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): **August 14, 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 2.02 Results of Operations and Financial Condition.

On August 14, 2023, Xilio Therapeutics, Inc. (the "Company") announced its financial results for the quarter ended June 30, 2023 and other business highlights. The full text of the press release issued in connection with the announcement is furnished as Exhibit 99.1 to this Current Report on Form 8-K and is incorporated by reference herein.

Item 7.01 Regulation FD Disclosure.

From time to time, the Company presents or distributes slide presentations to the investment community to provide updates and summaries of its business. The Company is posting a copy of its current corporate investor presentation to the "Investors & Media" portion of its website at https://ir.xiliotx.com. The information contained on, or accessible through, the Company's website is not incorporated by reference into this Current Report on Form 8-K and should not be considered to be a part hereof. A copy of the presentation is furnished as Exhibit 99.2 to this Current Report on Form 8-K.

The information in this Current Report on Form 8-K, including Exhibits 99.1 and 99.2, 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 2.02 and Item 7.01 of this Current Report on Form 8-K shall be deemed to be furnished and not filed:

Exhibit No.	Description
99.1	Press release issued by Xilio Therapeutics, Inc. on August 14, 2023
99.2	Corporate investor presentation of Xilio Therapeutics, Inc. as of August 14, 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: August 14, 2023

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

Exhibit 99.1

Xilio Therapeutics Announces Pipeline and Business Updates and Second Quarter 2023 Financial Results

Xilio entered into clinical trial collaboration with Roche to evaluate XTX101, a tumor-activated, Fc-enhanced anti-CTLA-4, in combination with atezolizumab (Tecentriq®), in patients with microsatellite stable (MSS) colorectal cancer

Xilio to host live virtual program spotlighting XTX101 on Thursday, August 17, 2023, at 12:30 p.m. ET

Anticipate reporting preliminary Phase 1/2 data for XTX202, a tumor-activated IL-2, in early November 2023

Anticipate reporting preliminary Phase 1 safety data for XTX301, a tumor-activated IL-12, in the fourth quarter of 2023

Ended second quarter of 2023 with $75.4 million in cash and cash equivalents, with cash runway anticipated into the end of the second quarter of 2024

WALTHAM, Mass., August 14, 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 pipeline progress and business updates and reported financial results for the second quarter ended June 30, 2023.

“In the second quarter, we reported encouraging initial monotherapy data from our Phase 1 trial of XTX101, a tumor-activated, Fc-enhanced anti-CTLA-4, including a partial response in a patient with advanced non-small cell lung cancer and a favorable preliminary safety profile at the recommended Phase 2 dose,” said René Russo, Pharm.D., chief executive officer of Xilio. “Building on these data, today we are pleased to announce a clinical trial collaboration with Roche to evaluate XTX101 in combination with atezolizumab in patients with MSS colorectal cancer. Currently, there are no approved immunotherapies for patients living with this cold tumor type. We believe the combination of our tumor-activated anti-CTLA-4 with an anti-PD-L1 represents a promising combination for evaluation in MSS colorectal cancer and potentially other cold tumor types with limited treatment options. We also look forward to reporting preliminary clinical data later this year from our ongoing trials of XTX202, a tumor-activated IL-2, and XTX301, a tumor-activated IL-12.”

Pipeline and Business Updates

XTX101: tumor-activated, Fc-enhanced anti-CTLA-4

XTX101 is an investigational tumor-activated, Fc-enhanced, high affinity binding anti-CTLA-4 designed to block CTLA-4 and deplete regulatory T cells when activated (unmasked) in the tumor microenvironment (TME). XTX101 has completed monotherapy dose escalation (Part 1A) and is currently being evaluated at the recommended Phase 2 dose and schedule of 150 mg once every six weeks (RP2D) in monotherapy dose expansion (Part 1B) of an ongoing Phase 1 clinical trial in patients with advanced solid tumors.

- Xilio today announced that it has entered into a clinical trial collaboration with Roche to evaluate XTX101 in combination with atezolizumab (Tecentriq®) in a Phase 1/2 clinical trial consisting of Phase 1 combination dose escalation in patients with advanced solid tumors and Phase 2 in patients with microsatellite stable colorectal cancer (MSS CRC). Under the clinical trial supply agreement, Xilio is eligible to receive specified cost-sharing payments from Roche, and each

company will supply its respective anti-cancer agent to support the clinical trial. Xilio will sponsor and conduct the Phase 1/2 clinical trial and retains global development and commercialization rights to XTX101.

- In May 2023, Xilio announced preliminary monotherapy data from its Phase 1 clinical trial evaluating XTX101 in patients with advanced solid tumors. These data included a confirmed partial response observed in a patient with advanced non-small cell lung cancer and a favorable preliminary safety profile observed at the RP2D. For more information, read the press release here.

- Xilio today announced updated monotherapy data from its Phase 1 clinical trial evaluating XTX101 in patients with advanced solid tumors at the RP2D. As of a data cutoff date of August 3, 2023, 11 patients had been treated at the RP2D. Across all dosing levels and dosing intervals, no Grade 4 or Grade 5 treatment-related adverse events (AEs) were reported by investigators. Among the 9 patients who received XTX101 administered at the RP2D and for whom safety data were available as of the data cutoff date, the most common treatment-related AEs (≥10% incidence) of any grade reported by investigators were diarrhea (11%), fatigue (11%), decreased appetite (11%) and dermatitis (11%). In these patients, no treatment-related colitis or infusion related reaction of any grade was observed. In addition to a previously reported Grade 3 treatment-related AE of diarrhea, which resolved after five days without steroid use, investigators observed one Grade 3 treatment-related AE of dermatitis. As of the data cutoff date of August 3, 2023, no patients who received XTX101 administered at the RP2D have discontinued treatment due to a treatment-related AE. In addition, Xilio reported data showing a durable, continuing partial response of 36 weeks in the previously reported patient with advanced non-small cell lung cancer, with treatment ongoing as of the data cutoff date.

Xilio anticipates activating clinical trial sites for the Phase 1 dose escalation portion of the clinical trial evaluating XTX101 in combination with atezolizumab in the fourth quarter of 2023.

XTX202: tumor-activated, engineered, beta-gamma biased IL-2

XTX202 is an investigational tumor-activated beta-gamma biased, engineered IL-2 molecule designed to potently stimulate CD8+ effector T cells and natural killer (NK) cells without concomitant stimulation of regulatory T cells when activated (unmasked) in the TME. XTX202 is currently being evaluated in an ongoing Phase 1/2 clinical trial in patients with advanced solid tumors.

- Xilio recently cleared the 2.8 mg/kg dose level (dose level six) in monotherapy dose escalation for the Phase 1 clinical trial. No signs or symptoms of vascular leak syndrome have been observed in patients through the 2.8 mg/kg dose level.

- Xilio is currently dosing patients at the 4.0 mg/kg dose level (dose level seven) in monotherapy dose escalation for the Phase 1 clinical trial. A maximum tolerated dose has not yet been determined, and enrollment in the Phase 1 clinical trial is ongoing.

- In addition, Xilio continues to dose patients at the 1.4 mg/kg dose level in the Phase 2 clinical trial evaluating XTX202 as a monotherapy in patients with unresectable or metastatic melanoma and metastatic renal cell carcinoma who have progressed on standard-of-care treatment. Based on continued Phase 1 monotherapy dose escalation, Xilio also plans to explore opportunities to evaluate XTX202 at an additional, higher dose level in the Phase 2 clinical trial.

Xilio anticipates reporting preliminary anti-tumor activity, safety, pharmacokinetic and pharmacodynamic data from the Phase 1/2 clinical trial in early November 2023. The company anticipates the reported data will include at least 20 evaluable patients across a range of solid tumors treated at dose levels of 1.0 mg/kg or higher across all cohorts in the Phase 1/2 clinical trial.

In addition, Xilio today announced the acceptance of an abstract for XTX202 at the Society for Immunotherapy of Cancer (SITC) 38th Annual Meeting on November 1-5, 2023.

XTX301: tumor-activated, engineered IL-12

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

- Xilio is currently dosing patients in monotherapy dose escalation of an ongoing Phase 1 clinical trial evaluating the safety and tolerability of XTX301 in patients with advanced solid tumors.
- Xilio anticipates reporting preliminary safety data from the Phase 1 clinical trial into the third dose level in the fourth quarter of 2023.

Corporate Highlights

- In August 2023, Xilio announced the promotion of Chris Frankenfield to Chief Operating Officer.

Virtual Spotlight Program on XTX101

Xilio will host a live virtual program on Thursday, August 17, 2023, at 12:30 p.m. ET spotlighting XTX101, including highlights from the recently reported Phase 1 monotherapy data for XTX101 and clinical development plans in MSS CRC.

- The event will feature members of Xilio's management team as well as Dr. Diwakar Davar, MBBS, M.Sc., a key opinion leader and assistant professor of medicine and a medical oncologist/hematologist from UPMC Hillman Cancer Center. Dr. Davar will discuss the anti-CTLA-4 treatment landscape, including recent advances observed in patients with previously I-O refractory cold tumors, such as MSS CRC. A live question and answer session will follow the presentation.
- To register in advance for the webcast, please click here. A live webcast of the event will also be available under "Events and Presentations" in the Investors & Media section of Xilio's website at https://ir.xiliotx.com. A replay of the webcast will be archived on Xilio's website for 90 days following the event.

Second Quarter 2023 Financial Results

- **Cash Position:** Cash and cash equivalents were $75.4 million as of June 30, 2023, compared to $120.4 million as of December 31, 2022.
- **Research & Development (R&D) Expenses:** R&D expenses were $13.2 million for the quarter ended June 30, 2023, compared to $16.2 million for the quarter ended June 30, 2022. The decrease was primarily driven by decreased manufacturing and clinical development activities for XTX101 and decreased manufacturing and preclinical activities for XTX301. These decreases were partially offset by increases in clinical activities for XTX202 and XTX301.
- **General & Administrative (G&A) Expenses:** G&A expenses were $6.9 million for the quarter ended June 30, 2023, compared to $8.3 million for the quarter ended June 30, 2022. The decrease was primarily driven by a decrease in personnel-related costs, including stock-based compensation.
- **Net Loss:** Net loss was $19.4 million for the quarter ended June 30, 2023, compared to $24.6 million for the quarter ended June 30, 2022.

Financial Guidance

Xilio continues to anticipate that its existing cash and cash equivalents will be sufficient to fund its operating expenses and capital expenditure requirements into the end of the second quarter of 2024.

About XTX101 (anti-CTLA-4) and the Phase 1 Monotherapy and Phase 1/2 Combination Clinical Trials

XTX101 is an investigational tumor-activated, Fc-enhanced, high affinity binding anti-CTLA-4 monoclonal antibody designed to block CTLA-4 and deplete regulatory T cells when activated (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 adult patients with advanced solid tumors. Xilio has completed monotherapy dose escalation (Part 1A) and is currently enrolling patients at the recommended Phase 2 dose and schedule of 150 mg once every six weeks in monotherapy dose expansion (Part 1B). Please refer to NCT04896697 on www.clinicaltrials.gov for additional details.

In addition, Xilio plans to evaluate the safety, tolerability and efficacy of XTX101 in combination with atezolizumab (Tecentriq®) in the Phase 1/2 clinical trial. The Phase 1 portion is designed to assess the safety and tolerability of XTX101 in combination with atezolizumab in dose escalation in patients with advanced solid tumors. The planned Phase 2 portion is designed to evaluate the safety and efficacy of the combination in patients with microsatellite stable colorectal cancer (MSS CRC).

About XTX202 (IL-2) and the Phase 1/2 Clinical Trials

XTX202 is an investigational tumor-activated beta-gamma biased, engineered IL-2 molecule designed to potently stimulate CD8+ effector T cells and natural killer (NK) cells without concomitant stimulation of regulatory T cells when activated (unmasked) in the tumor microenvironment (TME). The Phase 1 clinical trial for XTX202 is a first-in-human, multi-center, open-label trial designed to evaluate the safety and tolerability of XTX202 as a monotherapy in patients with advanced solid tumors. The Phase 2 clinical trial for XTX202 is a multi-center, open-label trial designed to evaluate the safety and efficacy of XTX202 as a monotherapy in patients with unresectable or metastatic melanoma and metastatic renal cell carcinoma who have progressed on standard-of-care treatment. Please refer to NCT05052268 on www.clinicaltrials.gov for additional details.

About XTX301 (IL-12) and the Phase 1 Clinical Trial

XTX301 is an investigational tumor-activated, engineered IL-12 molecule designed to potently stimulate anti-tumor immunity and reprogram the tumor microenvironment (TME) of poorly immunogenic “cold” tumors towards an inflamed or “hot” state. The Phase 1 clinical trial for XTX301 is a first-in-human, multi-center, open-label trial designed to evaluate the safety and tolerability of XTX301 as a monotherapy in patients with advanced solid tumors. Please refer to NCT05684965 on www.clinicaltrials.gov for additional details.

