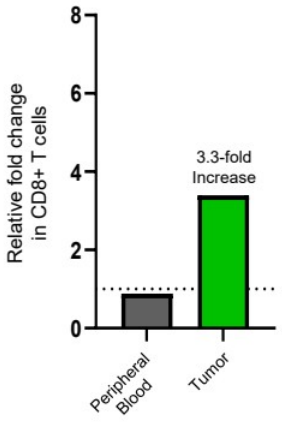


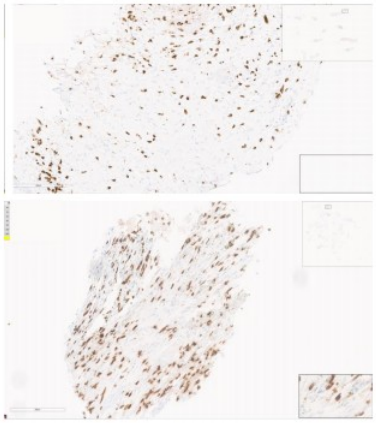
Patient had an optional on-treatment tumor biopsy and was one of the only two patients treated with XTX202 for whom a tumor biopsy analysis was available as of March 1, 2023.
CD8+ T cells assessed by FACS for peripheral blood and IHC for tumor. Relative fold-change in %CD8+ cells in tumor takes into account increase in stromal TILs and CD8+ count by IHC.

XTX202 Clinical Patient Data: Tumor-Selective Increases in CD8+ Effector T Cells Observed in Two Patients Following Treatment at Dose Levels 2 and 3

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

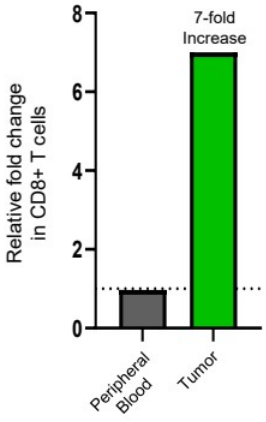
Relative Fold-Change in CD8+ T cells Compared to Pre-Treatment

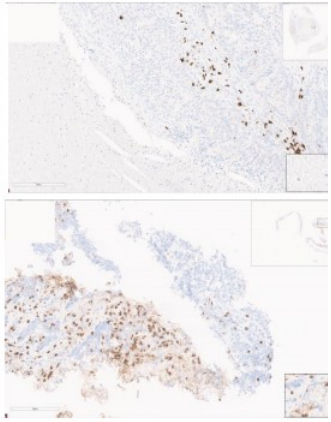




Patient #2: RCC patient treated with XTX202 at 0.53 mg/kg Q3W (dose level 3)

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





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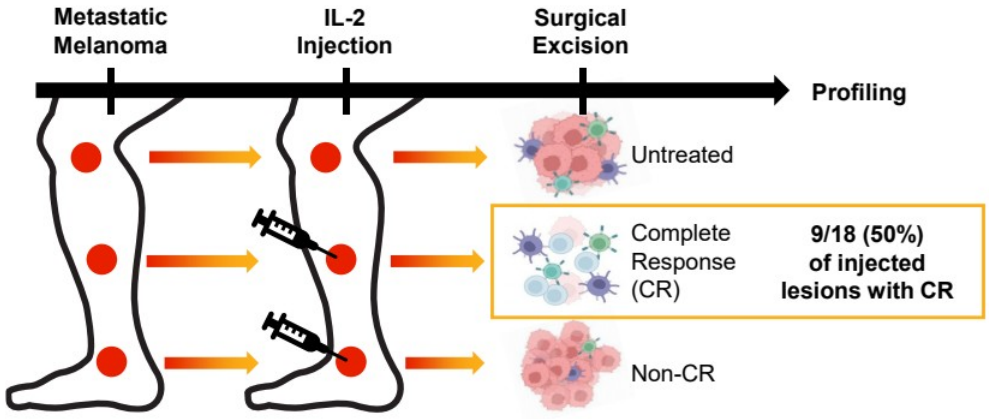
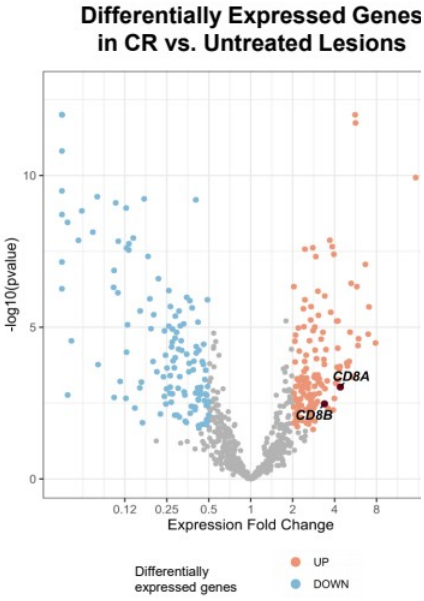
Patients had an optional on-treatment tumor biopsy and were the only two patients treated with XTX202 for whom a tumor biopsy analysis was available as of March 1, 2023. CD8+ T cells assessed by FACS for peripheral blood and IHC for tumor. Relative fold-change in CD8+ cells in tumor takes into account increase in stromal TILs and CD8+ IHC (%TIL post-treatment x %cCD8+ post-treatment over (%TIL pre-treatment x %CD8+ pre-treatment).

