

**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): **November 9, 2022**

Xilio Therapeutics, Inc.
(Exact Name of Registrant as Specified in Charter)

Delaware
(State or Other Jurisdiction
of Incorporation)

001-40925
(Commission
File Number)

85-1623397
(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 November 9, 2022, Xilio Therapeutics, Inc. (the “Company”) announced its financial results for the quarter ended September 30, 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 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 exhibits relating to Item 2.02 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 November 9, 2022
99.2	Corporate investor presentation of Xilio Therapeutics, Inc. as of November 9, 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: November 9, 2022

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

Xilio Therapeutics Announces Pipeline and Business Updates and Third Quarter 2022 Financial Results

XTX202, a tumor-activated IL-2, successfully reached target dose range of 1 mg/kg in ongoing Phase 1 clinical trial; preliminary evidence of increased CD8+ effector T cells and NK cells observed with no signs of vascular leak syndrome

XTX301, a tumor-activated IL-12, received FDA clearance for IND application; anticipate initiating patient dosing in Phase 1 clinical trial in first quarter of 2023

Plan to focus resources on advancing clinical-stage cytokine programs and will seek to partner XTX101, a tumor-activated anti-CTLA-4, to advance beyond ongoing Phase 1 monotherapy cohorts

\$139.1 million in cash and cash equivalents as of September 30, 2022, with anticipated cash runway into the second quarter of 2024

WALTHAM, Mass., November 9, 2022 -- Xilio Therapeutics, Inc. (Nasdaq: XLO), a biotechnology company developing tumor-activated immuno-oncology therapies for people living with cancer, today announced pipeline progress, business updates and reported financial results for the third quarter ended September 30, 2022.

“We continued to make meaningful progress advancing our clinical-stage cytokine programs, XTX202 and XTX301, during the quarter,” said René Russo, Pharm.D., chief executive officer of Xilio. “XTX202, our tumor-activated IL-2, has successfully reached the target dose range of 1 mg/kg in an outpatient setting in our ongoing Phase 1 clinical trial with no signs of vascular leak syndrome, and preliminary clinical data indicate evidence of IL-2 specific biology, including intra-tumoral pharmacodynamic effects in one patient for whom a tumor biopsy was available. We expect to report initial anti-tumor activity data for XTX202 in the third quarter of 2023. In addition, with the recent FDA clearance of our IND application for XTX301, our tumor-activated IL-12, we look forward to initiating a Phase 1 clinical trial in the first quarter of 2023 and evaluating the therapeutic potential of XTX301 across ‘cold’ and ‘hot’ tumor types.”

Dr. Russo continued, “While we remain enthusiastic about the potential for XTX101, our tumor-activated anti-CTLA-4, we plan to focus our existing resources on advancing our clinical-stage cytokine programs, and we will seek to partner XTX101 to advance the program beyond the ongoing Phase 1 monotherapy cohorts.”

Pipeline and Business Updates***XTX202: tumor-activated, engineered IL-2***

XTX202 is an investigational tumor-activated beta-gamma biased (non-alpha), 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. XTX202 is currently being evaluated in monotherapy dose-escalation of an ongoing Phase 1 clinical trial in patients with advanced solid tumors.

- Xilio recently began dosing patients at the 1 mg/kg dose level, which is in the target clinical dose range for XTX202, making it one of the first engineered IL-2 molecules to achieve a dose that is in line with that of traditional high dose treatment with aldesleukin.
 - As of November 7, 2022, 11 patients have been treated with XTX202 as outpatients in monotherapy dose-escalation at four dose levels ranging from 0.27 mg/kg to 1.0 mg/kg.
-

- Preliminary analyses indicated evidence of IL-2 specific biology in patients consistent with data observed in preclinical studies, including CD8+ effector T cells and NK cells increasing in peripheral circulation steadily over time.
- No signs of vascular leak syndrome (VLS) or decreases in albumin (an early sign of VLS) have been observed in patients to date.
- In addition, Xilio today reported preliminary intra-tumoral pharmacodynamic data for a single patient treated with XTX202 who had an optional on-treatment tumor biopsy and was the first patient for whom a tumor biopsy analysis was available to date. This patient tumor biopsy featured increased numbers of stromal tumor infiltrating lymphocytes (TILs), increased frequency of CD8+ effector T cells among these TILs and decreased frequency of immune suppressive regulatory T cells (TREGs). Importantly, in this patient, at the time of the tumor biopsy, these changes occurred in the absence of peripheral changes to either CD8+ effector T cells or TREGs.
- A maximum tolerated dose has not yet been determined, and enrollment in monotherapy dose-escalation is ongoing.