About Xilio Therapeutics

Xilio Therapeutics is a clinical-stage biotechnology company discovering and developing tumor-activated immuno-oncology (I-O) therapies with the goal of significantly improving outcomes for people living with cancer without the systemic side effects of current I-O treatments. The company is using its proprietary geographically precise solutions (GPS) platform to build a pipeline of novel, tumor-activated molecules, including antibodies, 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 reporting preliminary data from the Phase 1/2 clinical trial for XTX202, including the anticipated number of patients treated at the 1 mg/kg dose level or higher; evaluating XTX202 at a second dose level in the Phase 2 clinical trial; reporting preliminary safety data from the Phase 1 clinical trial for XTX301; activating clinical trial sites for Phase 1 combination dose escalation portion of the clinical trial evaluating XTX101 in combination with atezolizumab in patients with advanced solid tumors; the potential benefits of any of Xilio's current or future product candidates in treating patients; Xilio's ability to obtain and maintain sufficient cash resources to fund its operations beyond the end of the second quarter of 2024; 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 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; 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; Xilio's ability to successfully demonstrate the safety and efficacy of its product candidates and gain approval of its product candidates on a timely basis, if at all; results from preclinical studies or clinical trials for Xilio's product candidates, which may not support further development of such product candidates; actions of regulatory agencies, which may affect the initiation, timing and progress of current or future clinical trials; Xilio's ability to obtain, maintain and enforce patent and other intellectual property protection for current or future product candidates; Xilio's ability to obtain and maintain sufficient cash resources to fund its operations beyond the end of the second quarter of 2024; the impact of international trade policies on Xilio's business, including U.S. and China trade policies; and Xilio's ability to maintain its clinical trial collaboration with Roche to develop XTX101 in combination with atezolizumab. These and other risks and uncertainties are described in greater detail in the sections entitled "Risk Factor Summary" and "Risk Factors" in Xilio's filings with the U.S. Securities and Exchange Commission (SEC), including Xilio's most recent Quarterly Report on Form 10-Q and any other filings that Xilio has made or may make with the SEC in the future. Any forward-looking statements contained in this press release represent Xilio's views only as of the date hereof and should not be relied upon as representing its views as of any subsequent date. Except as required by law, Xilio explicitly disclaims any obligation to update any forward-looking statements.

This press release contains hyperlinks to information that is not deemed to be incorporated by reference in this press release.

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

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XILIO THERAPEUTICS, INC.

Condensed Consolidated Balance Sheets
(In thousands)
(Unaudited)

	June 30, 2023	December 31, 2022
Assets		
Cash and cash equivalents	$ 75,383	$ 120,385
Other assets	16,976	18,780
Total assets	$ 92,359	$ 139,165
Liabilities and Stockholders' Equity		
Liabilities	$ 24,982	$ 33,518
Stockholders' equity	67,377	105,647
Total liabilities and stockholders' equity	$ 92,359	$ 139,165

XILIO THERAPEUTICS, INC.

Condensed Consolidated Statements of Operations and Comprehensive Loss
(In thousands, except share and per share data)
(Unaudited)

	Three Months Ended June 30,		Six Months Ended June 30,	
	2023	2022	2023	2022
Operating expenses [1]				
Research and development	$ 13,218	$ 16,246	$ 29,349	$ 31,166
General and administrative	6,898	8,306	14,293	14,610
Total operating expenses	20,116	24,552	43,642	45,776
Loss from operations	(20,116)	(24,552)	(43,642)	(45,776)
Other income (expense), net				
Other income (expense), net	761	(61)	1,641	(190)
Total other income (expense), net	761	(61)	1,641	(190)
Net loss and comprehensive loss	$ (19,355)	$ (24,613)	$ (42,001)	$ (45,966)
Net loss per share, basic and diluted	$ (0.70)	$ (0.90)	$ (1.53)	$ (1.68)
Weighted average common shares outstanding, basic and diluted	27,468,668	27,384,614	27,451,058	27,376,043

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

	Three Months Ended June 30,		Six Months Ended June 30,	
	2023	2022	2023	2022
Research and development expense	$ 549	$ 637	$ 1,122	$ 1,233
General and administrative expense	1,251	2,072	2,469	3,505
Total stock-based compensation expense	$ 1,800	$ 2,709	$ 3,591	$ 4,738

Unleashing the Potential of Immuno-Oncology Therapies

August 14, 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 preliminary data from the Phase 1/2 clinical trial for XTX202, including the anticipated number of patients treated at the 1 mg/kg dose level or higher; evalu XTX202 at a second dose level in the Phase 2 clinical trial; reporting preliminary safety data from the Phase 1 clinical trial for XTX301; activating clinical trial sites for Phase 1 combination dose escala portion of the clinical trial evaluating XTX101 in combination with atezolizumab in patients with advanced solid tumors; the potential benefits of any of Xilio's current or future product candidates in treat patients; Xilio's ability to obtain and maintain sufficient cash resources to fund its operations beyond the end of the second quarter of 2024; and Xilio's strategy, goals and anticipated financial performa 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 managen current expectations and beliefs and are subject to a number of important risks, uncertainties and other factors that may cause actual events or results to differ materially from those expressed or impli any forward-looking statements contained in this presentation, including, without limitation, risks and uncertainties related to ongoing and planned research and development activities, including initiati 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 its operations beyon end of the second quarter of 2024; the impact of international trade policies on Xilio's business, including U.S. and China trade policies; and Xilio's ability to maintain its clinical trial collaboration with R to develop XTX101 in combination with atezolizumab.

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 June 30, 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 expl 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.

x·ilio THERAPEUTICS

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**

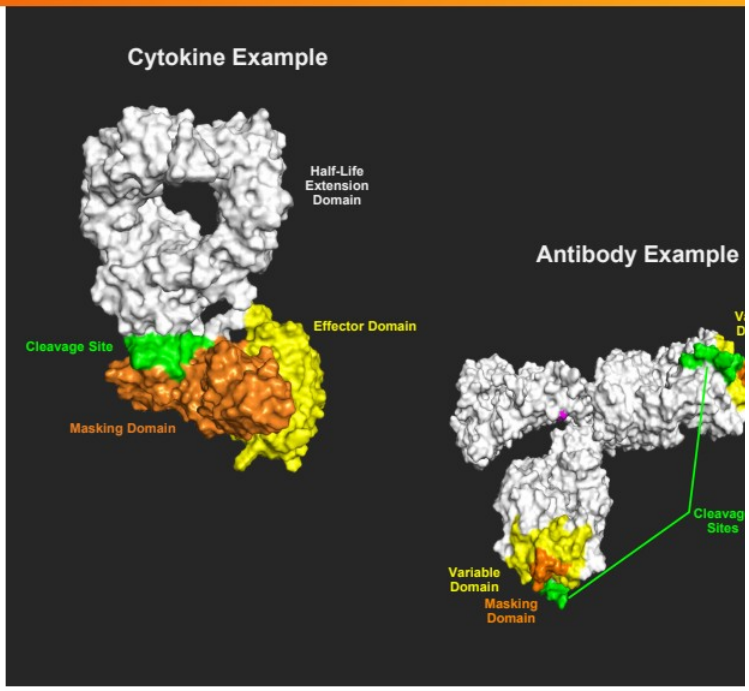
Xilio (*ex*-il-ee-oh) believes th next revolution in IO cancer therapies will **trick tumors int activating their own treatmen** while simultaneously **sparing healthy tissues and cells**

The Critical Challenge: Maximizing Efficacy While Improving Tolerability

xilio THERAPEUTICS

Xilio's Novel Tumor-Activated Molecules Are Designed to Overcome th 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)

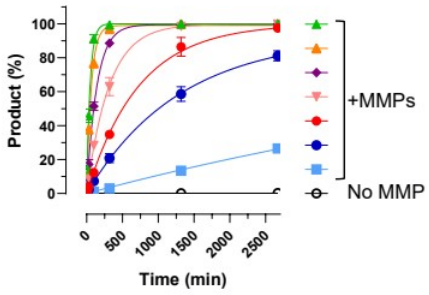


mAb: monoclonal antibody

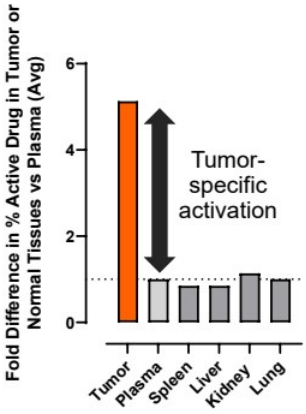
Xilio's Molecules Are Designed to Be Selectively Activated in the TME b MMPs

High activation efficiency across human solid tumors *ex vivo*

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)	XTX30 (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 and MSS CRC	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	●				

1. Xilio plans to evaluate XTX101 in combination with atezolizumab (Tecentriq®) in a Phase 1/2 clinical trial under a clinical trial collaboration with Roche. The Phase 1 portion is designed to assess the safety and tolerability of the combination in dose escalation in patients with advanced solid tumors, and the planned Phase 2 portion is designed to assess the safety and efficacy of the combination in patients with MSS CRC.
2. Initially evaluating 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 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; NSCLC: non-small cell lung cancer; RCC: renal cell carcinoma.


CTLA-4
Evolving Paradigm and Opportunity for
a Tumor-Activated Anti-CTLA-4
x·ilio
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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

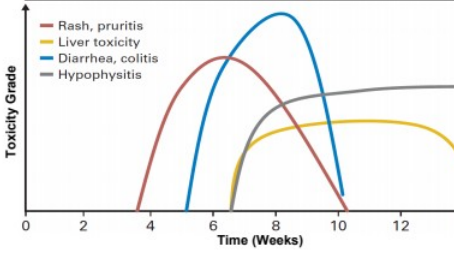
Improved efficacy seen with 10 mg/kg dose, but greater toxicity limits clinical use to 3 mg/kg dose

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



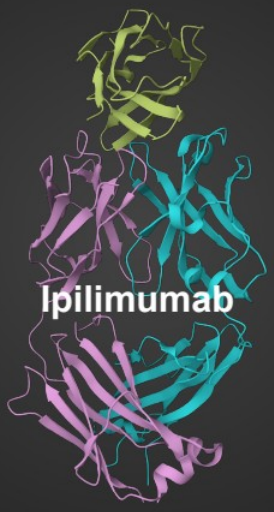
Trial conducted by Bristol Myers Squibb.
Ascierto et al., J Immunother Cancer (2020); Larkin et al., N Engl J Med (2015); Wolchok et al., Lancet (2010); Hamid et al., J Transl Med (2011); Lebbe et al., J Clin Oncol (2019); Weber et al., J Clin Oncol (2012).
AE: adverse event; irAE: immune-related adverse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

CTLA-4



High Dose CTLA-4 Improved Outcomes

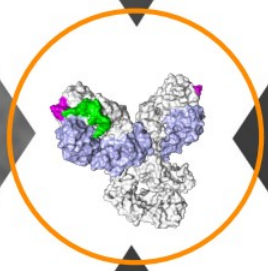
- Single high dose (300 mg x1) administration of tremelimumab in combination with an anti-PD-L1 resulted in improved efficacy compared to multiple low doses (75 mg x4 Q4W) (3)