In Patients Treated with Intralesional Injection of Aldesleukin, CRs Associate with Increase in CD8+ T Cells: 4-fold (Gene Expression) and 10-fold (IHC)





Pourmaleki et al., Cancer Immunology Research, 2022. **Left image:** Illustration adapted from same publication using BioRender. **Right image:** Differential Gene Expression data were obtained from Pourmaleki et al., Cancer Immunology Research, 2022. Volcano plots show significance of each gene (-log10[p-value], y-axis) plotted against the corresponding gene expression fold change (x-axis, log-scale). Each point is a gene and colors indicate genes that were significantly upregulated (red) or downregulated (blue). Genes encoding for CD8 (CD8A, CD8B) were annotated on the plot (darker points).

XTX202 Clinical Trial Progress

- Administered as an outpatient regimen
- PK supports once every three-week dosing schedule
- Surpassed target dose range of 1 mg/kg (dose level four) in Phase 1 monotherapy dose-escalation
  - No signs or symptoms of VLS observed through 1.4 mg / kg (dose level five)
  - Currently dosing patients at 2.8 mg/kg (dose level six)
- Robust tumor-selective increases in CD8+ effector T cells observed in two patients following XTX202 treatment *
- Patients received up to 13 cycles of treatment to date in Phase 1 monotherapy dose escalation
- Phase 2 open and dosing patients at initial RP2D of 1.4 mg/kg

Q3 2023

- Anticipate reporting preliminary anti-tumor activity, PK/PD, and safety data in ~15-20 evaluable patients treated at 1 mg/kg or higher from Phase 1/2 trial

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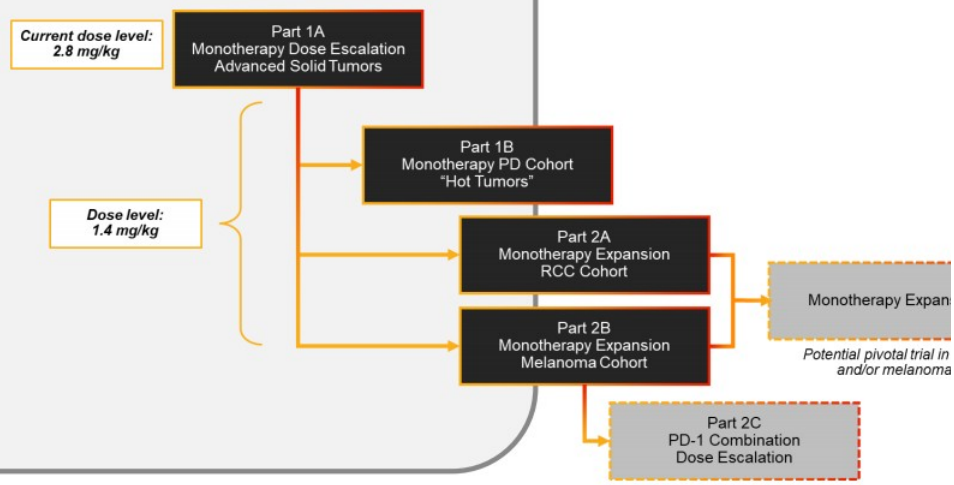
* Patients had an optional on-treatment tumor biopsy and were the only two patients treated with XTX202 for whom a tumor biopsy analysis was available as of March 1, 2023.

Anticipated Preliminary Clinical Data for XTX202 in Q3 2023

Anticipated Data

- ~15-20 evaluable patients treated at 1 mg/kg or higher across all cohorts in Part 1A/B and Part 2A/B
- Safety
- PK / PD
- Anti-tumor activity (ORR) *



