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 12, 2022**

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: **(617) 430-4680**

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 May 12, 2022, Xilio Therapeutics, Inc. announced its financial results for the quarter ended March 31, 2022 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. 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 Exhibit 99.1 and Exhibit 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 exhibits relating to Item 2.02 and Item 7.01 of this 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 May 12, 2022
99.2	Corporate investor presentation of Xilio Therapeutics, Inc. as of May 12, 2022
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 12, 2022

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

Exhibit 99.1

Xilio Therapeutics Reports Pipeline and Business Highlights and First Quarter 2022 Financial Results

Clinical programs for XTX202, a tumor-selective IL-2, and XTX101, a tumor-selective anti-CTLA-4, continue to advance with preliminary data anticipated in 2022

On track with plans to submit IND for XTX301, a tumor-selective IL-12, in second half of 2022

Strong financial position with $177 million in cash and cash equivalents as of March 31, 2022, with cash runway anticipated into first half of 2024

WALTHAM, Mass., May 12, 2022 – Xilio Therapeutics, Inc. (Nasdaq: XLO), a biotechnology company developing tumor-selective immuno-oncology therapies for people living with cancer, today announced pipeline and business highlights and reported financial results for the first quarter ended March 31, 2022.

"Leveraging our geographically precise solutions (GPS) platform, we are developing a pipeline of tumor-selective immunotherapies that have the potential to achieve meaningful anti-tumor activity while minimizing serious, systemic effects," said René Russo, Pharm.D., president and chief executive officer of Xilio. "We continue to progress enrollment in our Phase 1 clinical programs, XTX101 and XTX202, with planned preliminary data readouts later this year, and we remain on track with our plans to submit an IND application for XTX301 in the second half of 2022. With our strong financial position and an outstanding team in place, we believe we are well-positioned to advance our pipeline of tumor-selective immuno-oncology programs with the goal of transforming the lives of people living with cancer."

Pipeline and Business Progress

Cytokine Programs

- Enrollment is ongoing in the Phase 1 clinical trial evaluating XTX202 for the treatment of patients with solid tumors, with preliminary data anticipated to be reported in the second half of 2022. XTX202 is a tumor-selective interleukin-2 (IL-2) designed to localize activity in the tumor microenvironment, with the goal of overcoming the known tolerability challenges of existing IL-2 therapies while achieving enhanced anti-tumor activity as monotherapy and in combination with standard of care agents.

- Preclinical data from the XTX301 program was presented at the New York Academy of Sciences Frontiers in Cancer Immunotherapy 2022 conference on May 10, 2022. XTX301 demonstrated tumor-selective activation in patient-derived tumor explants, and a murine surrogate of XTX301 (mXTX301) induced significant tumor growth inhibition in a mouse model and improved tolerability compared to a non-tumor-selective version of mXTX301. View the poster online here.

- Xilio continues to anticipate submitting an investigational new drug application (IND) for XTX301, a tumor-selective interleukin-12 (IL-12), in the second half of 2022 for evaluation in patients with solid tumors.

Upcoming Presentations

- A trials-in-progress poster outlining details of the ongoing Phase 1/2 clinical trial for XTX202 will be presented at the American Society of Clinical Oncology (ASCO) 2022 Annual Meeting:

  Presentation title: A first-in-human, multicenter, phase 1/2, open-label study of XTX202, a masked and tumor-selective recombinant human interleukin-2 (IL-2) protein, in patients with advanced solid tumors

  Session date and time: Sunday, June 5, 2022, 8:00-11:00 AM CDT

  Abstract number: TPS2697

Checkpoint Inhibitor Program

- Enrollment is ongoing in the Phase 1 clinical trial evaluating XTX101, a tumor-selective anti-CTLA-4 monoclonal antibody, as a monotherapy and in combination with pembrolizumab, an anti-PD-1, for the treatment of patients with advanced solid tumors.

- Preliminary data for the Phase 1 clinical trial for XTX101 is anticipated to be reported from the monotherapy cohort in the middle of 2022 and from the combination cohort in the second half of 2022.

First Quarter 2022 Financial Results

- **Cash Position:** Cash and cash equivalents were $177.0 million as of March 31, 2022, as compared to $198.1 million as of December 31, 2021. The decrease was primarily driven by cash used in operations for the three months ended March 31, 2022.

- **Research & Development (R&D) Expenses:** R&D expenses were $14.9 million for the first quarter of 2022, compared to $11.6 million for the first quarter of 2021. The increase was primarily driven by increased costs associated with XTX301 and other preclinical programs, as well as higher personnel-related costs due to increased headcount.

- **General & Administrative (G&A) Expenses:** G&A expenses were $6.3 million for the first quarter of 2022, compared to $4.9 million for the first quarter of 2021. The increase was primarily driven by higher personnel-related costs due to increased headcount and other costs related to operating as a publicly traded company.

- **Net Loss:** Net loss was $21.4 million for the first quarter of 2022, compared to $16.7 million for the first quarter of 2021.

Financial Guidance

As a result of prioritization within the company's preclinical portfolio, Xilio now anticipates that its existing cash and cash equivalents will be sufficient to fund its operating expenses and capital expenditure requirements into the first half of 2024.

About Xilio Therapeutics

Xilio Therapeutics is a clinical-stage biotechnology company focused on harnessing the immune system to achieve deep and durable clinical responses to improve the lives of patients with cancer. The company is using its proprietary geographically precise solutions (GPS) platform to rapidly engineer novel molecules, including cytokines and other biologics, that are designed to optimize their therapeutic index. These molecules are designed to localize activity within the tumor microenvironment without systemic effect, resulting in the potential to achieve enhanced anti-tumor activity. Xilio is building a pipeline of wholly owned, tumor-selective, GPS-enabled cytokine and checkpoint inhibitor product candidates, including its clinical-stage programs, XTX101, a tumor-selective anti-CTLA-4 monoclonal antibody, and XTX202, a tumor-selective IL-2, as well as its earlier pipeline, including XTX301, a tumor-selective IL-12. For more information, please visit 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 and timing related to reporting preliminary Phase 1 clinical data for XTX101 and XTX202 and the submission of an IND for XTX301; the potential benefits of any of Xilio's current or future product candidates in treating patients; Xilio's ability to fund its operating expenses and capital expenditure requirements with its existing cash and cash equivalents; and Xilio's strategy, goals and anticipated financial performance, milestones, business plans and focus. The words "aim," "may," "will," "could," "would," "should," "expect," "plan," "anticipate," "intend," "believe," "estimate," "predict," "project," "potential," "continue," "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; Xilio's ability to successfully demonstrate the safety and efficacy of its product candidates and gain approval of its product candidates on a timely basis, if at all; results from preclinical studies or clinical trials for Xilio's product candidates, which may not support further development of such product candidates; actions of regulatory agencies, which may affect the initiation, timing and progress of current or future clinical trials; Xilio's ability to obtain, maintain and enforce patent and other intellectual property protection for current or future product candidates; Xilio's ability to obtain and maintain sufficient cash resources to fund current or future operating expenses and capital expenditure requirements; the impact of international trade policies on Xilio's business, including U.S. and China trade policies; and the impact of the COVID-19 pandemic on Xilio's business, operations, strategy, goals and anticipated milestones. 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 Annual Report on Form 10-K 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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Chief Financial Officer
investors@xiliotx.com