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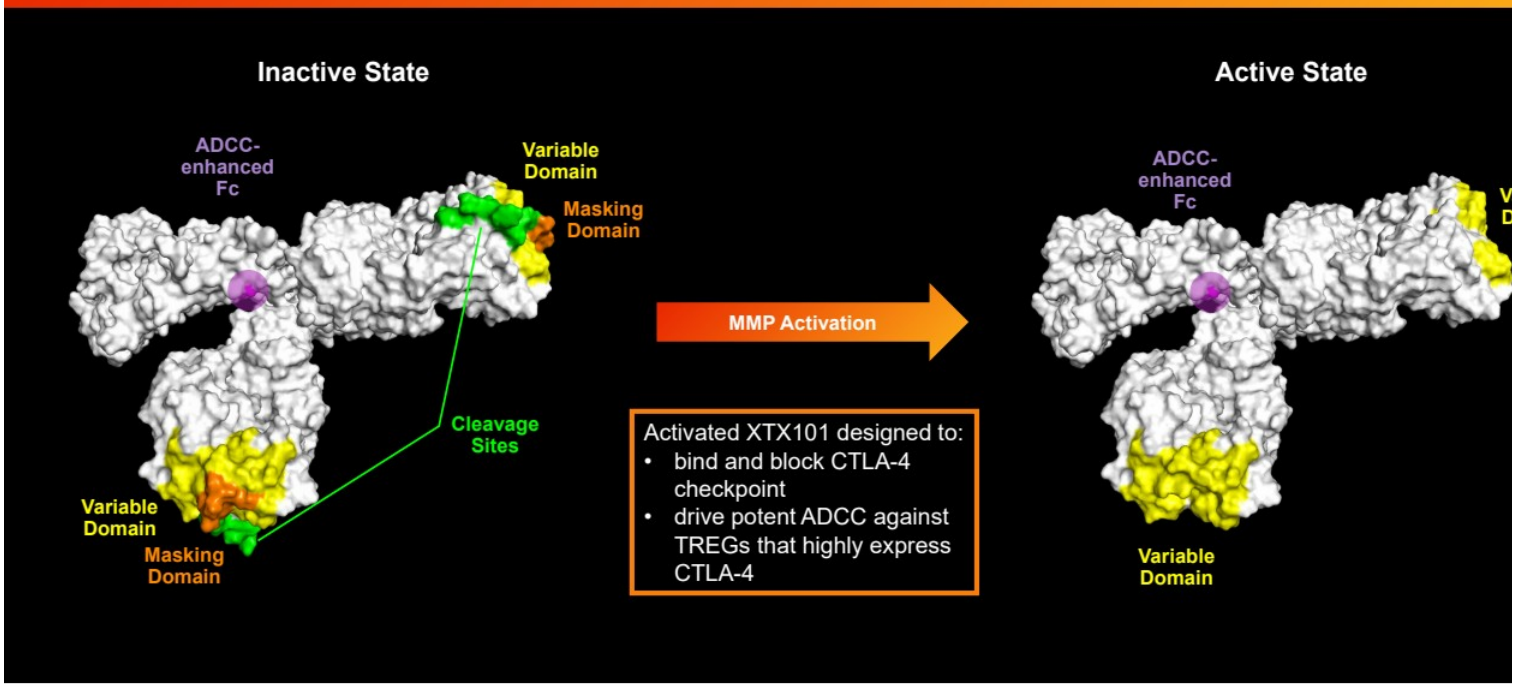
XTX101: Tumor-Activated, High Affinity Binding, Fc-Enhanced Anti-CTLA-



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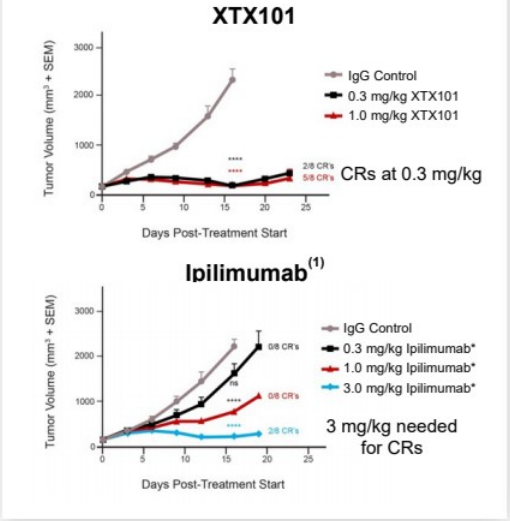
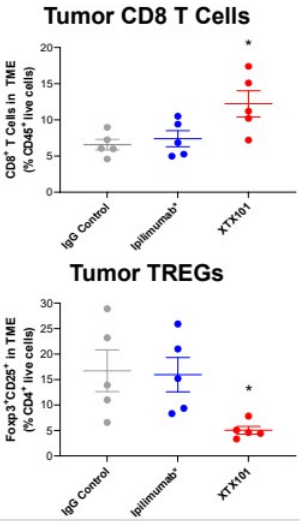
XTX101 Preclinical Profile Differentiated from Ipilimumab (10x Potency TREG Depletion, Safety) and AGEN1181 (Safety)

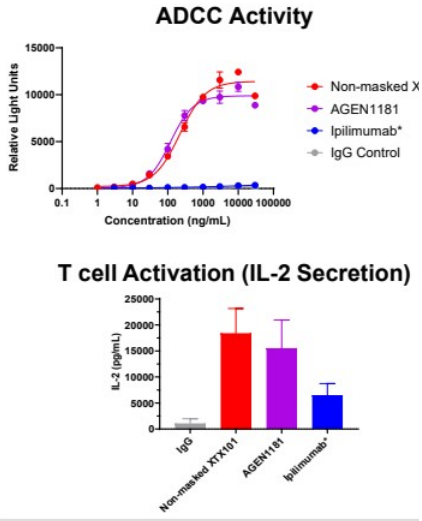
XTX101 is 10-fold more potent than ipilimumab[1] in *in vivo* studies



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

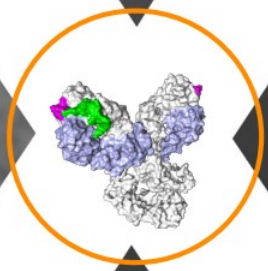


XTX101 exhibited enhanced AD and T cell activation vs ipilimum and in line with AGEN1181



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.

Phase 1 Clinical Trial Data for XTX101



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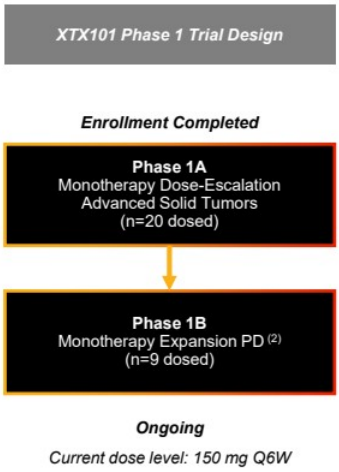
29 Patients Enrolled in Phase 1 Trial (Phase 1A and 1B) for XTX101 wi a Wide Range of Advanced and Treatment Refractory Solid Tumors



Patient Characteristics	Total (N=27)(1)
Demographics	
Age, median (range)	67 (49, 80)
Female	15 (56%)
ECOG PS 0	7 (26%)
ECOG PS 1	20 (74%)
Prior Lines of Anti-Cancer Treatment	**Median 4 (1-12)**
1	2 (7%)
2	4 (15%)
3	6 (22%)
4	7 (26%)
5	3 (11%)
6 and more	5 (19%)
Prior Treatment with IO	
≥1	12 (44%)

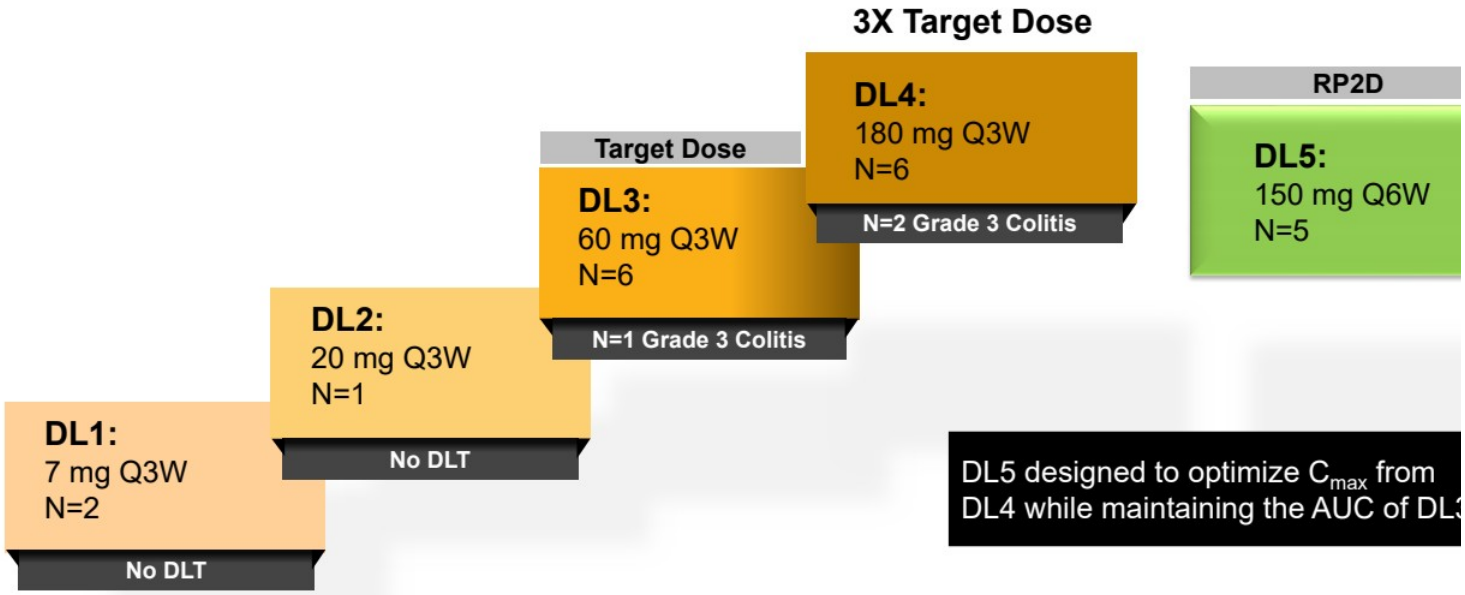
Tumor Types	Total (N=27)(1)
Colorectal	6
NSCLC	4
Pancreatic	3
Squamous cell skin	2
Breast	2
Uterine	2
Merkel cell carcinoma	2
Melanoma	1
Cervical	1
Prostate	1
Gastric	1
Fallopian tube cancer	1
Leiomyosarcoma	1

Treatment Status	Total (N=27)(1)
Continuing on Treatment	**3**
Discontinued Treatment	**24**
Progressive Disease	14
Adverse Events	4
Consent Withdrawal (Hospice)	3
Death Due to Progressive Disease	1
Other	2

Data cutoff date: August 3, 2023. 29 patients have been dosed across all dose levels, including 20 patients dosed in Phase 1A and 9 patients dosed in Phase 1B.
1. Among the 29 patients dosed, data was not available for two patients as of the data cutoff date.
2. 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

150 mg Q6W Identified as RP2D for XTX101 in Phase 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.

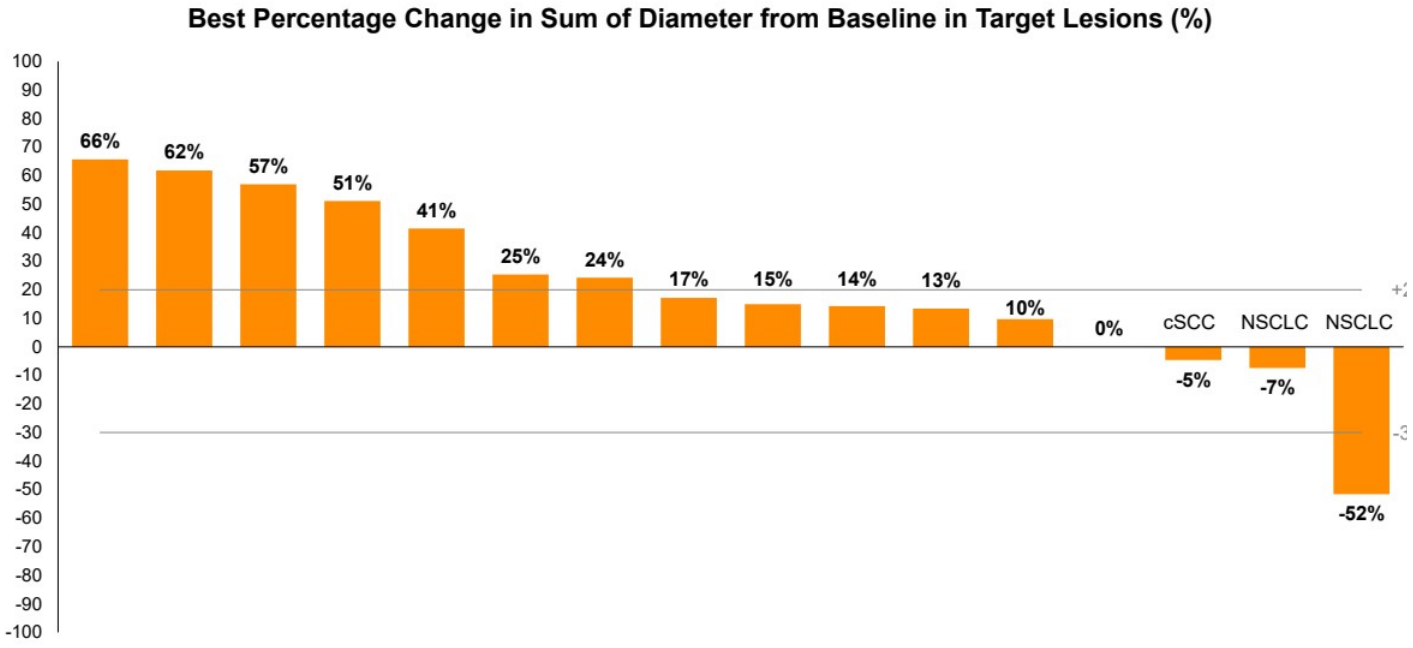
150 mg Q6W Identified as Optimal Dose and Schedule for XTX101