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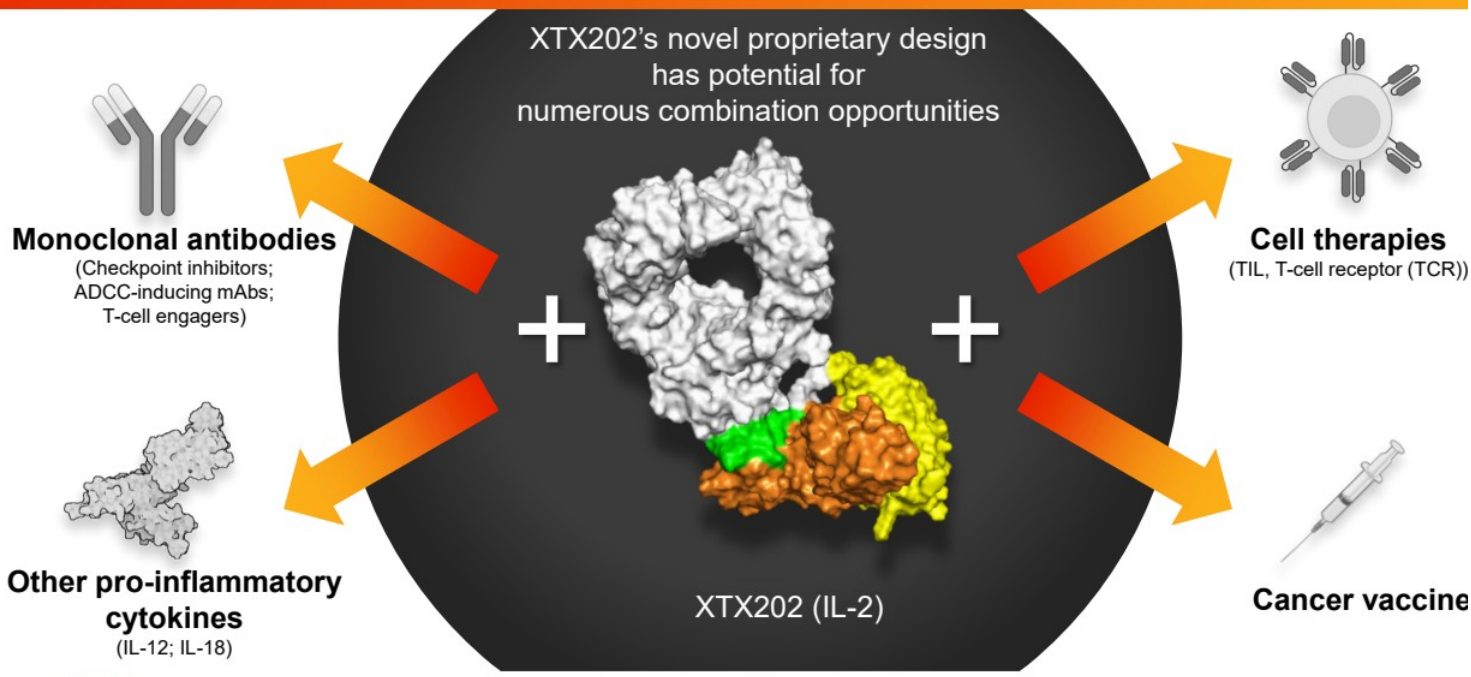
* Target ORR similar to aldesleukin of ~10-15%

Multiple Combination Opportunities Enabled by XTX202 Properties: Tumor-Activated, Well-Tolerated Preclinically and Clinically-Validated Target



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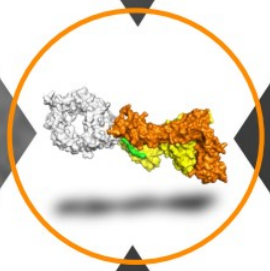
XTX301

Tumor-Activated IL-12



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The Compelling Potential of IL-12 as a Therapeutic Agent

- IL-12 has significant potential as a potent IO 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 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 si
agent objectiv
responses in pati
but poorly tolera
(MTD <500 ng/k
repeat dosing

xilio THERAPEUTICS®

INFγ is a pleiotropic molecule with associated antiproliferative, pro-apoptotic and antitumor mechanisms. Th1-type cytokines tend to produce the proinflammatory responses responsible for killing intracellular parasites and for perpetuating autoimmune responses.
INFγ: interferon gamma; MTD: maximum tolerated dose; ng/kg: nanograms/kilogram.

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

Cold Tumor

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

Hot Tumor

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

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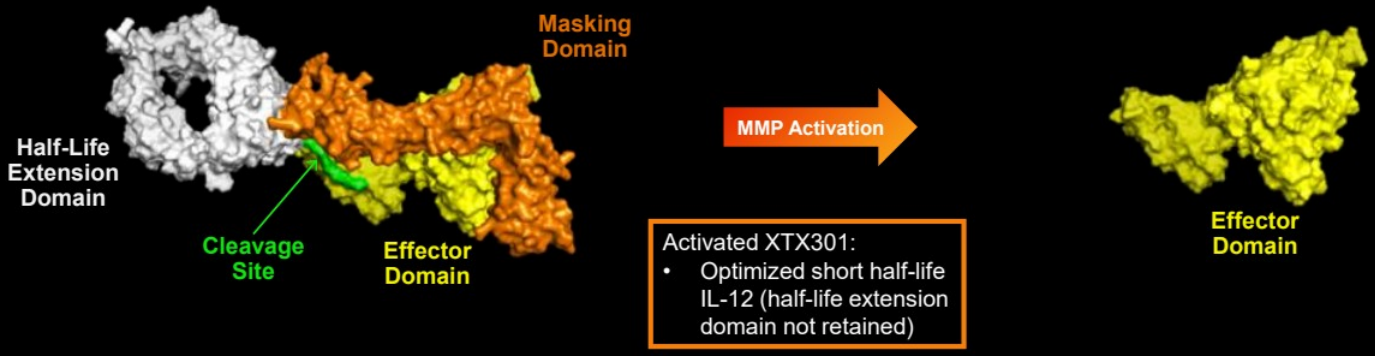
Adapted from "Cold vs Hot Tumors", by BioRender.com, 2022. Retrieved from https://app.biorender.com/biorender-templates Barraondo et al., Clin. Cancer Res., 2018. Nguyen et al., Front. Immunol., 2020.
MDSC: myeloid-derived suppressor cells