For Media Inquiries:
Julissa Viana
Vice President, Corporate Communications
media@xiliotx.com

XILIO THERAPEUTICS, INC.

Condensed Consolidated Balance Sheets
(In thousands)
(Unaudited)

	March 31, 2022	December 31, 2021
Assets		
Cash and cash equivalents	$ 176,959	$ 198,053
Other assets	19,393	20,007
Total assets	$ 196,352	$ 218,060
Liabilities and Stockholders' Equity		
Liabilities	$ 30,231	$ 32,631
Stockholders' equity	166,121	185,429
Total liabilities and stockholders' equity	$ 196,352	$ 218,060

XILIO THERAPEUTICS, INC.

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

	Three Months Ended March 31,	
	2022	**2021**
Operating expenses [1]		
Research and development	$ 14,920	$ 11,621
General and administrative	6,304	4,899
Total operating expenses	21,224	16,520
Loss from operations	(21,224)	(16,520)
Other expense, net		
Other expense, net	(129)	(147)
Total other expense, net	(129)	(147)
Net loss and comprehensive loss	$ (21,353)	$ (16,667)
Net loss per share, basic and diluted	$ (0.78)	$ (23.53)
Weighted average common shares outstanding, basic and diluted	27,367,377	708,264

[1] Operating expenses include the following amounts of non-cash equity-based compensation expense:

	Three Months Ended March 31,	
	2022	**2021**
Research and development expense	$ 596	$ 135
General and administrative expense	1,433	659
Total equity-based compensation expense	$ 2,029	$ 794

XILIO THERAPEUTICS (NASDAQ: XLO)

HARNESSING THE IMMUNE SYSTEM TO IMPROVE THE LIVES OF PEOPLE WITH CANCER

MAY 12, 2022

© 2022 Xilio Therapeutics, Inc.

Forward-looking statements

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Expert leadership team across oncology drug discovery, development and commercialization

Collectively contributed to > 40 INDs and > 30 NDAs, sNDAs or BLAs, including pembrolizumab, dostarlimab, niraparib, docetaxel and trastuzumab

René Russo, Pharm. D.
CHIEF EXECUTIVE OFFICER, PRESIDENT AND BOARD MEMBER

- 20+ years leading biotech companies, R&D and commercialization organizations
- Co-founder and chairman of Adagio Therapeutics; previously President and CEO of Arsanis; VP global medical affairs at Cubist Pharmaceuticals; R&D at BMS

Martin Huber, M.D.
PRESIDENT OF R&D AND CHIEF MEDICAL OFFICER

- 25+ years of academic, biotech and pharma drug development, including multiple cancer immunotherapy programs
- Key medical roles at Tesaro, Merck, Schering-Plough, Hoffmann-La Roche, Rhone-Poulenc Rorer, MD Anderson Cancer Center

Salvatore Giovine
CHIEF FINANCIAL OFFICER

- ~20 years healthcare finance leadership experience across operations, capital strategies, investments and business development
- ~15 years at J&J/Janssen Biotech, Inc.

Li Malmberg, Ph.D.
CHIEF TECHNOLOGY & MANUFACTURING OFFICER

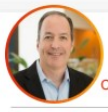
- ~25 years of scientific and executive leadership across CMC strategies, intellectual property and collaborations
- Established and led scientific and engineering teams at Magenta, Celgene and AbbVie

Uli Bialucha, Ph.D.
SENIOR VICE PRESIDENT, RESEARCH

- ~15 years of academic and industry experience including discovery research leadership roles in pharma and biotech
- Successful track record progressing oncology/immuno-oncology projects from discovery through early clinical development

Chris Frankenfield
GENERAL COUNSEL

- ~15 years leading biotechnology companies through R&D and commercialization, including Blueprint Medicines
- Executed numerous public and private financings and strategic transactions for life sciences companies



Timothy D. Hunt
CHIEF CULTURE AND CORPORATE AFFAIRS OFFICER

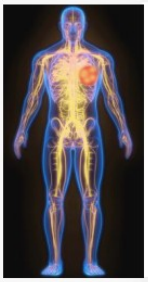
- 20+ years biotech leadership in human resources, market development, communication, policy and government affairs
- Key senior roles at Editas Medicine, Cubist and Biogen

Building a robust pipeline of tumor-selective immunotherapy programs

Tumor-Selective Programs	Mechanism of Action	Discovery	IND-Enabling	Phase 1	Phase 2	Phase 3	Anticipated Upcoming Milestones
XTX101 [1]	Anti-CTLA-4						Preliminary Phase 1 monotherapy data mid-2022
XTX202 [2]	IL-2						Preliminary Phase 1 data 2H 2022
XTX301	IL-12						IND submission 2H 2022

Continuing to leverage GPS platform with the goal of expanding pipeline and developing additional tumor-selective immunotherapies, including product candidates with a range of tumor targeting approaches

Today's I-O agents offer curative potential but are limited due to systemic toxicity



Compelling Efficacy

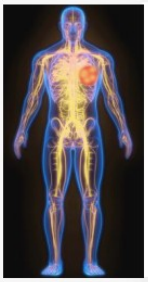
- Improved survival achieved with high dose ipilimumab (anti-CTLA-4) at 10 mg/kg
- 10-year durable CRs achieved in melanoma with high dose IL-2 as a monotherapy
- Tumor shrinkage observed in patients with IL-12