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)		RP2D 150 mg Q6W (n=9)	
	Any	Grade 3	Any	Grade 3
Diarrhea or Colitis	7 (39%)	4 (22%)	1 (11%)	1 (11%)
Diarrhea	*5 (28%)*	*1 (6.0)*	*1 (11%)*	*1 (11%)* [1]
Colitis	*5 (28%)*	*4 (22.0)*	*0*	*0*
Nausea	3 (17%)	0	0	0
Vomiting	3 (17%)	0	0	0
Abdominal pain	2 (11%)	0	0	0
Infusion related reaction [2]	5 (28%)	3 (17%)	0	0
Fatigue	1 (6%)	0	1 (11%)	0
Decreased appetite	1 (6%)	0	1 (11%)	0
Dermatitis			1 (11%)	1 (11%)
Dose reduction due to AE	3		1	
Treatment discontinuation due to TRAE [3]	4		0	

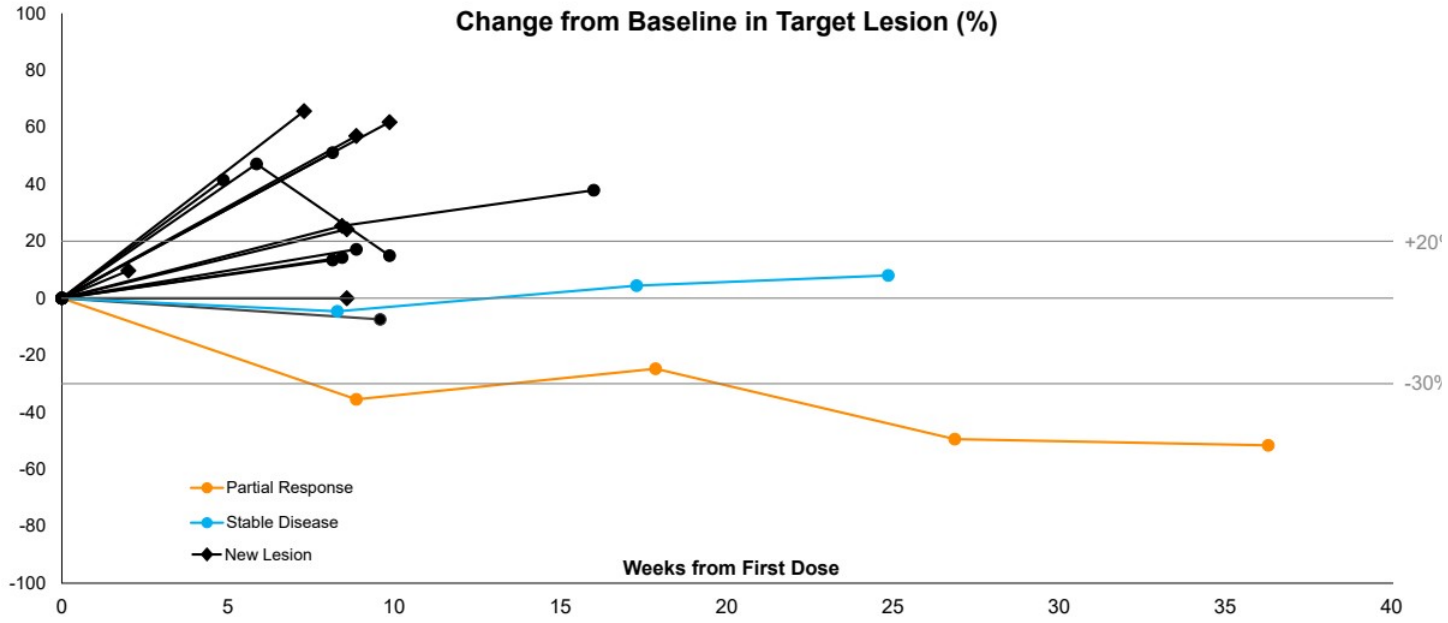
Data cutoff date: August 3, 2023. As of the data cutoff date, safety data were available for 27 patients across all dose levels, including 20 patients dosed in Phase 1A and 7 patients dosed in Phase 1B.
1. Grade 3 diarrhea with onset 10 weeks after the start of treatment (after 2 doses), resolved within 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.

XTX101 Demonstrated Evidence of Anti-Tumor Activity in Phase 1 Trial (Phase 1A and 1B)



cSCC: cutaneous squamous cell carcinoma
Data cutoff date: August 3, 2023.

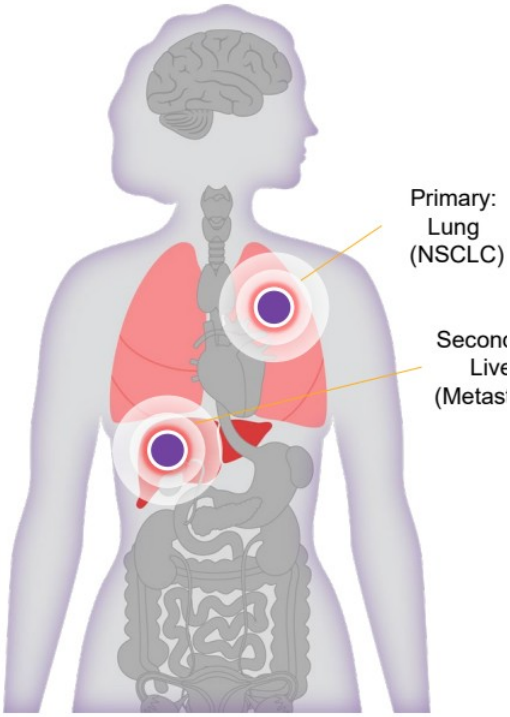
XTX101 Demonstrated Prolonged Anti-Tumor Activity in a Patient with PD-L1 Negative NSCLC and Hepatic Metastases



Data cutoff date: August 3, 2023. As of the data cutoff date, treatment ongoing for one NSCLC patient with confirmed partial response, and all other patients shown in figure have discontinued treatment.

XTX101 Anti-Tumor Activity in a Patient with PD-L1 Negative NSCLC and 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:** 7 doses of XTX101 administered (continuing on treatment, 36+ weeks)
- **Related AE**: Only Grade 1 fatigue



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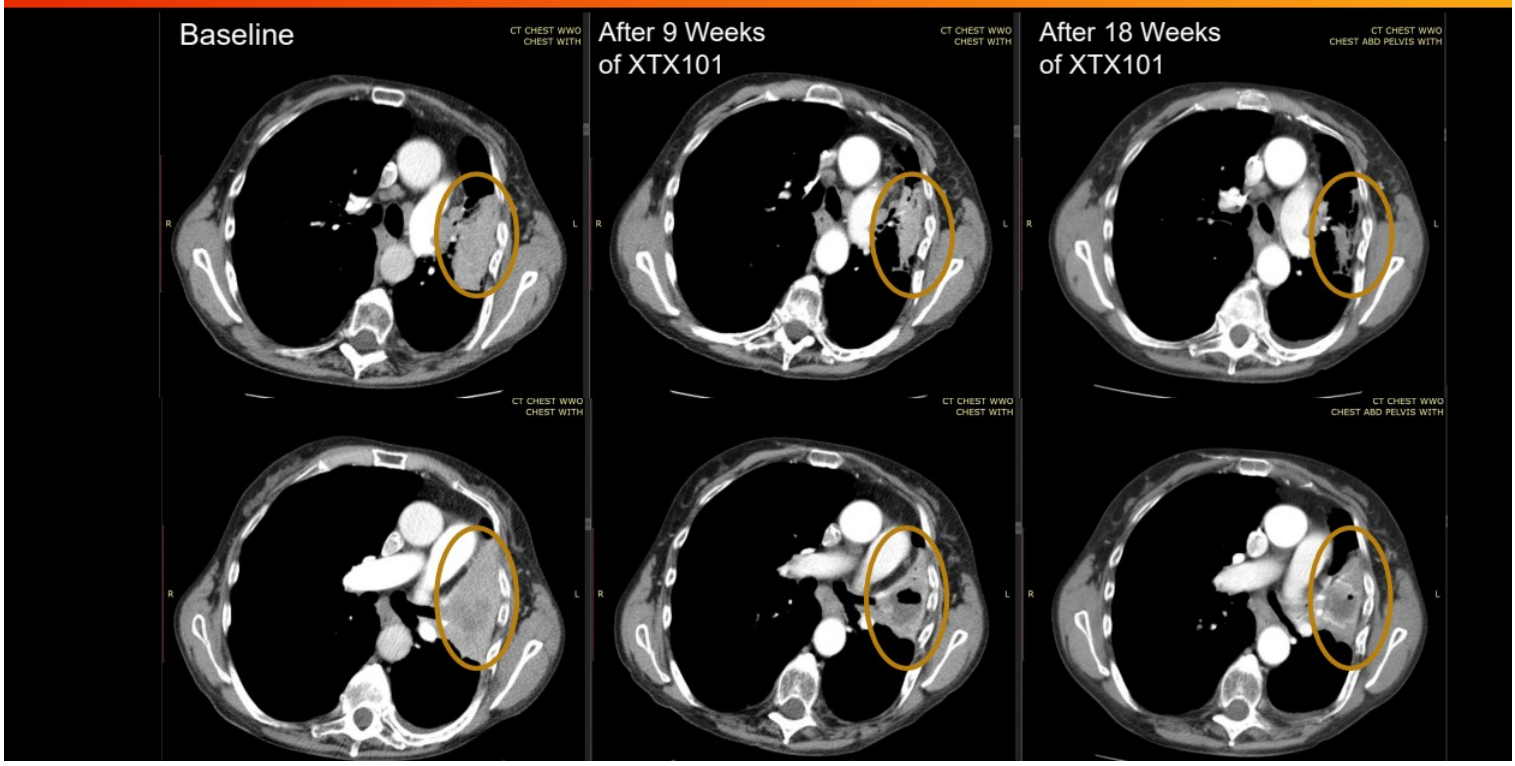
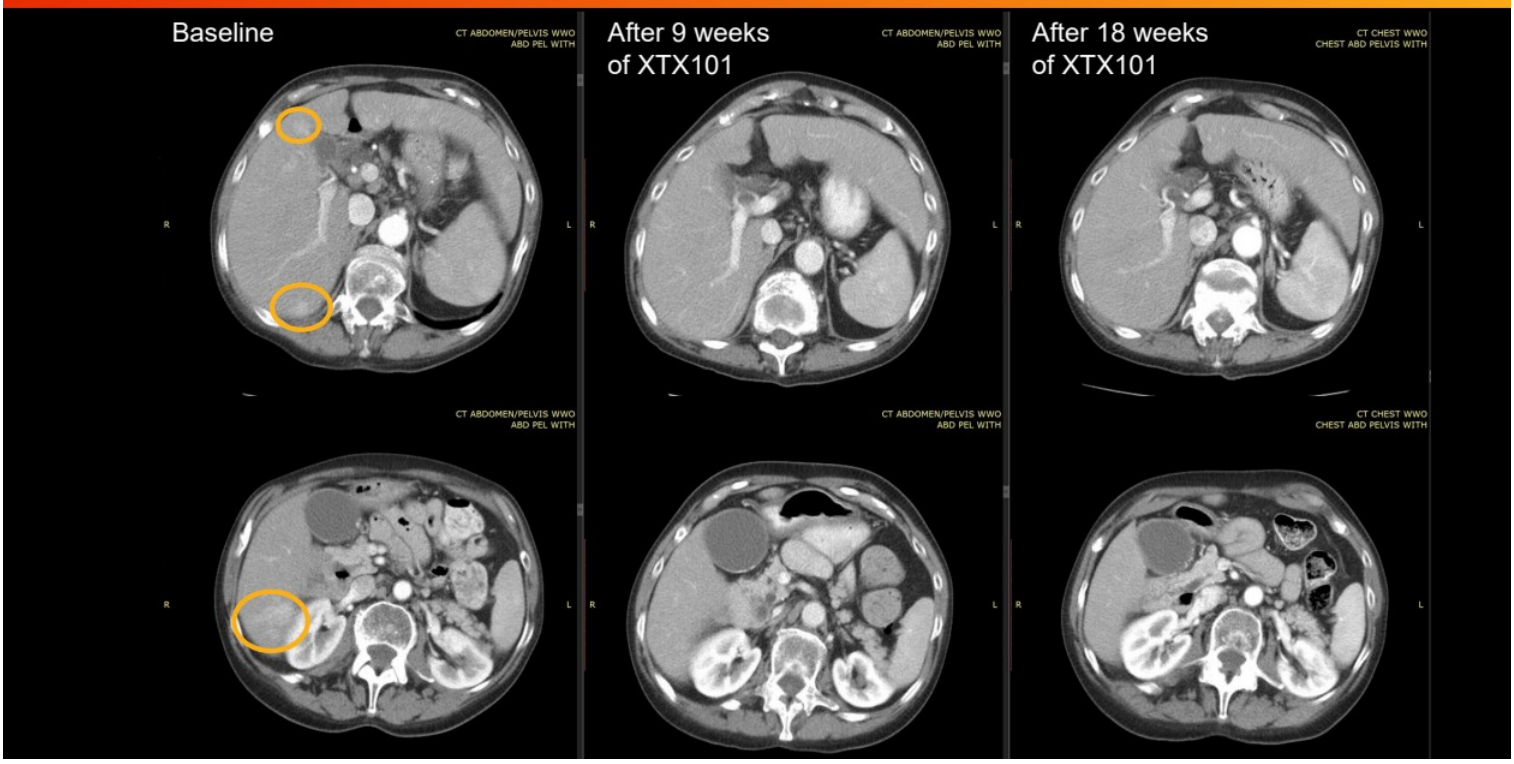
Data cutoff date: August 3, 2023.