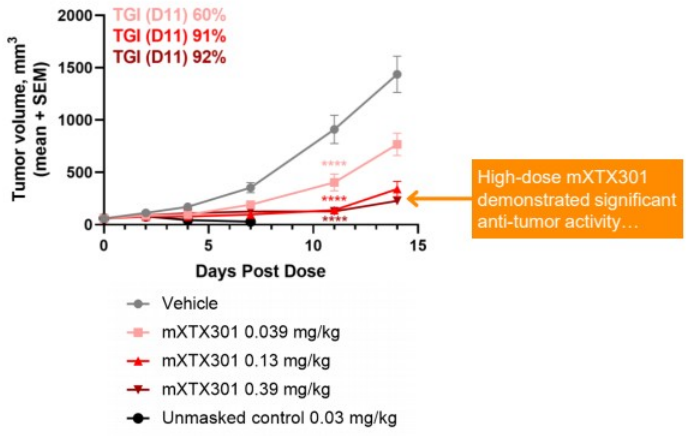
XTX301: Tumor-Activated IL-12 Designed to Overcome the Limitations of Systemic Recombinant Human IL-12



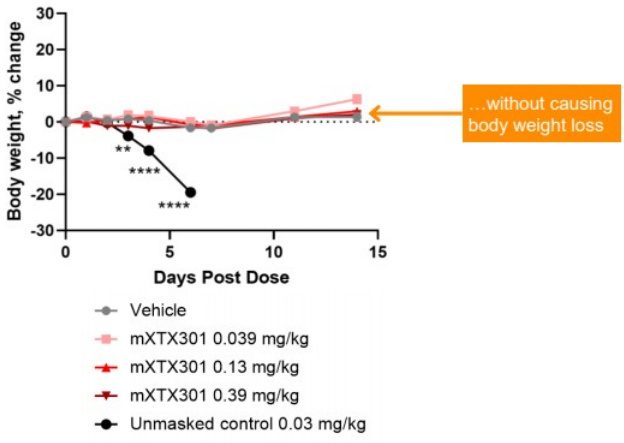
Activated XTX301:
- Optimized short half-life IL-12 (half-life extension domain not retained)

mXTX301 Demonstrated Dose-Dependent Anti-Tumor Activity Without Body Weight Loss *In Vivo*

Tumor Growth



Body Weight



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

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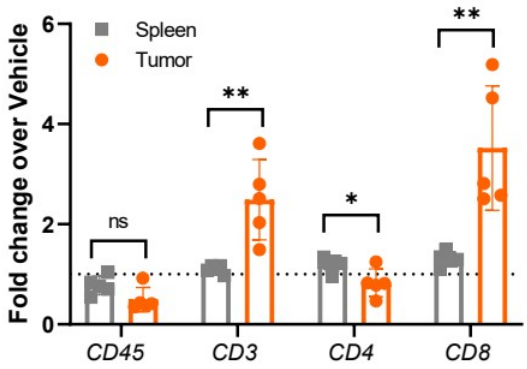
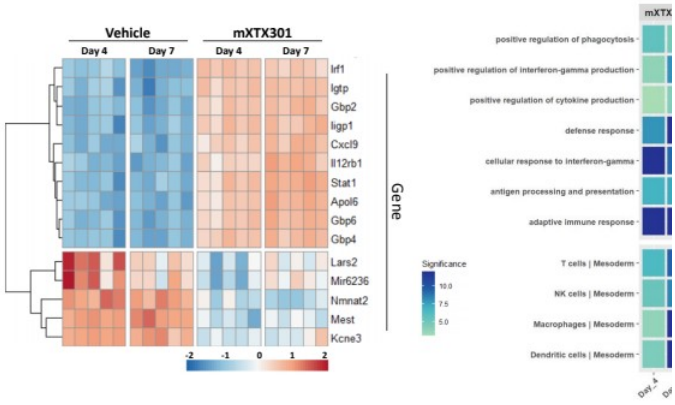
mXTX301 is a murine surrogate for XTX301.
MC38 model: s.c. 0.5x106 cells; single IV dose of mXTX301 and mXTX302 on Day 0. Tumor growth data shown as mean±SEM. Tumor volume data was assessed by a two-way ANOVA followed by Bonferroni post hoc test on Day 11 compared to vehicle treated animals. ****p<0.0001 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 Induced Tumor-Specific Pharmacology *In Vivo*

mXTX301 induced specific T cell recruitment into the tumor with minimal peripheral effects



mXTX301 induced pro-inflammatory gene programs and broadly remodeled TME toward inflamed state