Dose-limiting Toxicity

- Multi-organ AEs and peripheral side effects of potent I-O therapy can be lethal
- Often results in dose reductions, interruptions or discontinuations for many patients
- Many I-O agents remain completely untapped (IL-12)

AEs: Adverse Events; CR: Complete response; I-O: Immuno-oncology

Today's I-O agents offer curative potential but are limited due to systemic toxicity



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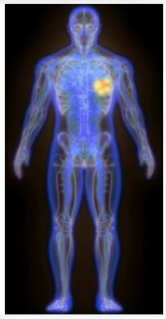
- Many I-O agents remain completely untapped (IL-12)

Geographically precise solutions (GPS) are designed to solve this problem by localizing the desired I-O effect in the tumor

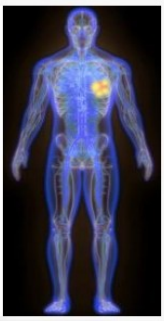
Xilio's GPS Platform:

- ✓ Engineer highly potent I-O molecules
- ✓ Designed to be systemically inactive
- ✓ Activated locally in the tumor microenvironment



GPS-enabled therapies are designed to unlock the full potential of immuno-oncology

Geographically precise solutions (GPS) are designed to solve this problem by localizing the desired I-O effect in the tumor

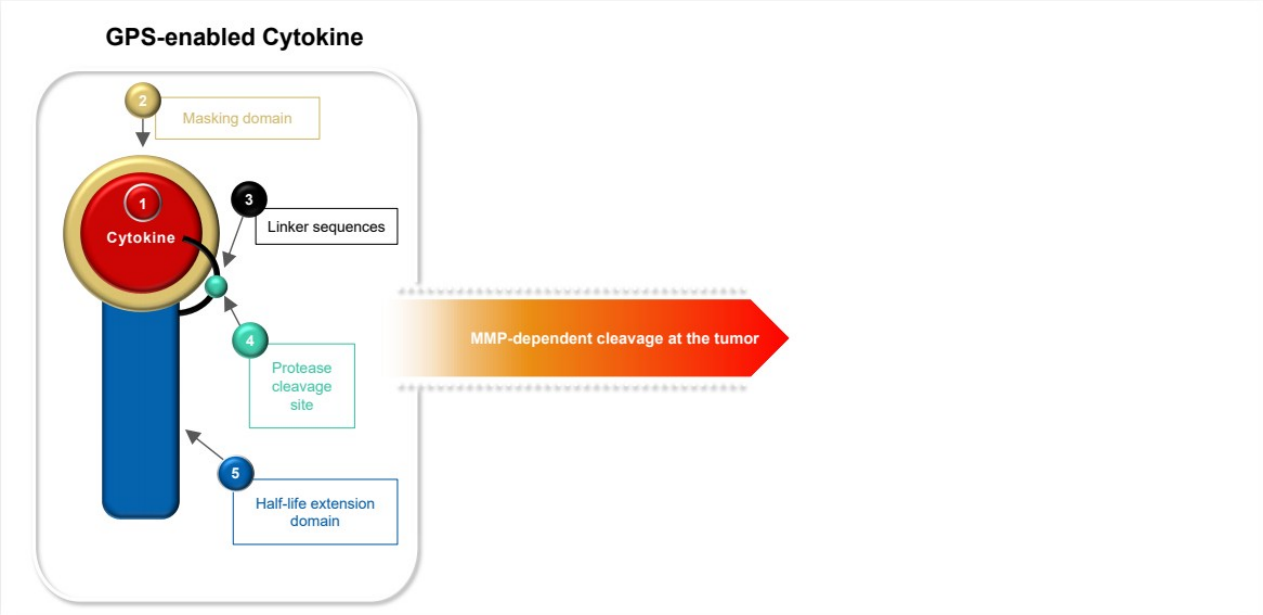


Xilio's GPS Platform:

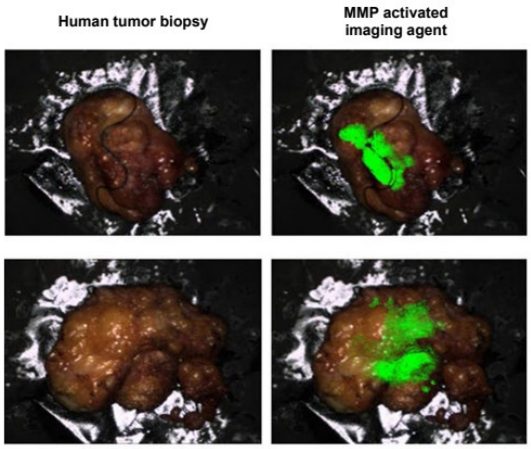
- ✓ Engineer highly potent I-O molecules
- ✓ Designed to be systemically inactive
- ✓ Activated locally in the tumor microenvironment

	1st generation cytokines (aldesleukin)	2nd generation systemically active engineered cytokines	Opportunity for GPS-enabled cytokines
Efficacy	✓	—	✓
Tolerability	—	✓	✓
Therapeutic Index	—	—	✓

GPS platform components designed to work synergistically to improve I-O therapeutic index