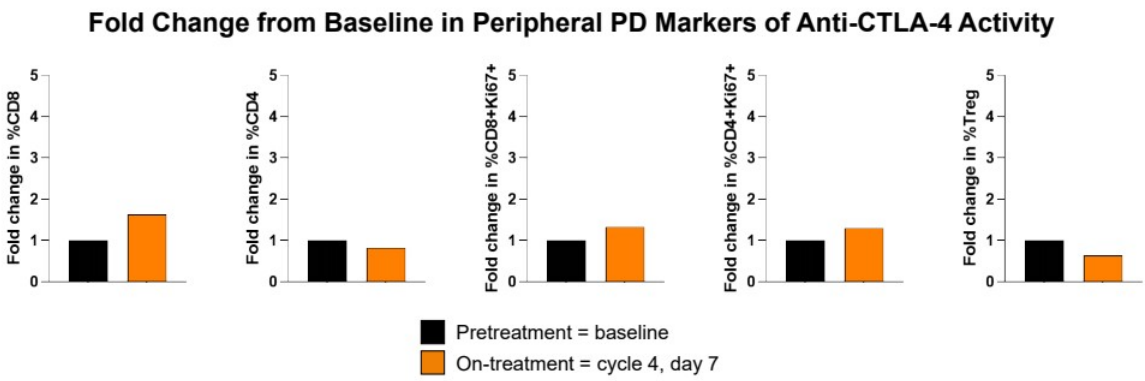
Primary Lung Lesion Decreased in Size and Developed Cavitation on XTX101 Monotherapy



Hepatic Metastases Resolved on XTX101 Monotherapy



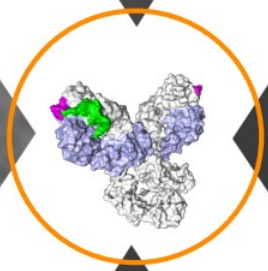
XTX101 Tumor-Selective Activity Demonstrated by Minimal Changes in Peripheral PD Markers in PD-L1 Negative NSCLC Patient with Confirmed PR



PR: partial response

XTX101 Clinical Development Path

Pursuing XTX101 in Combination with Atezolizumab in MSS CRC



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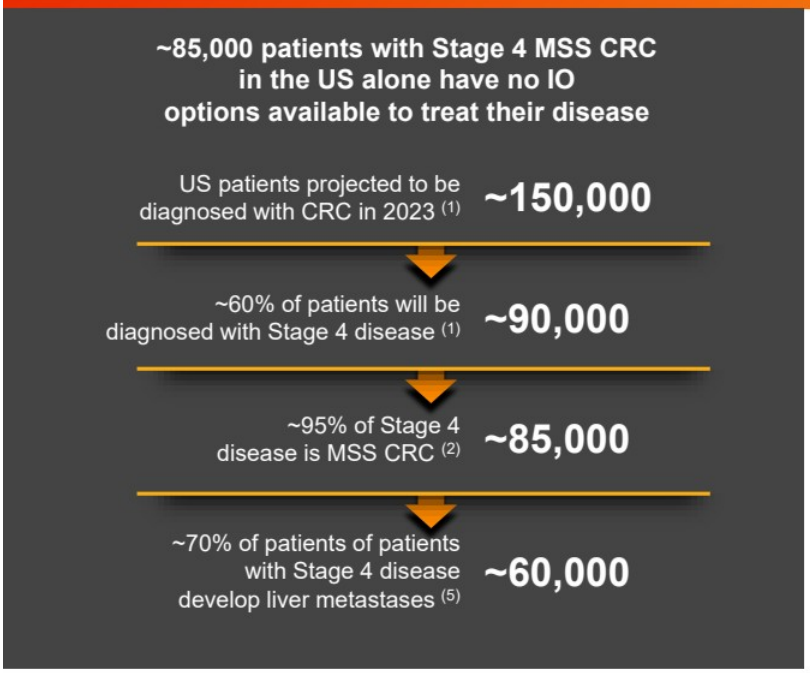
Colorectal Cancer (CRC) – A Growing Threat to Young Adults

- In the US, colorectal cancer ranks second in cancer-related deaths overall and is the leading cause in men younger than 50 (1)
  - Over 150,000 patients diagnosed annually, with ~60% anticipated to have Stage 4 disease at diagnosis (1)
  - 52,550 CRC deaths projected in 2023, with nearly 4,000 in adults younger than 50 (1)
- Majority of patients diagnosed with metastatic disease (~60%) do not have surgery (2)
  - Primary treatment approach includes chemotherapy and radiation for most patients
  - Only 2-4% of Stage 4 patients classified as MSI-H are eligible for treatment with immunotherapy, and a subset of these quickly develop immune resistance (3)

MSI-H: Microsatellite Instability-High

1. Siegel et al, Colorectal Cancer Statistics, (2023).
2. Cerner Enviza, CancerMPact®Treatment Architecture (2022).
3. Weng et al, Journal of Hematology & Oncology, (2022).

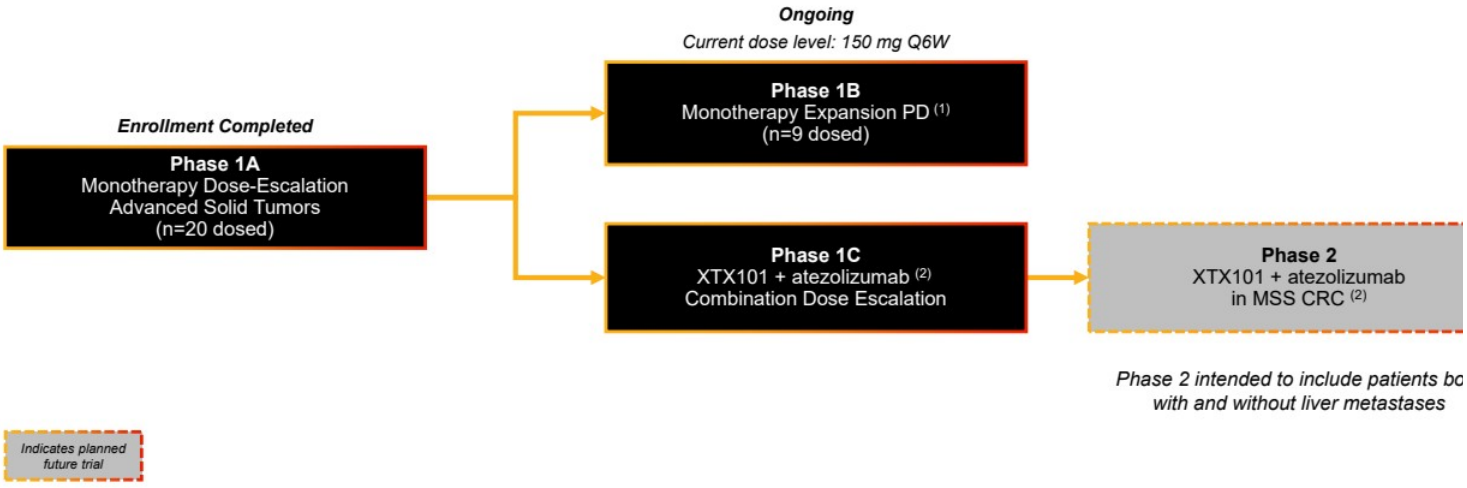
Vast Majority of Metastatic Colorectal Cancer is MSS CRC with No Approved IO Treatment Options



- MSS CRC represents the vast majority of metastatic CRC (95%) (2)
  - Characterized by tumors with weak immunogenicity and limited immune cells (making it a “cold tumor”)
  - Checkpoint inhibitors ineffective in MSS CRC to date
  - Opportunity exists for IO combinations that together can help mount an adequate immune response
- Liver is most common site of metastases in CRC
  - Over 80% of patients with liver metastases from CR have unresectable lesions (4)
  - Long-term survival remains rare, with these patients often excluded from clinical trials, particularly for IO

1. Siegel et al, Colorectal Cancer Statistics, (2023).
2. Ooki et al, Journal of Anus Rectum Colon, (2021).
3. Valderrama-Trevino et al, EJOHG, (2017).
4. Sheth et al, Clinics in Colon and Rectal Surgery (2005).
5. Cerner Enviza, (2023).

Clinical Development Plan for XTX101



Plan to activate clinical trial sites for combination dose escalation to evaluate XTX101 in combination with atezolizumab in Q4 2023

Data cutoff date: August 3, 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.
2. Clinical trial research collaboration with Roche to evaluate XTX101 in combination with atezolizumab (Tecentriq®).

XTX101 Clinical Trial Progress and Anticipated Milestones

- RP2D defined at 150 mg Q6W with differentiated safety profile
- Preliminary PK analyses demonstrated dose-proportional drug exposure and limited active (unmasked) molecule in the periphery
- 150 mg dose provided a 2-fold higher C_{max} (adjusted for 10x higher potency) compared to ipilimumab 10 mg/kg
- Monotherapy confirmed partial response in a patient with PD-L1 negative NSCLC reported at 150 mg Q6W with resolution of hepatic metastases [1]
  - Tumor-selective activation for XTX101 demonstrated by minimal peripheral PD in this patient

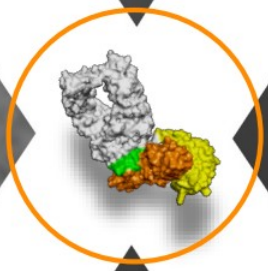
Q4
2023

- Anticipate activating clinical trial sites for Phase 1 dose escalation evaluating XTX101 in combination with atezolizumab in Q4 2023

Data cutoff date: August 3, 2023.
1. Tumor response was assessed by RECIST version 1.1.

XTX202

Tumor-Activated, Beta-Gamma IL-2



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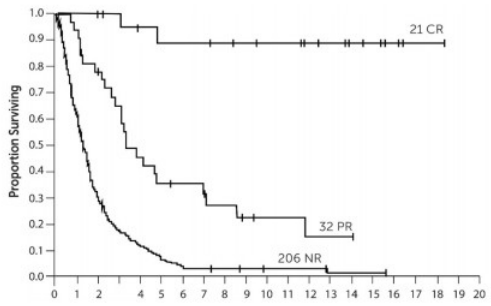
High-Dose IL-2 has Curative Potential but Limited by High Systemic Toxic

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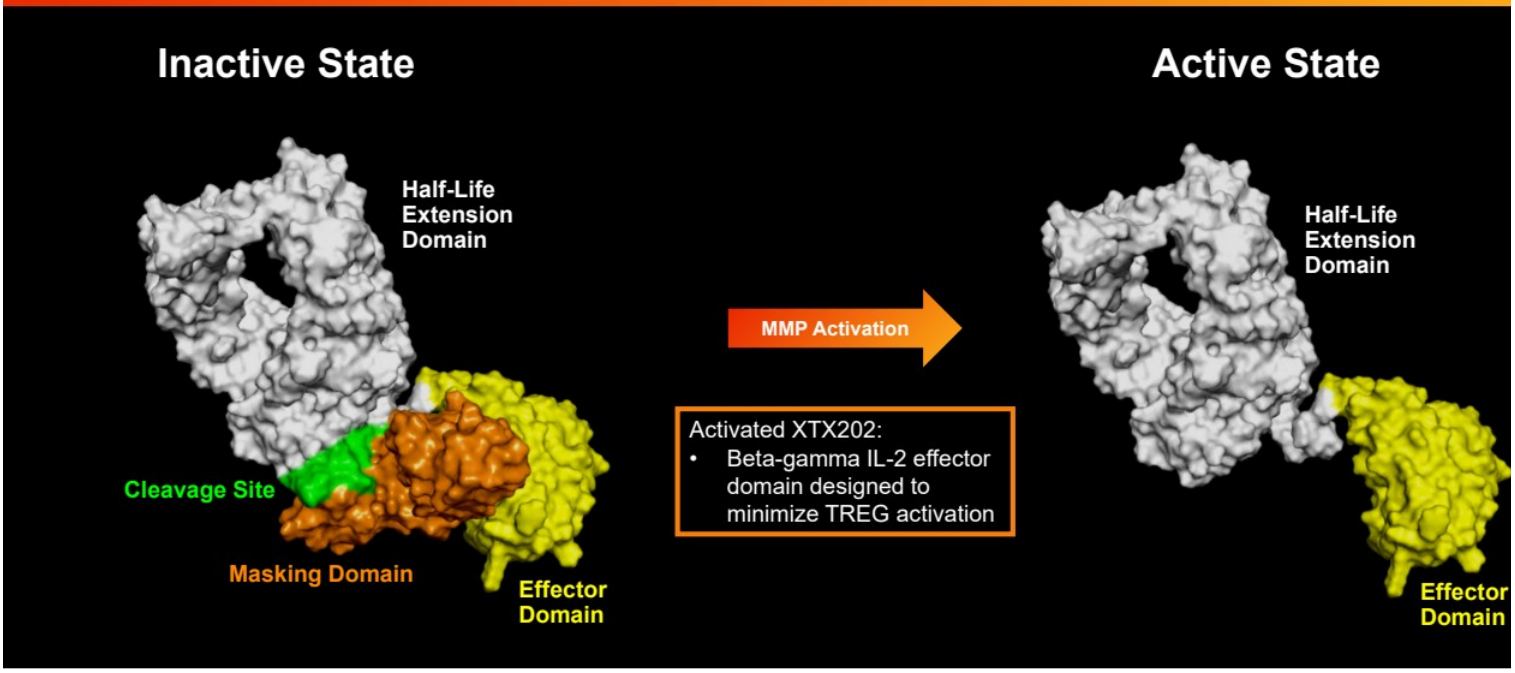
Data represents all patients that received high dose IL-2 (no control group).
NR: no response; PFS: progression free survival.