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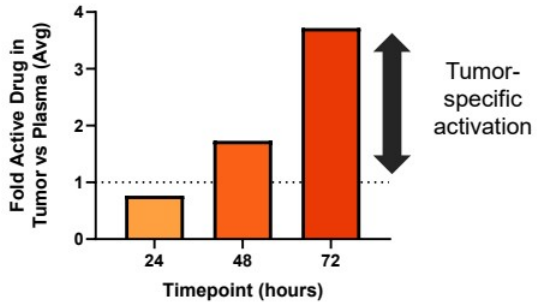
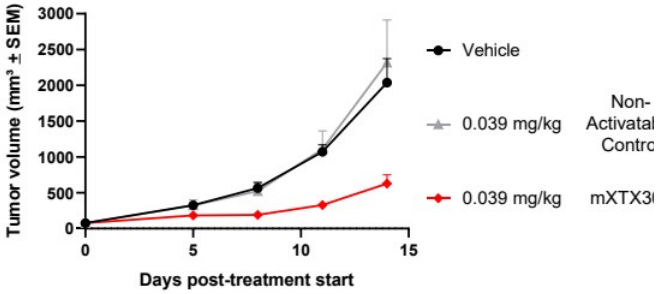
mXTX301 is a murine surrogate for XTX301.
Left panel: MC38 tumor bearing mice (n= 5 per group) were treated with a single IV dose of mXTX301 at 0.39 mg/kg or vehicle and immune cells were phenotyped using FACS. The number of cells for each immune phenotype was calculated per g of tissue and the ratio of cells after mXTX301 treatment to after vehicle treatment is presented as mean ± SD. Changes in the ratio of each cell type in spleen and tumor were assessed by an unpaired t test. *P < 0.05, **P < 0.005. **Right panel:** Tumors from mice treated with vehicle, 0.39 mg/kg mXTX301 were profiled by RNAseq.
Left Heatmap: Color tracks with z-score-transformed relative expression of each gene across samples (blue, under-expression compared to the mean; red: over-expression compared to the mean).
Right Heatmap: Color shows significance (-log10 Fisher_PVal) of pathway enrichment (rows are pathways or gene-sets).

mXTX301 was Preferentially Activated in Tumors vs. Plasma *In Vivo*

mXTX301 demonstrated tumor-specific activation *in vivo*



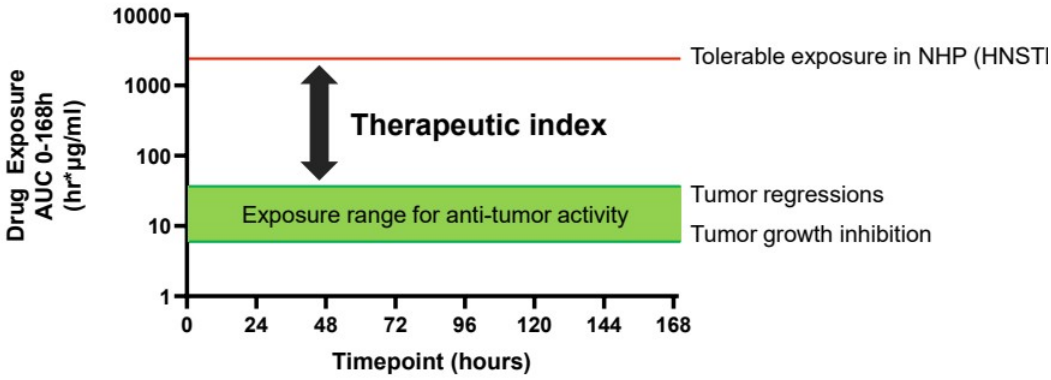
mXTX301 treatment resulted in cleavage-dependent enhancement in activity vs non-activatable control



mXTX301 is a murine surrogate for XTX301.
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.

XTX301 Preclinical Data Support Potential for Broad Therapeutic Index

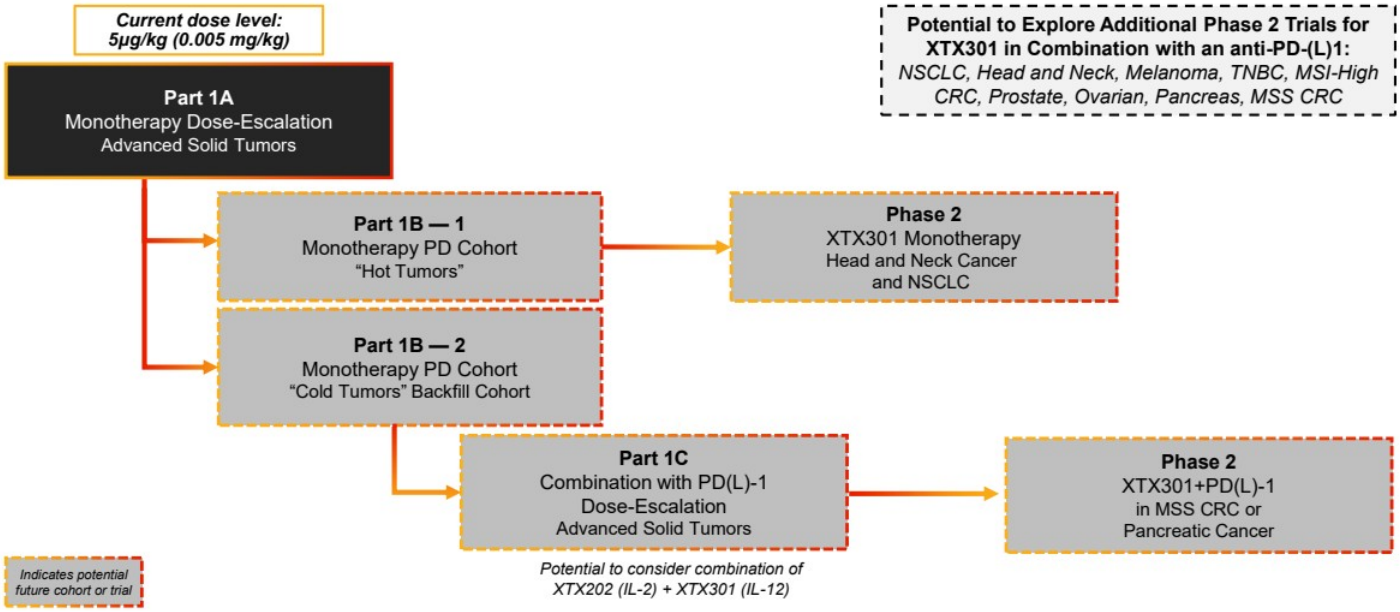
- XTX301 was tolerated at doses up to 2.0 mg/kg Q1W x4 in NHP (HNSTD)
- mXTX301 induced tumor regressions in murine model following a **single dose** of 0.13 mg/kg