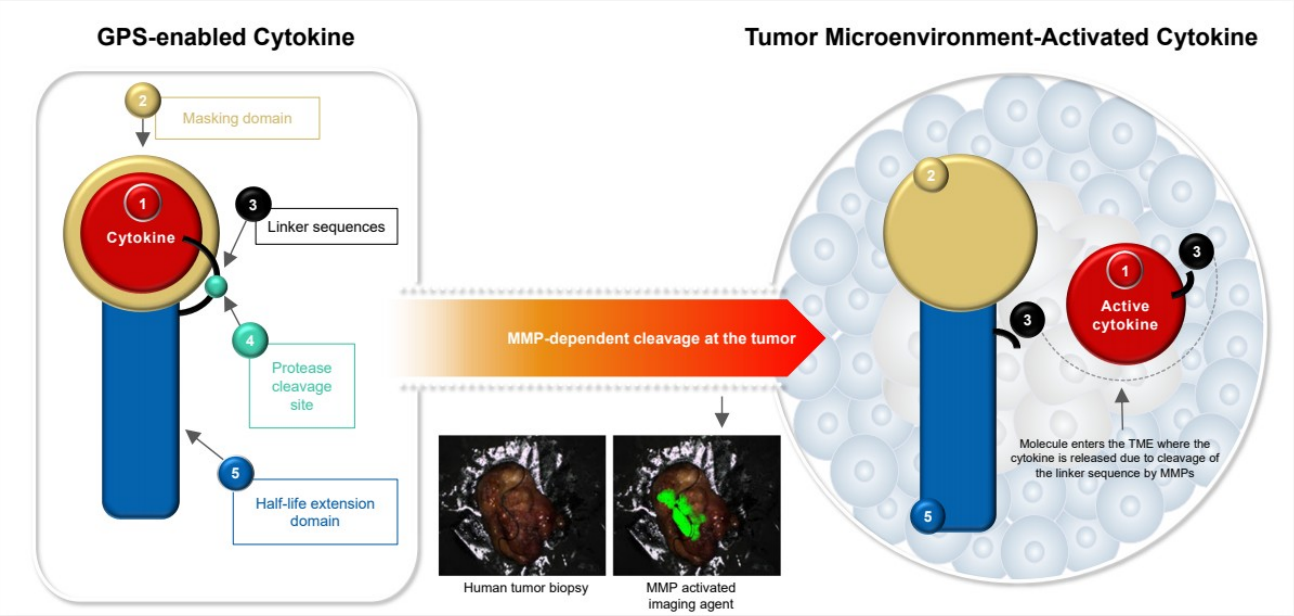
Clinical validation of MMP-activated imaging agent in tumor microenvironment in patients



Third-party MMP activated imaging agent AVB-620 validates tumor-dependent MMP expression; selectively highlights tumor tissue in human clinical studies;
Breakthrough Designation granted as diagnostic for breast cancer

Images: Unkart J.T. et al., (2017) Ann. Surg. Oncol.

GPS platform components designed to work synergistically to improve I-O therapeutic index



Xilio product candidates are cleaved in the majority of tumor samples from patients

XTX101 [1]		
Cancer Type	Sample Size	% of Samples Cleaving XTX101
Colon	11	91%
Bladder	5	80%
Breast	4	75%
Liver	5	60%
Melanoma	7	71%
NSCLC	9	67%
Ovarian	11	64%
RCC	30	57%

XTX202 [2]		
Cancer Type	Sample Size	% of Samples Cleaving XTX202
Colon	5	100%
H&N	6	83%
Lung	7	57%
Ovarian	2	50%
Prostate	4	75%
RCC	33	67%

XTX301 [3]		
Cancer Type	Sample Size	% of Samples Cleaving XTX301
Colon	6	83%
H&N	4	75%
Lung	8	50%
Ovarian	4	50%
Prostate	12	67%
RCC	6	83%

H&N: Head and neck cancer; NSCLC: non-small cell lung cancer; RCC: Renal cell carcinoma. Using fresh tumor biopsies obtained from human patients, Xilio demonstrated the capacity of human tumors to activate XTX101, XTX202 and XTX301 in a protease-dependent manner in preclinical studies. 1. Data presented at New York Academy of Sciences (NYAS) Frontiers in Cancer Immunotherapy 2021 Conference in May 2021. 2. Data on file. 3. Data presented at NYAS Frontiers in Cancer Immunotherapy 2022 Conference in May 2022.


XTX101
TUMOR-SELECTIVE ANTI-CTLA-4 PRODUCT CANDIDATE
xilio
THERAPEUTICS
12

High-dose ipilimumab (aCTLA-4) improved survival, but utility is limited due to known toxicity

Ipilimumab Melanoma Randomized Phase 3 Trial

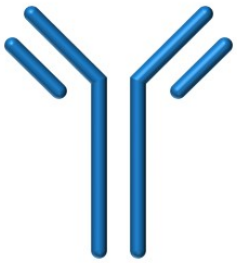
	Dose	Median OS	Adverse Events: Grade 3/4 irAEs / discontinuations (%)
Standard Approved Dose	3 mg/kg	11.5 mo	14 / 19
	10 mg/kg	15.7 mo	30 / 31

- Improved efficacy seen with 10 mg/kg dose but greater toxicity limits clinical use to 3 mg/kg dose
- Further reduced in combination with anti-PD-1, typically to 1 mg/kg of ipilimumab
- 3-fold increase in therapeutic index has high potential for transformational outcome

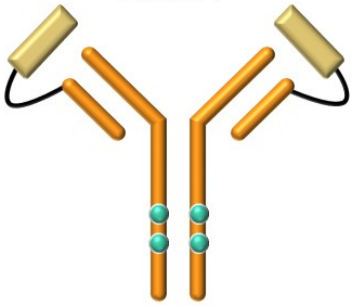
irAE: Immune-related adverse event; OS: Overall survival
Trial conducted by Bristol Myers Squibb
Ascierto (2016); Larkin et al., NEJM (2015); Wolchok et al., Lancet (2010); Hamid et al., J. Trans. Med (2011); Lebbe et al., J. Clin. Onc (2019)

XTX101 (aCTLA-4) achieved 10-fold wider therapeutic index than ipilimumab analog in preclinical studies

Ipilimumab



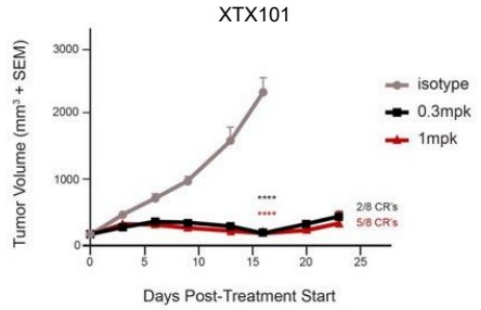
XTX101



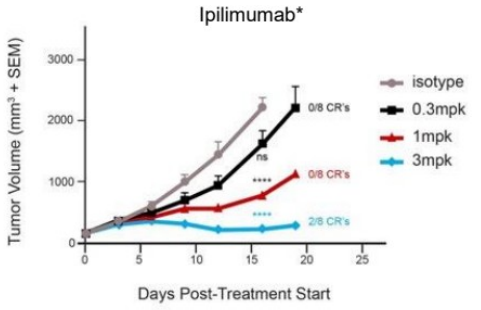
- Improved activity, higher CTLA-4 binding affinity and enhanced Fc-driven effector function
- Lower peripheral toxicity potential due to masking and tumor-selective activation

XTX101 (aCTLA-4) demonstrated improved therapeutic index and 10-fold greater potency than ipilimumab analog *in vivo*

0.3 mg/kg XTX101 Achieved Complete Responses



3 mg/kg Ipilimumab Analog Required to Achieve Complete Responses[2]



Jenkins *et al.*, Frontiers in Cancer Immunotherapy 2021

- [1] MB49 cells were inoculated subcutaneously into C57BL/6-huCTLA-4 mice. When tumors reached approximately 150 mm^3, 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).
- [2] Ipilimumab analog comprising a monoclonal antibody of identical amino acid sequence to ipilimumab that was produced at Xilio for research purposes.