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



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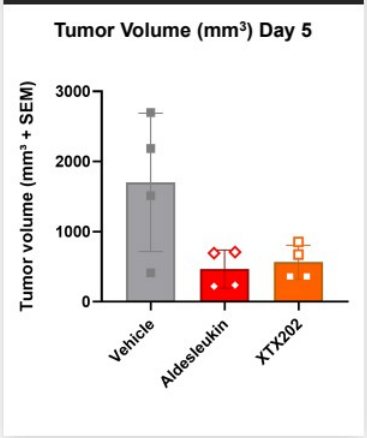
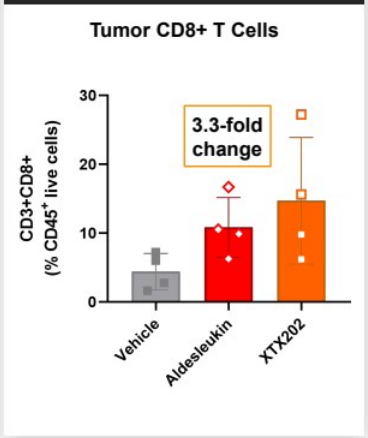
XTX202 Demonstrated TIL Expansion (CD8+ Effector T Cells and NK) and Anti-Tumor Activity Without Significant TREG Stimulation *In Vivo*

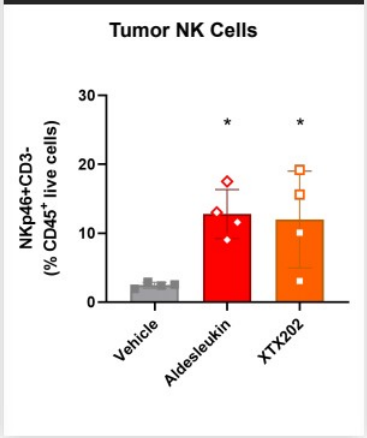
XTX202 and aldesleukin featured comparable anti-tumor activity



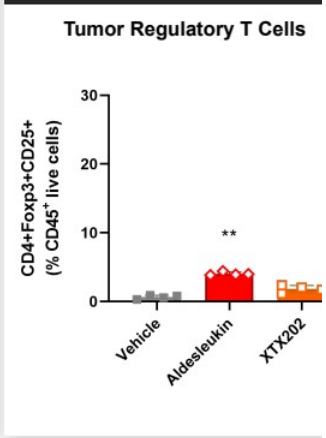
XTX202 and aldesleukin treatment increased CD8+ T cells in tumors



XTX202 and aldesleukin treatment increased NK cells in tumors



Aldesleukin increased TREGs in tumors while XTX202 had minimal effe



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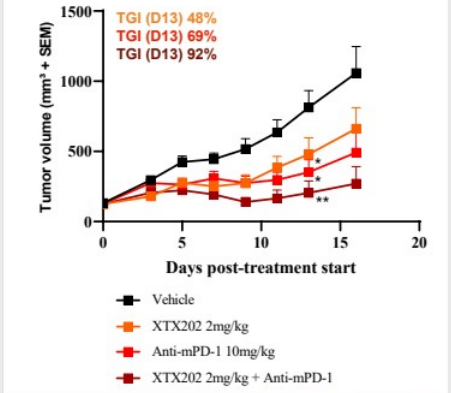
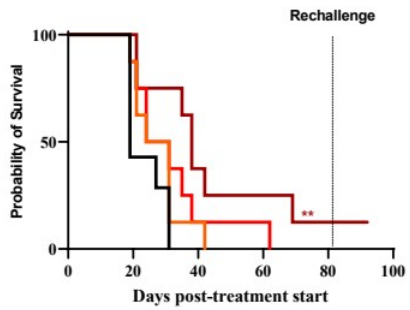
MC38 tumor-bearing mice were treated with either vehicle, aldesleukin (3 mg/kg BID) or XTX202 10mg/kg QDx5. Tumor volume was recorded at day 5 post first dose and tumor infiltrating immune cells were phenotyped and enumerated using flow cytometry. One-way ANOVA was performed to determine statistical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

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

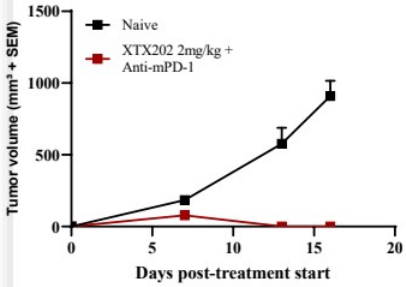
Enhanced *in vivo* activity observed with combination of XTX202 and anti-PD-1 mAb



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



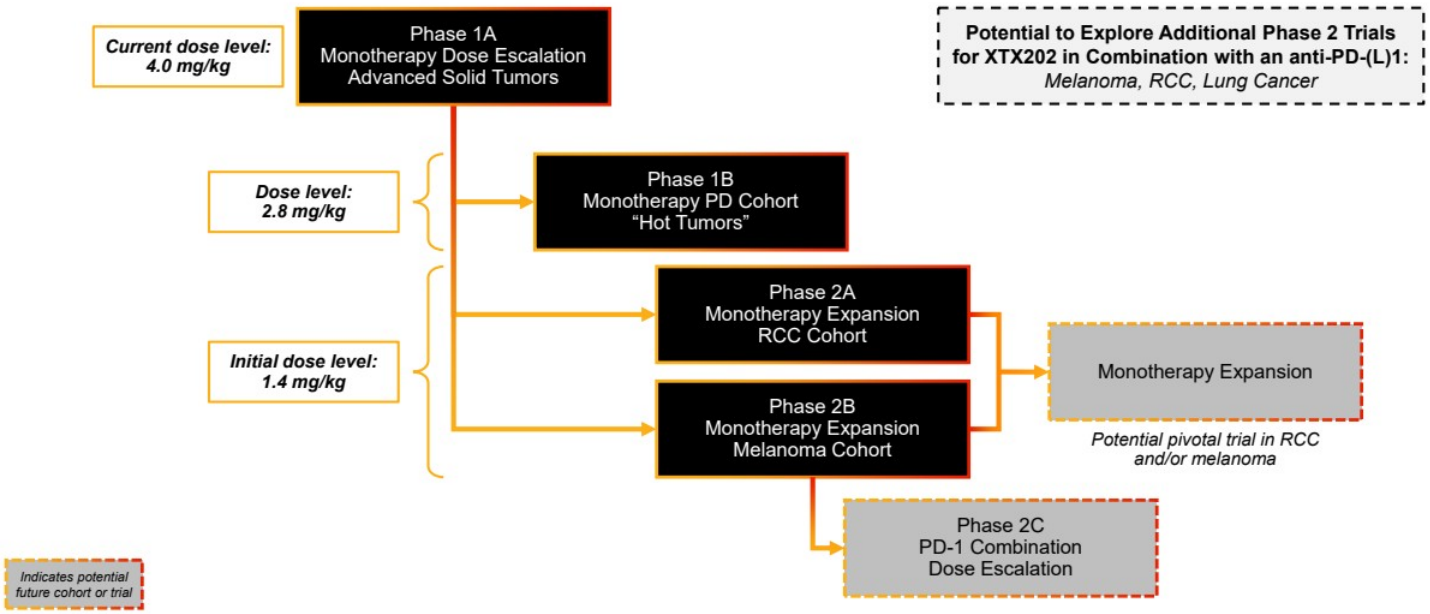
Complete responders rejected tumors upon rechallenge, indicati evidence of memory response



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.
mAb: monoclonal antibody; TGI: tumor growth inhibition.

Clinical Development Plan for XTX202



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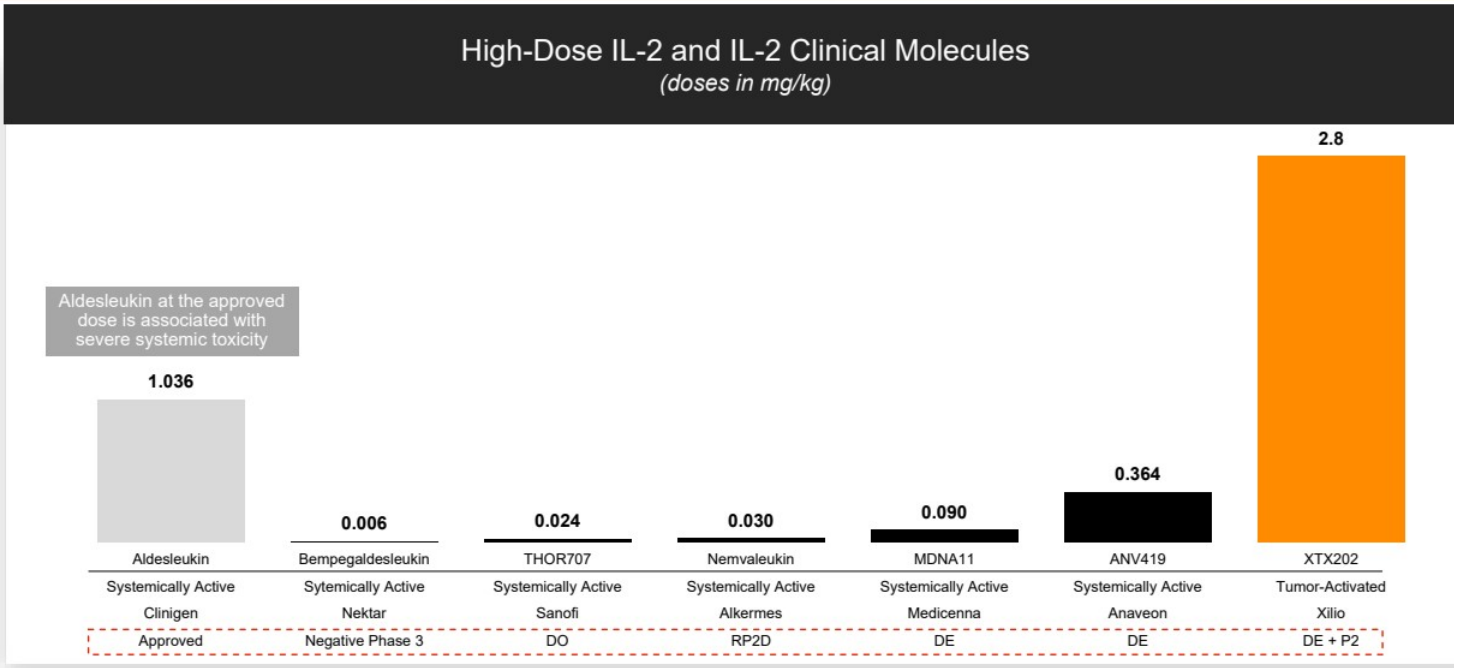
As of August 14, 2023

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

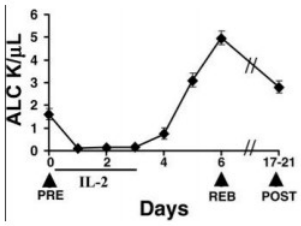


Aldesleukin dose if full indicated administration completed (0.037mg/kg*14 over 5 days + 9 days rest + 0.037 mg/kg*14 over 5 days). In preclinical studies, XTX202 at a total dose of 20 mg/kg had similar activity for tumor growth inhibition and PD to aldesleukin at a total dose of 24 mg/kg.
DO: dose optimization;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

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

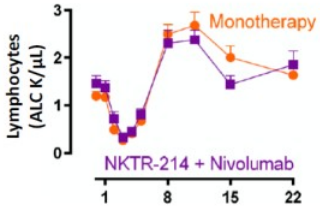
Aldesleukin [1]
hr IL-2
First Generation

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



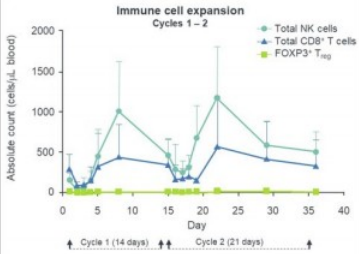
Bempegaldesleukin [2]
NKTR-214
Second Generation

Dose: 0.006 mg/kg



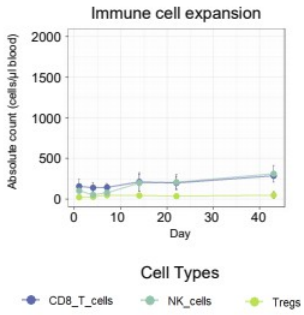
Nemvaleukin Alfa [3]
ALKS-4230
Second Generation

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 ben

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.