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	**67**
XTX301	**Safety** (NHP)	2.0	2540	

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

Clinical Development Plans for XTX301



MSI: microsatellite instability; µg: micrograms.

XTX301 Progress and Anticipated 2023 Clinical Milestones

- Demonstrated dose-dependent anti-tumor activity without significant body weight l *in vivo*
- Preferentially activated in tumors vs plasma *in vivo*
- Preferentially activated in human patient tumors vs. plasma *ex vivo*
- Phase 1 initiated at starting dose of 5µg/kg (0.005 mg/kg) Q3W
  - 10x higher than the MTD for recombinant human IL-12 of 0.5 µg/kg [1]

Q4 2023

- Anticipate reporting preliminary Phase 1 safety data into at least the third dose leve in Q4 2023

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1. Portielje et al. Clin Cancer Res. 1999 Dec;5(12):3983-9.

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

	Preclinical Proof-of-Concept	Human Translational Proof-of-Concept	Peripheral Masking In Clinic	Tumor-Activation in Clinic	Clinica Anti-Tum Activit
XTX101 (Anti-CTLA-4) Phase 1A Dosing Complete Phase 1B Dosing	✓	✓	✓	✓	✓
XTX202 (IL-2) Phase 2 Dosing	✓	✓	✓	✓	Anticipate Q3 2023
XTX301 (IL-12) Phase 1A Dosing	✓	✓	Anticipated Q4 2023		
Multifunctional (PD-1/IL-2) Research Program	✓	✓			

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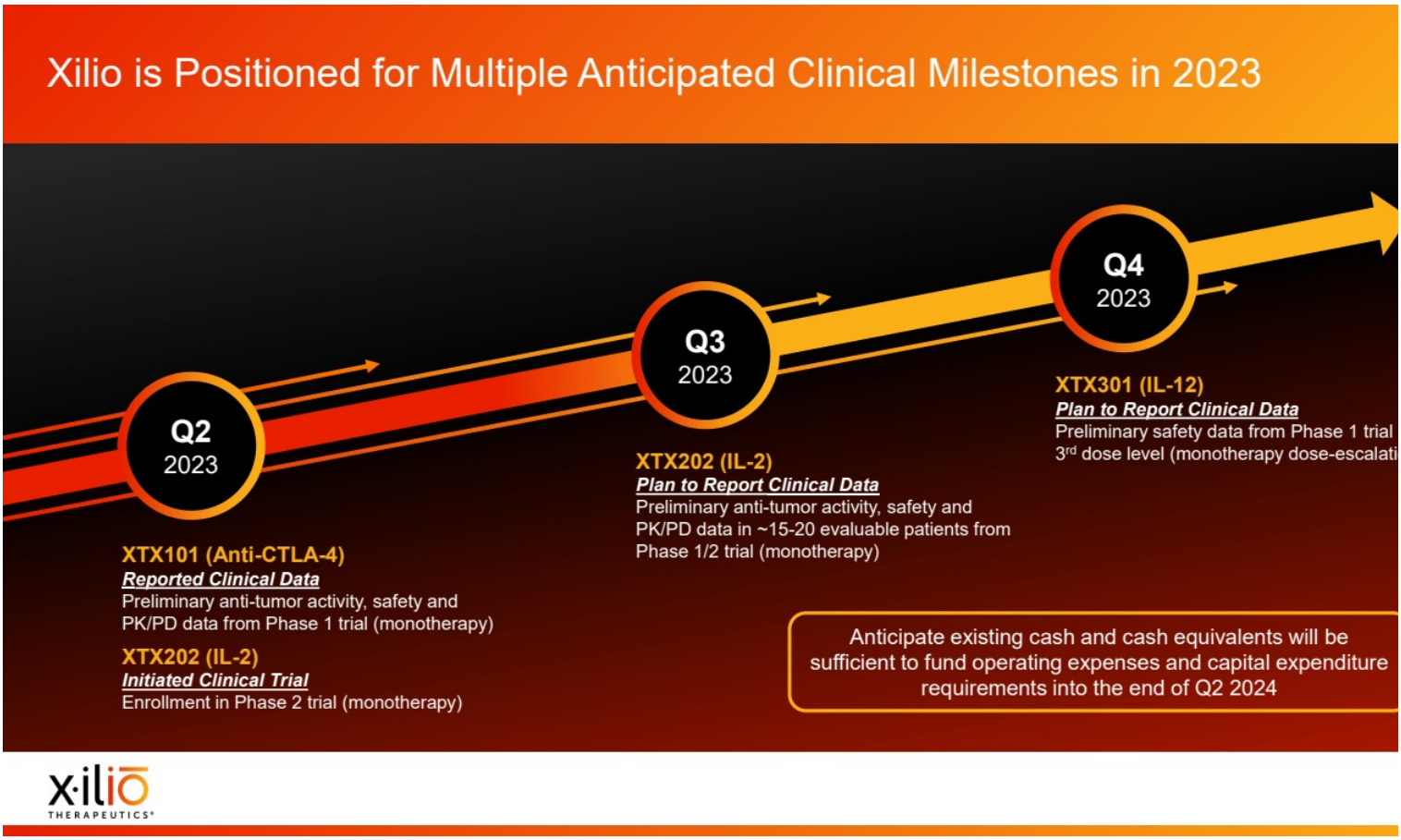
Xilio is Positioned for Multiple Anticipated Clinical Milestones in 2023
Q2
2023
Q3
2023
Q4
2023
XTX101 (Anti-CTLA-4)
Reported Clinical Data
Preliminary anti-tumor activity, safety and
PK/PD data from Phase 1 trial (monotherapy)
XTX202 (IL-2)
Initiated Clinical Trial
Enrollment in Phase 2 trial (monotherapy)
XTX202 (IL-2)
Plan to Report Clinical Data
Preliminary anti-tumor activity, safety and
PK/PD data in ~15-20 evaluable patients from
Phase 1/2 trial (monotherapy)
XTX301 (IL-12)
Plan to Report Clinical Data
Preliminary safety data from Phase 1 trial
3rd dose level (monotherapy dose-escalati
Anticipate existing cash and cash equivalents will be sufficient to fund operating expenses and capital expenditure requirements into the end of Q2 2024
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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
xilio THERAPEUTICS
Patient