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[2] Ipilimumab analog comprising a monoclonal antibody of identical amino acid sequence to ipilimumab that was produced at Xilio for research purposes.

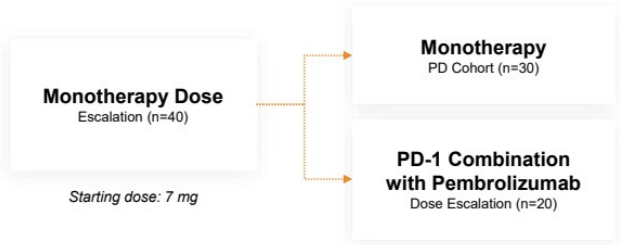
Clinical plan for XTX101 (aCTLA-4) enables efficient path to POC with substantial opportunities for expansion

Initiated patient dosing in September 2021;
Preliminary monotherapy data anticipated in mid-2022

Objectives

- Establish safety POC at target pharmacokinetic exposure
- Evaluate anti-tumor activity at tolerable dose
- Establish safety in combination with anti-PD-1
- Establish recommended Phase 2 dose

Phase 1 Trial Design



Additional Opportunities with Combination Strategies

Melanoma, NSCLC, renal cell carcinoma, hepatocellular carcinoma, MSI-high colorectal cancer

Clinical trial collaboration and supply agreement established with Merck in May 2021 to evaluate XTX101 in combination with KEYTRUDA® (pembrolizumab)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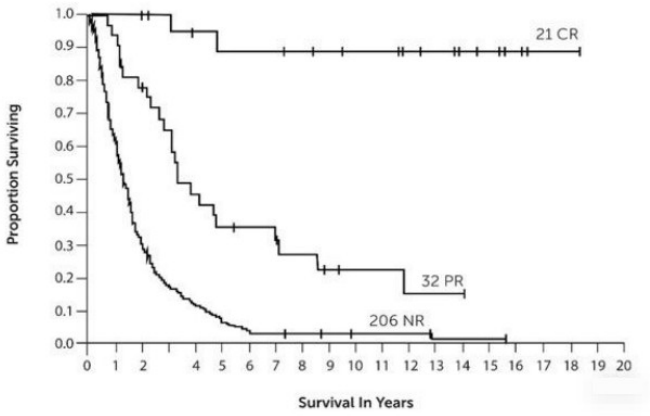
High-dose IL-2 offered curative potential, but usage limited in patients due to life-threatening VLS

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

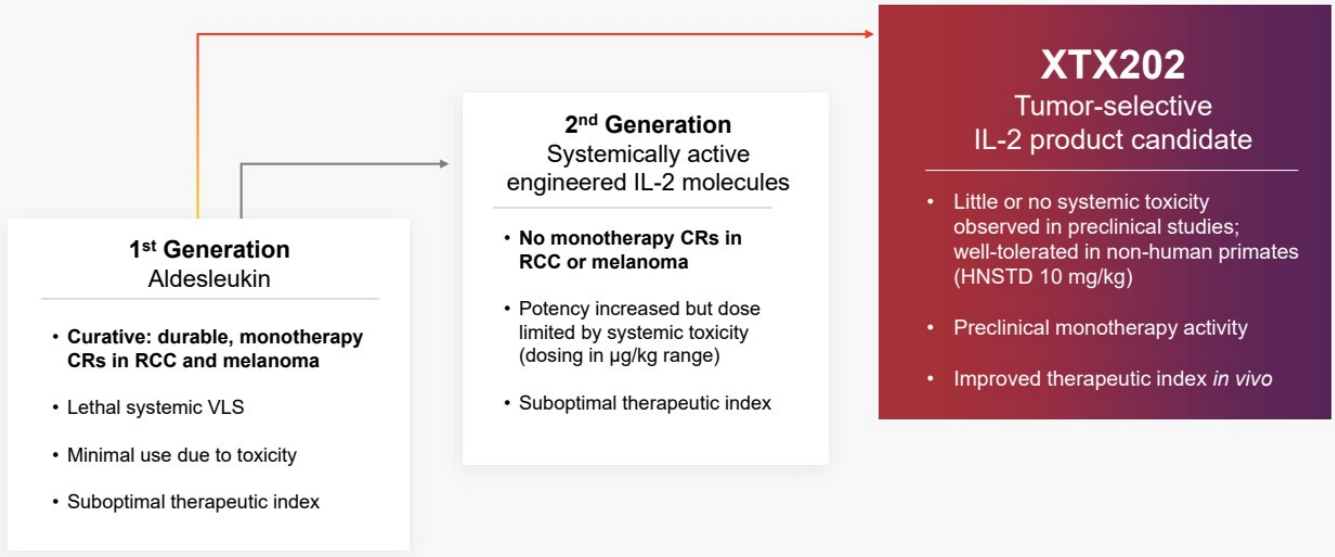


Data represents all patients that received IL-2 (no control group)

Limited use of high-dose IL-2 in patients with cancer

- Must have normal cardiac and pulmonary function
- Most develop hypotension, despite strict requirements
- Unable to receive full dose due to life-threatening toxicity
- Treatment restricted to use at specialized centers

GPS-enabled IL-2 candidate designed to overcome known limitations of 1st and 2nd generation approaches