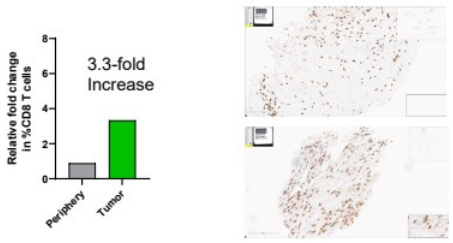
Peripheral lymphocytosis is a PD marker of IL-2 biology.
hr: human recombinant; ALC: absolute lymphocyte count

Tumor-Selective Increases in CD8+ Effector T Cells Observed with XTX202 in Patients

- 3.4 average increase in CD8 cell count observed in tumors treated with XTX202 from baseline
- Clinical data consistent with 3.3-fold change observed in preclinical data

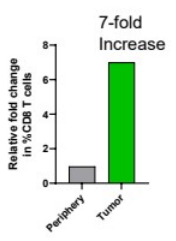
Patient #1: Melanoma patient treated with XTX202 at 0.38mg/kg Q2W (dose level 2)

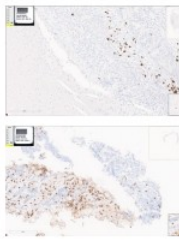
Relative Fold-Change in CD8+ T cells Compared to Pre-Treatment



Patient #2: RCC patient treated with XTX20 0.53mg/kg Q2W (dose level 3)

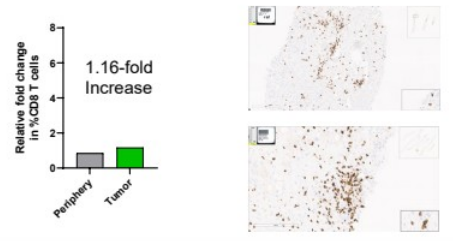
Relative Fold-Change in CD8+ T cells Compared to Pre-Treatm





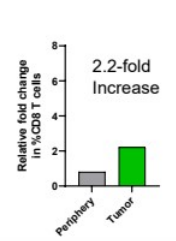
Patient #3: RCC patient treated with XTX202 at 1mg/kg Q2W (dose level 4)

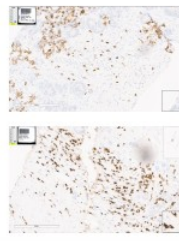
Relative Fold-Change in CD8+ T cells Compared to Pre-Treatment



Patient #4: Rectal patient treated with XTX2 2.8mg/kg Q2W (dose level 6)

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





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

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 2.8 mg / kg (dose level six)
  - Currently dosing patients at 4.0 mg/kg (dose level seven)
- Tumor-selective increases in CD8+ effector T cells observed in four patients following XTX202 treatm
- Patients received up to 17 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
  - Based on continued Phase 1 dose-escalation, plan to explore opportunities to evaluate XTX202 at an additional, higher dose level in Phase 2

- Plan to report preliminary anti-tumor activity, PK/PD and safety data in at least 20 evaluable patients treated at dose levels at or above 1 mg/kg in the Phase 1/2 trial in early November 2023

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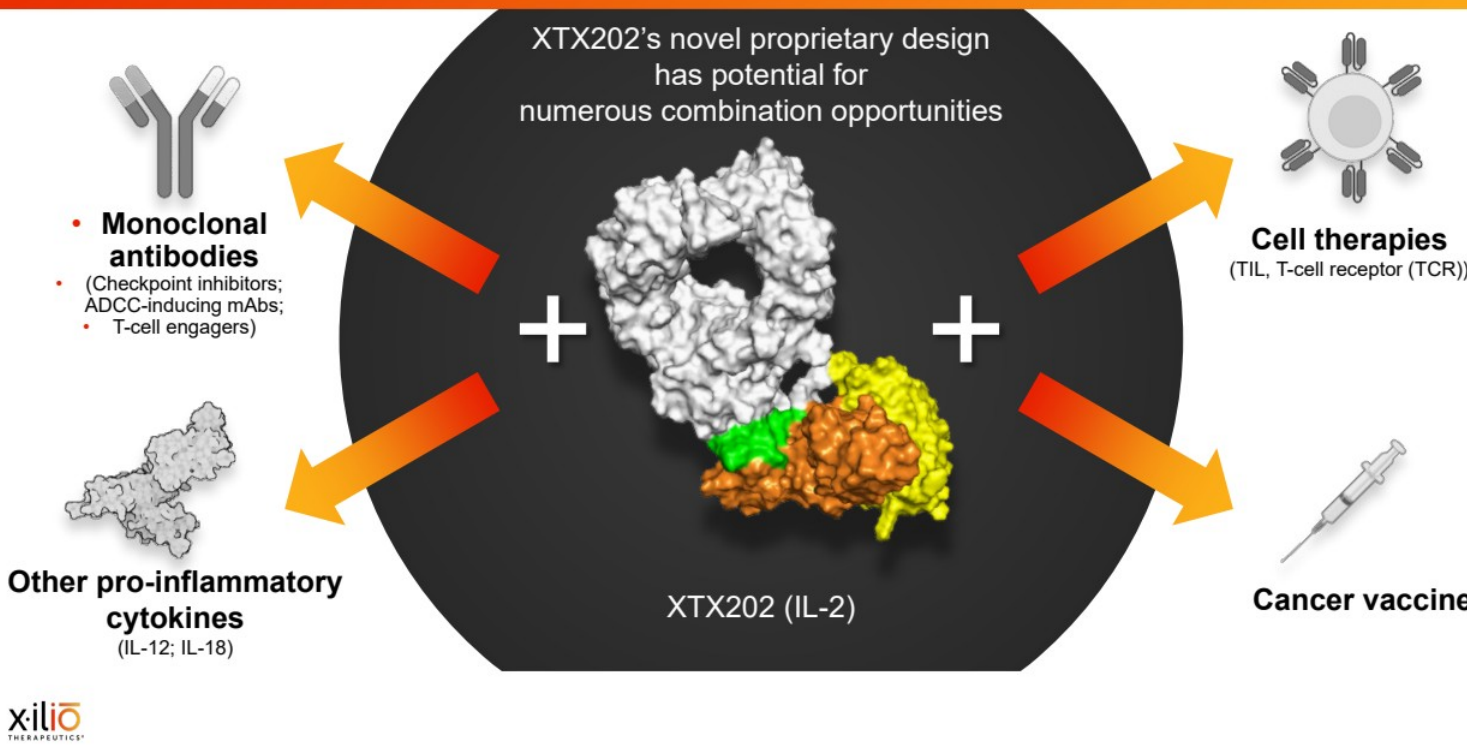
Multiple Combination Opportunities Enabled by XTX202 Properties: Tumor-Activated, Well-Tolerated Preclinically and Clinically-Validated Target



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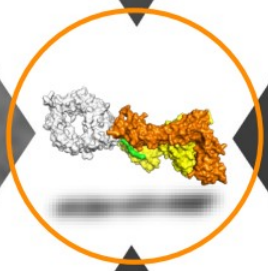
XTX301

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

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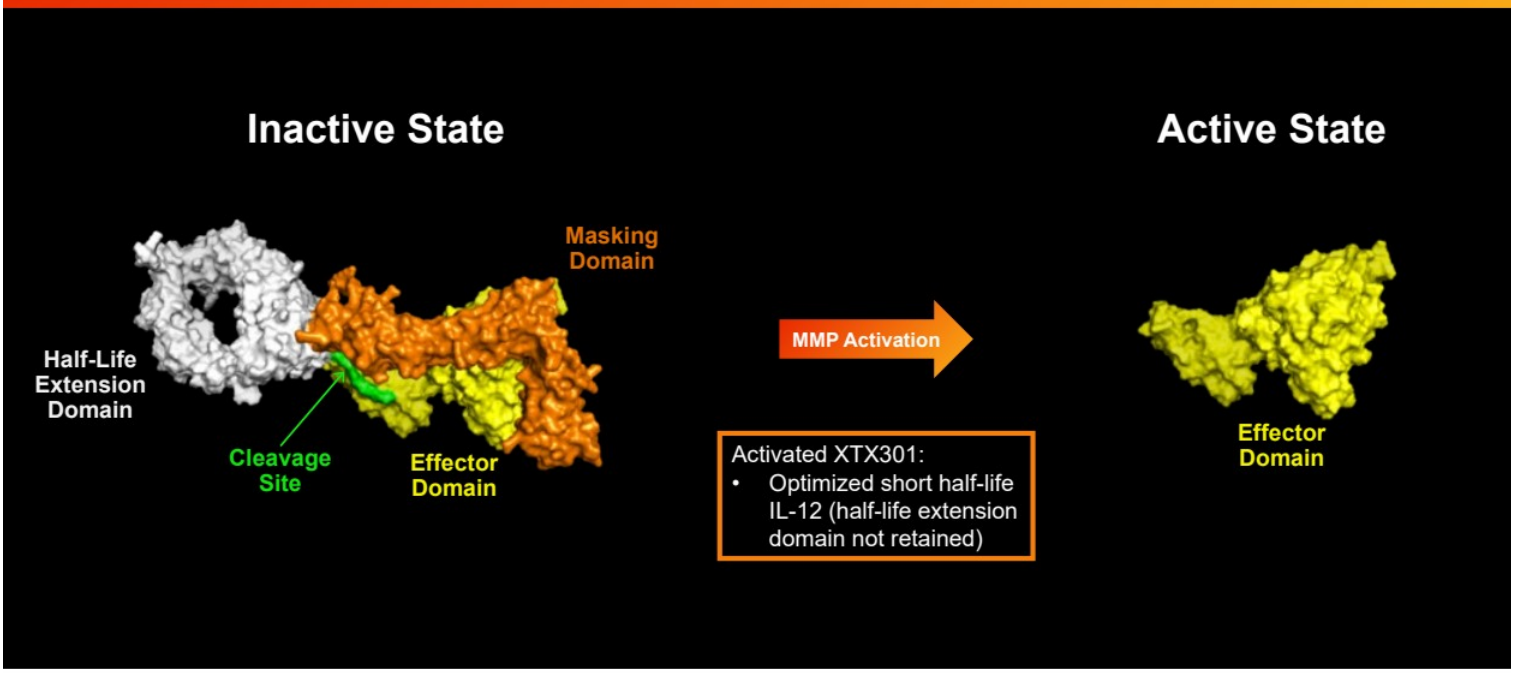
Adapted from "Cold vs Hot Tumors", by BioRender.com, 2022. Retrieved from https://app.biorender.com/biorender-templates Barraondo et al., Clin. Cancer Res., 2018. Nguyen et al., Front. Immunol., 2020.
MDSC: myeloid-derived suppressor cells

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



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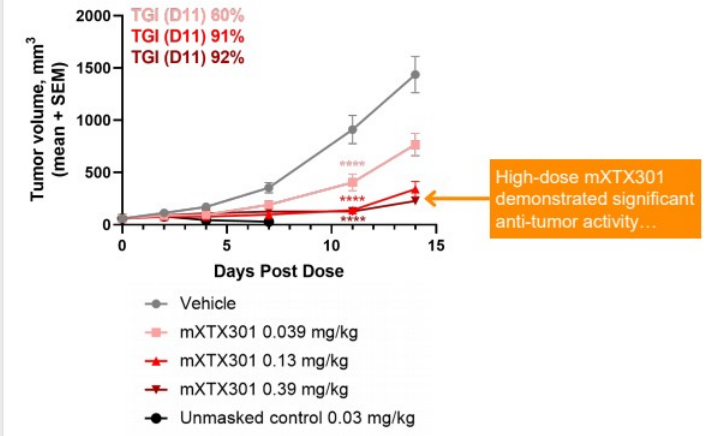
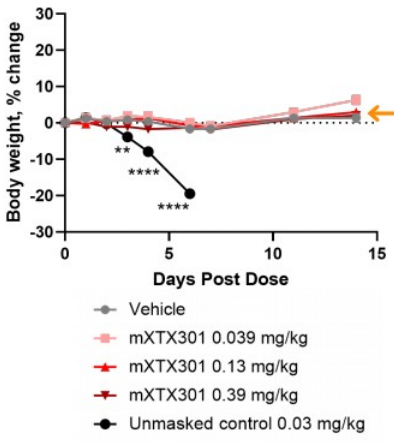
mXTX301 Demonstrated Dose-Dependent Anti-Tumor Activity Without Body Weight Loss *In Vivo*