Exhibit 99.2

Xilio Therapeutics Announces Preliminary Clinical Data from Phase 1 Trial of XTX101, a Tumor-Activated, Fc-Enhanced Anti-CTLA-4, in Patients with Advanced Solid Tumors

Encouraging preliminary anti-tumor activity observed in a patient with PD-L1 negative advanced non-small cell lung cancer

Favorable preliminary safety profile for XTX101 observed at the recommended Phase 2 dose of 150 mg once every six weeks

WALTHAM, Mass., May 25, 2023 – 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 preliminary data from its Phase 1 clinical trial evaluating XTX101, an investigational tumor-activated, Fc-enhanced anti-CTLA-4, in patients with advanced solid tumors.

“We are encouraged by the preliminary data from the Phase 1 trial for XTX101 showing evidence of tumor-selective activation,” said Martin Huber, M.D., president and head of research and development at Xilio. “Following treatment with XTX101 monotherapy at the recommended Phase 2 dose of 150 mg once every six weeks, we observed a partial response in a patient with PD-L1 negative advanced non-small cell lung cancer. Importantly, this anti-tumor activity occurred in the absence of meaningful observed activation of the immune system in the periphery, suggesting tumor-selective activation of XTX101. Based on these Phase 1 data, we plan to explore opportunities to evaluate XTX101 in combination with an anti-PD-(L)1 in historically immunotherapy-resistant tumor types.”

Data from the Ongoing Phase 1 Clinical Trial for XTX101

As of a data cutoff date of May 2, 2023, 25 patients had been treated with XTX101, including dose levels ranging from 7 mg to 180 mg administered once every three weeks (Q3W) and one dose level at 150 mg administered once every six weeks (Q6W). Of these patients, 20 patients were dosed in monotherapy dose-escalation (Part 1A) and five patients were dosed in monotherapy dose-expansion (Part 1B).

Patients had a wide range of advanced and treatment-refractory solid tumors, including colorectal cancer (CRC), non-small cell lung cancer (NSCLC) and pancreatic cancer. In addition, 76% of patients had been previously treated with at least three prior lines of anti-cancer therapy, and 44% had been previously treated with at least one immuno-oncology (I-O) agent. As of the data cutoff date, three patients were continuing on treatment with XTX101, and 22 patients had discontinued treatment with XTX101.

Preliminary Safety Data

A recommended Phase 2 dose (RP2D) and schedule of 150 mg Q6W was determined based on the favorable preliminary safety, pharmacokinetic (PK) and pharmacodynamic (PD) data for XTX101. At the RP2D, no dose-limiting toxicities were observed, and there was no reported evidence of immune-related endocrine or skin adverse events (AEs) that are commonly associated with systemically active anti-CTLA-4 agents. In addition, evidence of effective masking of XTX101 was demonstrated by low levels of unmasked drug detected in peripheral circulation, and XTX101 achieved target PK exposure at the RP2D, reaching the targeted area under the curve (AUC) and peak concentration (C_{max}).

As of the data cutoff date:

- Across all dosing levels and dosing intervals, no Grade 4 or Grade 5 treatment-related AEs were reported by investigators.