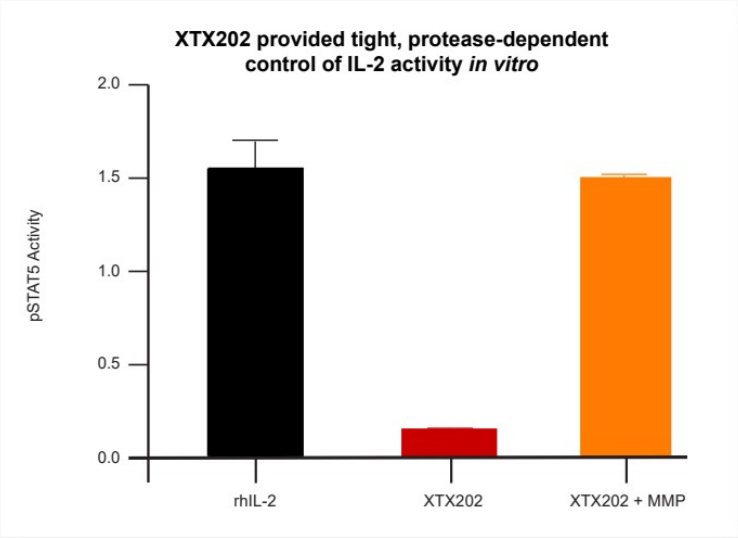
RCC: Renal cell carcinoma; VLS: Vascular leak syndrome; HNSTD: Highest non-severely toxic dose

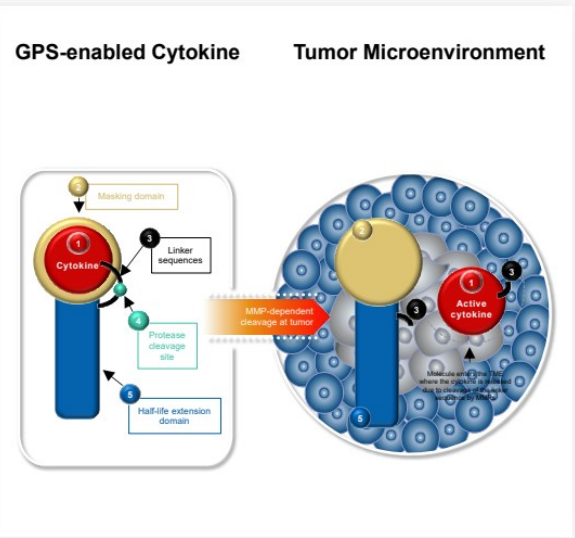
Aldesleukin Remains the Efficacy Bar for XTX202

Aldesleukin	NKTR-214 (bempegaldesleukin)	XTX202
• **High dose:** 0.5-1.0 mg/kg over 4 days	• **Low dose:** 0.006 mg/kg	• **High dose:** Phase 1 starting dose 0.27 mg/kg *(45x higher than R2PD for bempeg in patients)*
• **Systemically active**	• **Systemically active**	• **Activated selectively within the TME** using GPS platform
• **Poor tolerability:** AE profile requires ICU-level supervision	• **Dose limited by systemic toxicity**	• **Lack of systemic activity observed preclinically**: supports potential for mg/kg dosing in patients
• **Demonstrated monotherapy responses:** ORR of ~15% with monotherapy in melanoma and RCC patients, including *long-term durable CRs*	• **No objective responses observed with monotherapy** in Phase 1 trial (including 24 patients treated at RP2D or higher)	• **Monotherapy Phase 2 trial:** designed to evaluate monotherapy response rate

AE = adverse event; CR = complete response; MTD = maximum tolerated dose; ORR = objective response rate; RCC = renal cell carcinoma; RP2D = recommended Phase 2 dose; TME = tumor microenvironment

XTX202 (IL-2) designed to improve therapeutic index through tumor-selective activation

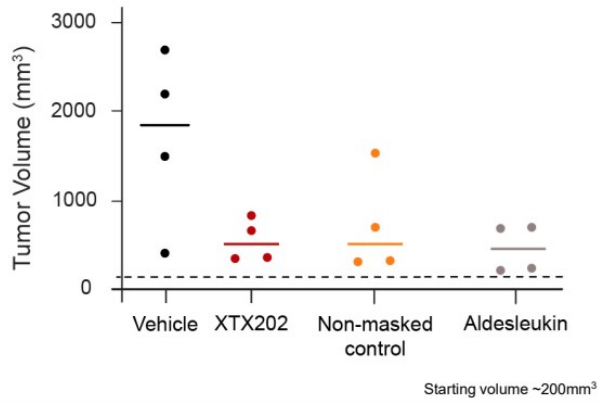




HEK-Blue IL-2 reporter cells engineered by stable transfection of IL-2Rα,β,γ, JAK, and STAT genes to monitor IL-2 dependent activation of JAK-STAT pathway. Activation of STAT5 leads to production of secreted embryonic alkaline phosphatase. pSTAT5 activity expressed as absorbance at 625 nanometers. Data shown are for recombinant human IL-2 (rhIL-2) and XTX202+MMP assayed at 50 pM and XTX202 assayed at 57 pM.

XTX202 (IL-2) improved therapeutic index *in vivo*: Tumor growth inhibition with substantially less toxicity compared to aldesleukin at its MTD

Tumor Growth Inhibition at Day 5



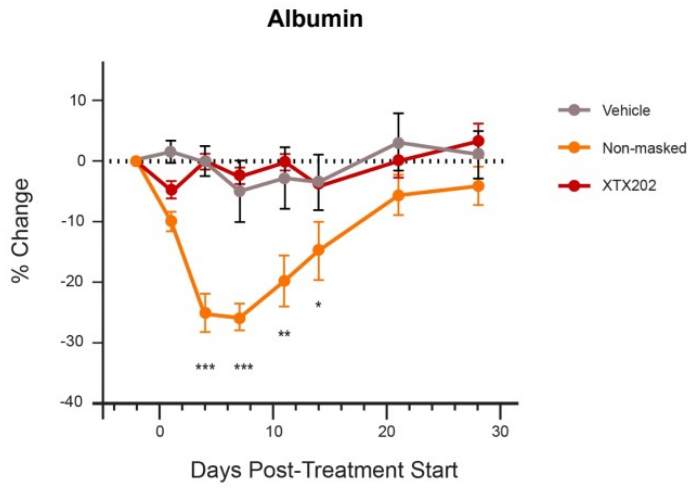
Starting volume ~200mm^3

High Dose XTX202 Well-Tolerated *In Vivo*

- Aldesleukin at MTD of 3 mg/kg BID for 4 days (24 mg/kg total) induced body weight loss and mortality
- Non-masked control at MTD of 0.5 mg/kg on day 0 and 3 (1 mg/kg total) induced body weight loss and mortality
- XTX202 at 10 mg/kg on day 0 and 3 (20 mg/kg) was well-tolerated with no body weight loss; doses up to 25 mg/kg resulted in reversible, mild body weight loss with no mortality