Tumor Growth



High-dose mXTX301 demonstrated significant anti-tumor activity…

Body Weight



…without causing body weight loss

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

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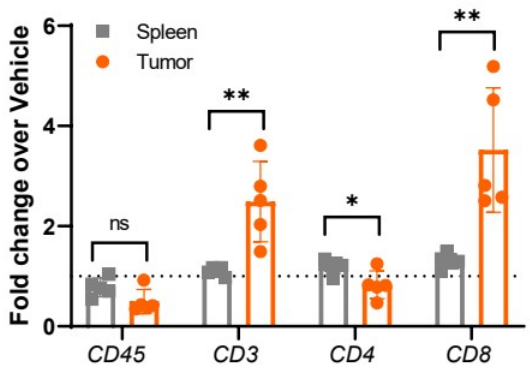
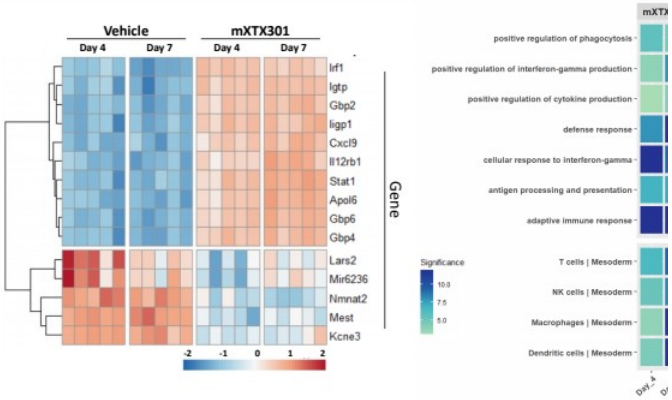
mXTX301 is a murine surrogate for XTX301.
MC38 model: s.c. 0.5x106 cells; single IV dose of mXTX301 and mXTX302 on Day 0. Tumor growth data shown as mean±SEM. Tumor volume data was assessed by a two-way ANOVA followed by Bonferroni post hoc test on Day 11 compared to vehicle treated animals. ****p<0.0001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



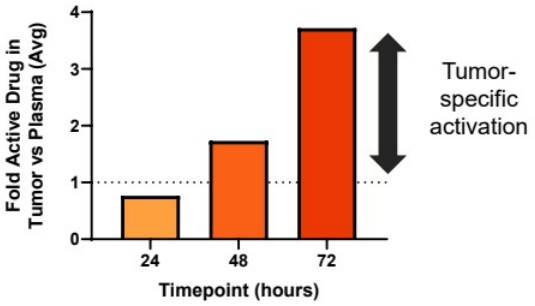
mXTX301 induced pro-inflammatory gene programs and broadly remodeled TME toward inflamed state



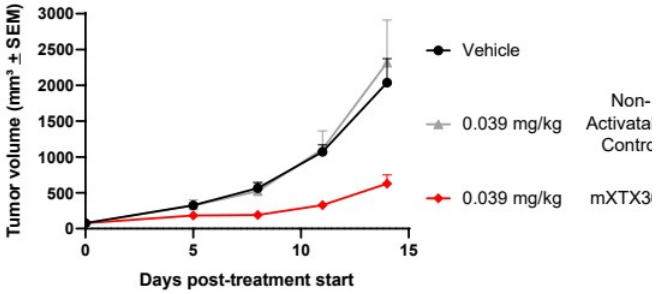
mXTX301 is a murine surrogate for XTX301.
Left panel: MC38 tumor bearing mice (n= 5 per group) were treated with a single IV dose of mXTX301 at 0.39 mg/kg or vehicle and immune cells were phenotyped using FACS. The number of cells for each immune phenotype was calculated per g of tissue and the ratio 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 treatment resulted in cleavage-dependent enhancement in activity vs non-activatable control



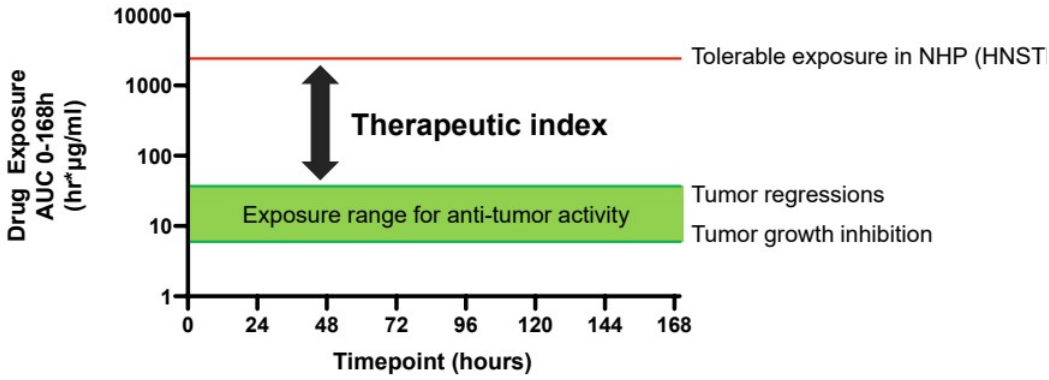
mXTX301 treatment resulted in cleavage-dependent enhancement in activity vs non-activatable control



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	

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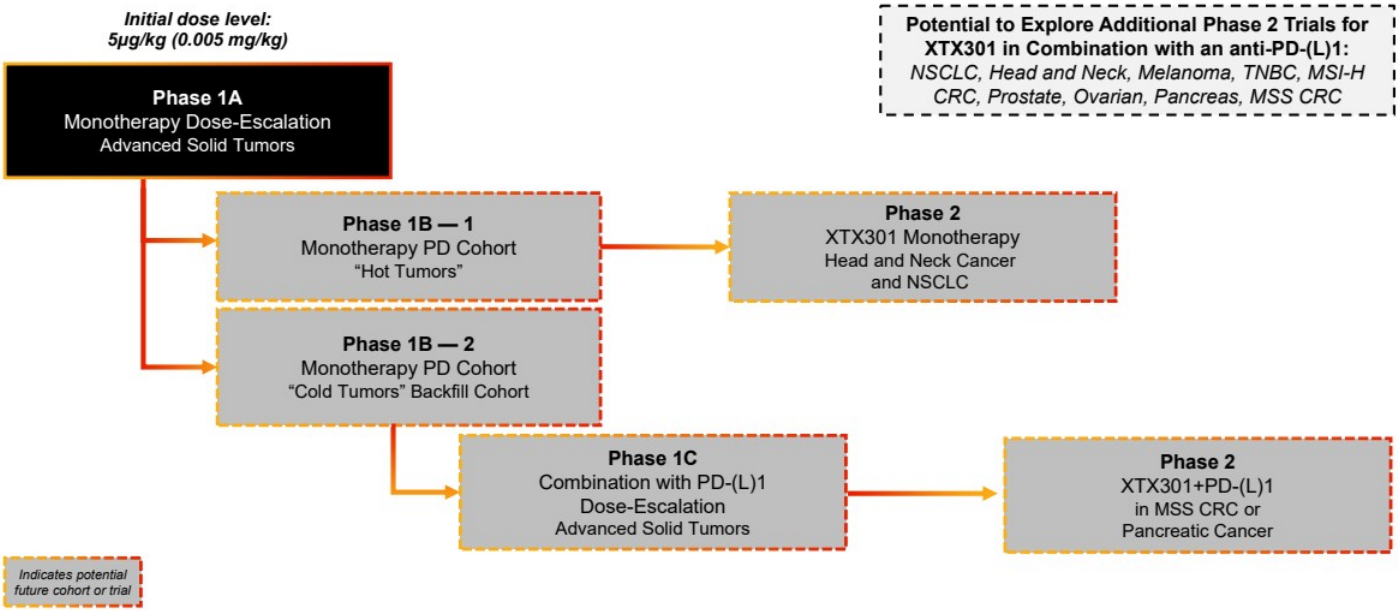
HNSTD: highest non-severely toxic dose; Q1W: once every week.

Clinical Development Plans for XTX301



µg: micrograms.

XTX301 Progress and Anticipated 2023 Clinical Milestones

- Demonstrated dose-dependent anti-tumor activity without significant body weight loss *in viv*
- 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 3rd dose level 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 Complete Phase 1B Dosing	✓	✓	✓	✓	✓
XTX202 (IL-2) Phase 1B and Phase 2 Dosing	✓	✓	✓	✓	✓ Anticipat Early Novemb
XTX301 (IL-12) Phase 1A Dosing	✓	✓	✓ Anticipated Q4 2023	✓	✓
Multifunctional (PD-1/IL-2) Research Program	✓	✓	✓	✓	✓

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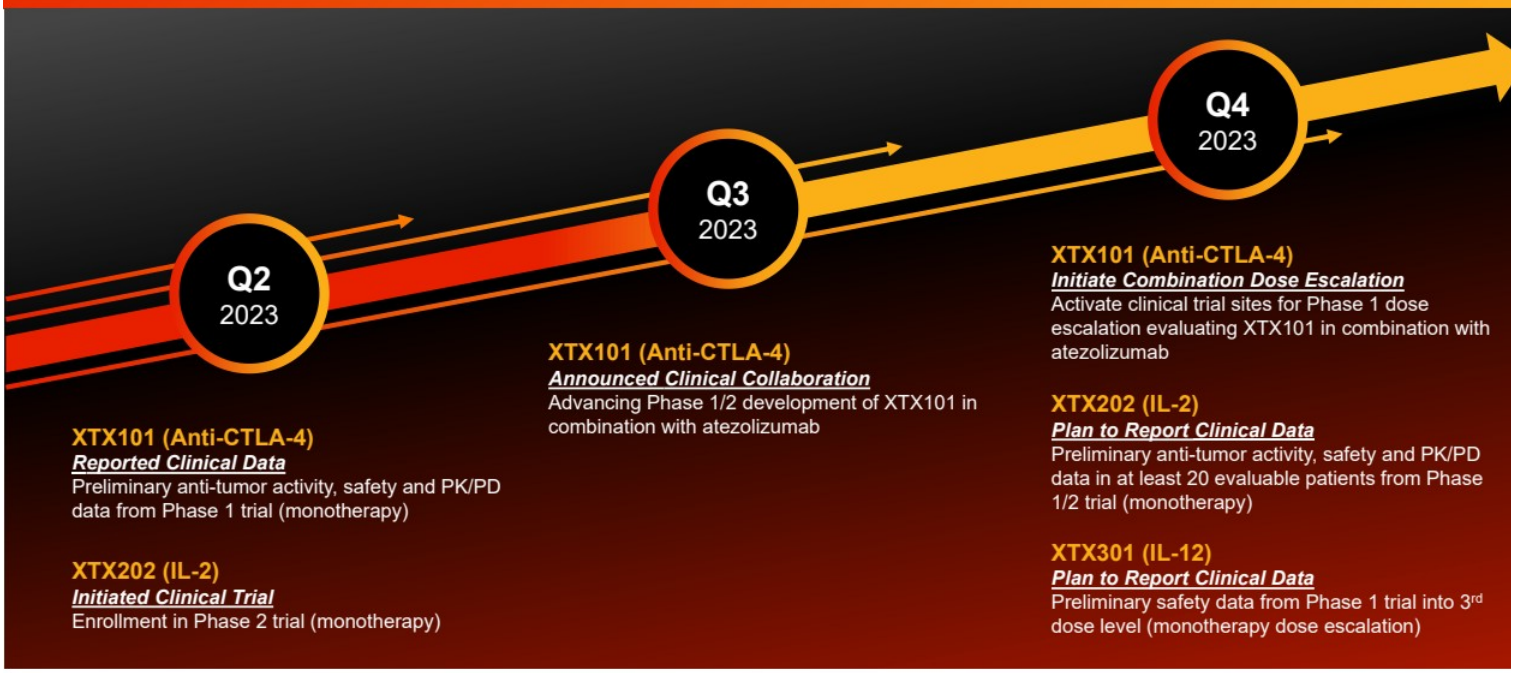
Xilio is Positioned for Multiple Anticipated Clinical Milestones



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Anticipate Existing Cash and Cash Equivalents Sufficient to Fund Operating Expenses and Capital Expenditure Requirements Into the End of Q2 2024

Balance Sheet

	June 30, 2023*	December 31, 2022
Cash and Cash Equivalents	$75.4M	$120.4

Statement of Operations

	Three Months Ended June 30	
	2023*	2022*
Research & Development Expenses	$13.2M	$16.2
General & Administrative Expenses	$6.9M	$8.3
Loss from Operations	$(20.1M)	$(24.6

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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
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