- Among seven patients who received XTX101 administered at the RP2D of 150 mg on a Q6W dosing schedule, the most common treatment-related AEs (≥10% incidence) of any grade reported by investigators were diarrhea (14%), fatigue (14%) and decreased appetite (14%). In these patients, no treatment-related colitis or infusion related reaction of any grade was observed. Investigators reported only one Grade 3 treatment-related AE of diarrhea, which occurred after two doses and resolved after five days without steroid use. This patient tolerated two additional doses of XTX101 after dose reduction to 75 mg Q6W without any symptom recurrence. At the RP2D of 150 mg Q6W, this was the only patient with a dose reduction due to an AE, and no patients discontinued treatment due to a treatment-related AE.

- Among 18 patients who received XTX101 administered on a Q3W dosing schedule, the most common treatment-related AEs (≥10% incidence) of any grade reported by investigators were diarrhea (28%), colitis (28%), infusion related reaction (28%), nausea (17%), vomiting (17%) and abdominal pain (11%). Of these, investigators reported the following Grade 3 treatment-related AEs: diarrhea (6%), colitis (22%) and infusion related reaction (17%). Infusion related reactions were associated with antidrug antibodies. Across all dose levels administered Q3W, two patients had dose reductions due to AEs, and four patients discontinued treatment due to an infusion related reaction.

Preliminary Anti-Tumor Activity

A partial response was observed at nine weeks in one patient with advanced PD-L1 negative NSCLC with hepatic metastases treated with XTX101 at the 150 mg Q6W dose level and confirmed after the data cutoff date at week 27. The only treatment-related AE reported for this patient was Grade 1 fatigue. In addition, PD markers for anti-CTLA-4 reported for this patient showed minimal immune activation in peripheral circulation, demonstrating evidence of tumor-selective activation of XTX101. The patient is currently continuing on treatment with XTX101.

Clinical Development Plan for XTX101

Enrollment in monotherapy dose-expansion (Part 1B) of the Phase 1 trial is currently ongoing, with the goal of further characterizing the safety, PK and PD of XTX101 at the RP2D of 150 mg Q6W. In addition, mandatory tumor biopsies will be obtained from patients in Part 1B to examine intra-tumoral PK and PD for XTX101.

Xilio plans to continue to explore strategic opportunities to advance XTX101 with a partner beyond the current Phase 1 monotherapy cohorts, including in potential Phase 1 dose escalation evaluating XTX101 in combination with a PD-(L)1 and in a potential Phase 2 trial evaluating XTX101 in combination with a PD-(L)1 in patients with microsatellite stable CRC.

About XTX101 (anti-CTLA-4) and the Phase 1 Clinical Trial

XTX101 is an investigational tumor-activated, Fc-enhanced anti-CTLA-4 monoclonal antibody designed to deplete regulatory T cells when activated (unmasked) in the tumor microenvironment (TME). The Phase 1 clinical trial is a first-in-human, multi-center, open-label trial designed to evaluate the safety and tolerability of XTX101 for the treatment of patients with advanced solid tumors. The primary outcome measures were the incidence of dose-limiting toxicities (DLTs) and the incidence of treatment-related adverse events, and changes in clinical laboratory abnormalities. Please refer to NCT04896697 on www.clinicaltrials.gov for additional details.

About Xilio Therapeutics

Xilio Therapeutics is a clinical-stage biotechnology company discovering and developing tumor-activated immuno-oncology (I-O) therapies with the goal of significantly improving outcomes for people living with cancer without the systemic side effects of current I-O treatments. The company is using its proprietary geographically precise solutions (GPS) platform to build a pipeline of novel, tumor-activated molecules, including cytokines and other biologics, which are designed to optimize their therapeutic index and localize anti-tumor activity within the tumor microenvironment. Xilio is currently advancing multiple programs for tumor-activated I-O treatments in clinical development, as well as programs in preclinical development. Learn more by visiting www.xiliotx.com and follow us on Twitter (@xiliotx) and 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, timing and expectations related to: the ongoing Phase 1 monotherapy dose expansion cohort for XTX101; plans to continue to explore strategic opportunities to advance XTX101 with a partner beyond the current Phase 1 monotherapy cohorts; the potential safety and anti-tumor activity of any of Xilio's current or future product candidates in treating patients, including without limitation XTX101; and Xilio's strategy, goals and anticipated financial performance, milestones, business plans and focus. The words "aim," "may," "will," "could," "would," "should," "expect," "plan," "anticipate," "intend," "believe," "estimate," "predict," "project," "potential," "continue," "seek," "target" and similar expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words. Any forward-looking statements in this press release are based on management's current expectations and beliefs and are subject to a number of important risks, uncertainties and other factors that may cause actual events or results to differ materially from those expressed or implied by any forward-looking statements contained in this press release, including, without limitation, risks and uncertainties related to the following: 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 programs; Xilio's ability to replicate in future preclinical studies or clinical trials positive data results from earlier preclinical studies or clinical trials, such as the preliminary safety and anti-tumor data observed in the Phase 1 clinical trial for XTX101 as of the data cutoff date; 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; the potential for results from preclinical studies or clinical trials for Xilio's product candidates not supporting 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 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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