O'Neill *et al.*, ASCO 2021

XTX202 (IL-2) was well-tolerated in NHPs and overcame toxicity observed with non-masked control



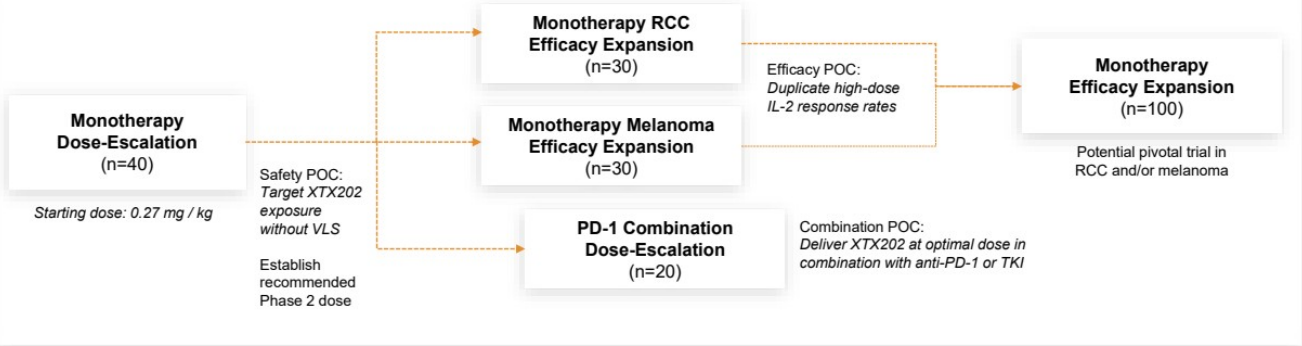
- XTX202 did not cause peripheral lymphocyte expansion or capillary leakage at repeat doses (weekly x4) up to 10 mg/kg in completed GLP toxicology studies
- XTX202 half-life in NHPs of 5.3 days, suggesting potential for Q3W dosing in patients

PK: Pharmacokinetics; Q3W: every three weeks
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).

Clinical plan for XTX202 (IL-2) enables efficient path to POC with substantial opportunities for expansion

Initiated patient dosing in January 2022
Preliminary Phase 1 data anticipated in 2H 2022

Phase 1/2 Trial Design



Additional Opportunities with Combination Strategies

NSCLC, head & neck cancer, ovarian cancer, bladder cancer, melanoma, renal cell carcinoma

FDA: U.S. Food and Drug Administration; NSCLC: Non-small cell lung cancer; POC: Proof-of-concept; TKI: Tyrosine kinase inhibitor; VLS: Vascular leak syndrome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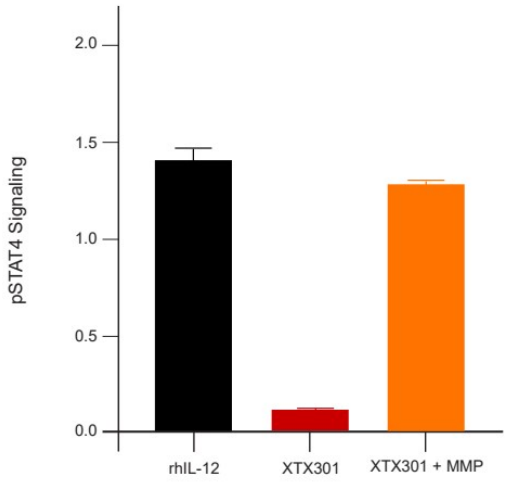
IL-12 has potential for meaningful anti-tumor activity in a range of tumors but is limited by severe systemic toxicity

- IL-12 induces objective responses in patients
- Systemic IL-12 therapy causes severe life-threatening hepatotoxicity
- Currently no FDA-approved IL-12 therapies

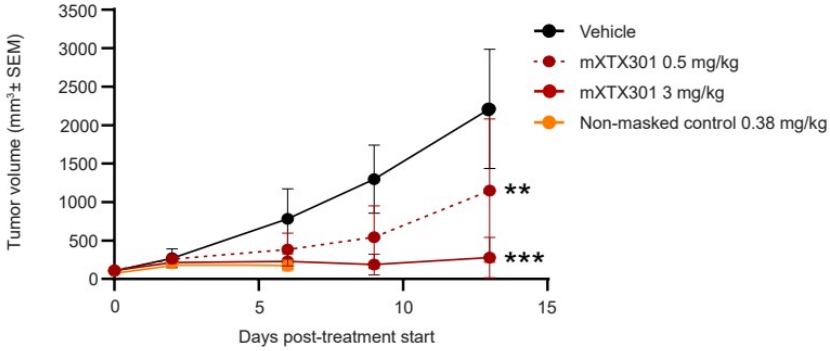
XTX301 provided tight, protease-dependent control of IL-12 activity *in vitro*



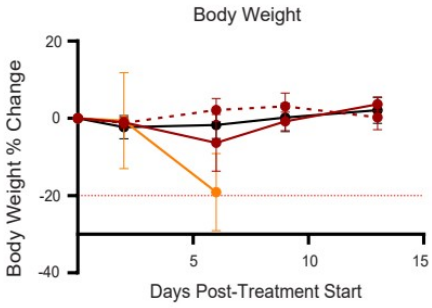
HEK-Blue IL-12 reporter cells engineered by stable transfection of IL-12Rβ1, IL-12Rβ2, JAK, and STAT genes to monitor IL-12 dependent activation of JAK-STAT pathway. Activation of STAT4 leads to production of secreted embryonic alkaline phosphatase. pSTAT4 activity expressed as absorbance at 625 nanometers. Data shown are for recombinant human IL-12 (rhIL-12) and XTX301+MMP assayed at 228 pM and XTX301 assayed at 143 pM

XTX301 (IL-12) demonstrated improved therapeutic index *in vivo*

Tumor Growth Inhibition[1]



Body Weight[2]

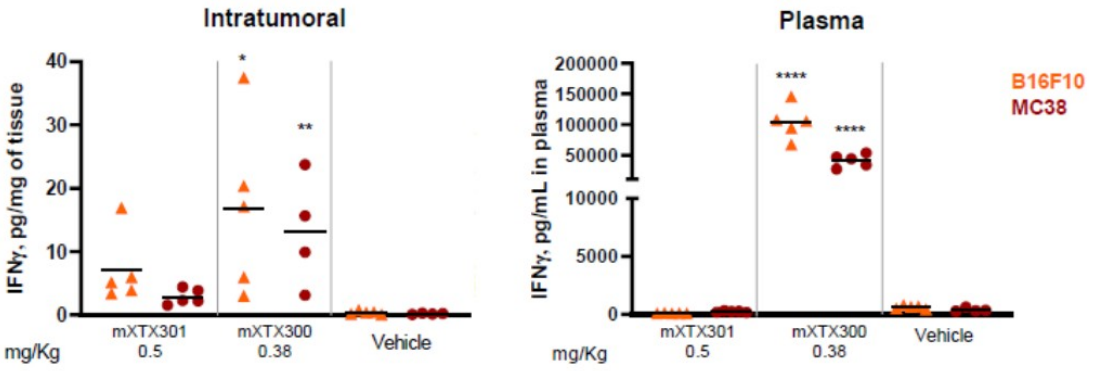


mXTX301: murine XTX301

- **Safety in NHPs:** XTX301 was well-tolerated in multiple dose studies at doses up to 1.5 mg/kg, while non-masked control was not tolerated (fatal toxicity) at doses down to 0.03 mg/kg

[1] A one-way ANOVA Dunnet's multiple comparison post-test was performed to determine the statistical significance of treatment vs vehicle (*P<0.05; **P<0.01; ***P<0.001; ****P<0.0001).
[2] Mice bearing established tumors received a single dose of either vehicle, 0.38 mg/kg of the non-masked mouse IL-12 cytokine or 3 mg/kg of mXTX301.

mXTX301, a mouse surrogate for XTX301 (IL-12), elicited pharmacodynamic effects in tumors and exhibited effective peripheral masking in mouse models



- Treatment with mXTX301 resulted in intra-tumoral induction of IFNg in B16F10 and MC38 tumor bearing mice with low peripheral exposure

1. A one-way ANOVA followed by Bonferroni post-hoc test was performed (#p = 0.17, *p < 0.05, **p < 0.005, ****p < 0.0001)
2. Mice bearing established tumors received a single dose of either vehicle, 0.4 mg/kg of the non-masked control (mXTX300) or 0.5 mg/kg of mXTX301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Building a robust pipeline of tumor-selective immunotherapy programs

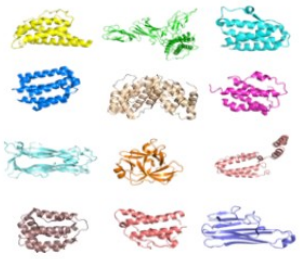
Tumor-Selective Programs	Mechanism of Action	Discovery	IND-Enabling	Phase 1	Phase 2	Phase 3	Anticipated Upcoming Milestones
XTX101 [1]	Anti-CTLA-4						Preliminary Phase 1 monotherapy data mid-2022
XTX202 [2]	IL-2						Preliminary Phase 1 data 2H 2022
XTX301	IL-12						IND submission 2H 2022

Continuing to leverage GPS platform with the goal of expanding pipeline and developing additional tumor-selective immunotherapies, including product candidates with a range of tumor targeting approaches

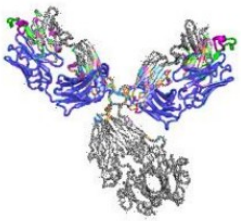
1 Plan to initially evaluate XTX101 as a monotherapy and as a combination therapy for the treatment of advanced solid tumors
2 Plan to initially evaluate XTX202 as a monotherapy and as a combination therapy for the treatment of renal cell carcinoma and melanoma prior to potential expansion into additional cancer indications

GPS platform has potential to deliver highly potent, geographically localized immunotherapies beyond cancer

Masked Cytokines



Masked Antibodies

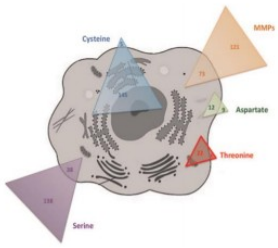


Pro- and Anti-Inflammatory Processes

IL-2
IL-12
IL-15
IL-17
IL-23
IL-22
GM-CSF
IL-18
TNF-a
IL-1
IL-7
IL-6
INF-y

IL-2
IL-4
IL-5
IL-9
IL-10
IL-13
IL-25
IL-27
IL-35
TGF-B
LIF

Proteases in Diseases of Immune Dysregulation



Potential to harness unique protease profiles of different diseases to deliver therapeutics that enhance or inhibit immune activity at the disease site without systemic toxicity

Building a team that is passionately committed to oncology innovation to transform patients' lives

First quarter 2022 financial results

Balance Sheet	March 31, 2022	December 31, 2021
Cash and Cash Equivalents	$177.0M	$198.1M

Statement of Operations	Three Months Ended March 31,	
	2022*	2021*
Research & Development Expenses	$14.9M	$11.6M
General & Administrative Expenses	$6.3M	$4.9M
Net Loss	$(21.4)M	$(16.7)M

Anticipate existing cash and cash equivalents will be sufficient to fund operating expenses and capital expenditure requirements into the first half of 2024

Focused on harnessing the immune system to achieve deep and durable clinical responses in cancer

Harness the power of highly potent, tumor-selective I-O therapies to provide effective, tolerable and durable therapeutic options for patients and their physicians

- ✓ GPS platform enables engineered molecules that localize activity within the tumor microenvironment
- ✓ XTX101 (anti-CTLA-4) preliminary Phase 1 monotherapy cohort data anticipated in mid-2022 and preliminary Phase 1 combination cohort data anticipated in 2H 2022
- ✓ XTX202 (IL-2) preliminary Phase 1 data anticipated in 2H 2022
- ✓ XTX301 (IL-12) IND submission anticipated in 2H 2022
- ✓ Anticipate existing cash and cash equivalents will be sufficient to fund operating expenses and capital expenditure requirements into 1H 2024