Xilio anticipates multiple milestones for XTX202 through the end of 2023:

- Initiate patient enrollment in a monotherapy expansion cohort of the Phase 1 clinical trial in the fourth quarter of 2022.
- Initiate patient enrollment in a Phase 2 monotherapy clinical trial in the first half of 2023.
- Report preliminary anti-tumor activity and safety data from the Phase 1/2 clinical trial in the third quarter of 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 tumor microenvironment (TME) of poorly immunogenic “cold” tumors towards an inflamed, or “hot,” state. IL-12 plays a key role in bridging innate and adaptive cellular immunity, making it a compelling target for immunotherapy. However, life-threatening toxicity observed with systemically active IL-12, including severe liver toxicity, have limited the therapeutic potential of IL-12 agents. Preclinical studies using a murine surrogate molecule for XTX301 demonstrated *in vivo* anti-tumor activity at doses as low as 0.04 mg/kg, and XTX301 demonstrated favorable tolerability in non-human primates at doses up to 2 mg/kg given weekly over four cycles.

- Xilio today announced that the U.S. Food and Drug Administration has cleared the company’s investigational new drug (IND) application for the evaluation of XTX301 as a potential treatment for patients with advanced solid tumors.

Xilio anticipates multiple milestones for XTX301 through the end of 2023:

- Initiate patient enrollment in monotherapy dose-escalation in a Phase 1 clinical trial in the first quarter of 2023 evaluating the safety and tolerability of XTX301 in patients with advanced solid tumors.
 - Report preliminary safety data from the Phase 1 clinical trial in the fourth quarter of 2023.
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XTX101: tumor-activated anti-CTLA-4

XTX101, an Fc-enhanced, tumor-activated anti-CTLA-4, is currently being evaluated in monotherapy dose-escalation of an ongoing Phase 1 clinical trial in patients with advanced solid tumors.

- Xilio is currently dosing patients at 150 mg once every six weeks (Q6W) in the monotherapy dose-escalation cohort, which the company anticipates completing by the end of 2022. Enrollment in a monotherapy dose expansion cohort is currently ongoing.
- Preliminary pharmacokinetic (PK) analyses continue to demonstrate dose-proportional drug exposure, with limited active (unmasked) XTX101 in peripheral circulation consistent with PK data observed in preclinical studies.
- Xilio anticipates reporting preliminary data from the Phase 1 clinical trial in the second quarter of 2023.
- Xilio plans to continue to explore opportunities for strategic collaborations to advance XTX101 and does not plan to initiate an anti-PD-1 combination cohort in the Phase 1 clinical trial or initiate a Phase 2 clinical trial for XTX101 without a partner.

Corporate Highlights

- In September 2022, Xilio announced the appointment of Tomas J. Heyman as a member of the board of directors and John Maraganore, Ph.D. joined as a strategic advisor to the company.
- In August 2022, Xilio announced the promotion of Uli Bialucha, Ph.D. to Chief Scientific Officer and Chris Frankenfield to Chief Legal and Administrative Officer.

Upcoming Presentations

Xilio will present a poster outlining preclinical data demonstrating anti-tumor activity and sustained memory T-cell response in mice for XTX202 in combination with immune checkpoint blockade at the Society for Immunotherapy in Cancer 37th Annual Meeting.

- **Presentation title:** XTX202, a tumor-activated protein-engineered IL-2, exhibited enhanced anti-tumor activity in combination with checkpoint inhibition in mice
- **Session date and time:** Thursday, November 11, 2022, at 11:40 am to 1:10 pm and 7:30 pm to 9:00 pm ET
- **Abstract number:** 841

Uli Bialucha, Ph.D., Xilio's chief scientific officer, will present at the 14th Annual Protein & Antibody Engineering Summit (PEGS) Europe meeting and will highlight preclinical data for XTX301, a tumor-activated IL-12, and Xilio's emerging research portfolio developing tumor-activated multifunctional biologics.

- **Presentation title:** Engineering Tumor-Selective Biologics for Immune-Oncology
- **Session date and time:** Monday, November 14, 2022, at 3:20 pm CET (10:20 am ET)

Third Quarter 2022 Financial Results

- **Cash Position:** Cash and cash equivalents were \$139.1 million as of September 30, 2022, compared to \$198.1 million as of December 31, 2021.
 - **Research & Development (R&D) Expenses:** R&D expenses were \$13.0 million for the third quarter of 2022, compared to \$10.5 million for the third quarter of 2021. The increase was primarily driven by higher personnel-related costs mainly due to increased headcount and a \$0.2
-

million increase in non-cash equity-based compensation expense, as well as increased costs associated with XTX301 preclinical, clinical and manufacturing development activities.

- **General & Administrative (G&A) Expenses:** G&A expenses were \$7.2 million for the third quarter of 2022, compared to \$5.5 million for the third quarter of 2021. The increase was primarily driven by higher personnel-related costs, primarily due to increased headcount and a \$0.6 million increase in non-cash equity-based compensation expense, as well as certain costs related to operating as a publicly traded company.
- **Net Loss:** Net loss was \$19.8 million for the third quarter of 2022, compared to \$16.3 million for the third quarter of 2021.

Financial Guidance

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

About the Phase 1/2 Clinical Trial for XTX202 (IL-2)

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 1 clinical trial is designed to enroll up to approximately 119 patients across all cohorts at multiple sites in the United States, Europe and other international sites. Please refer to NCT05052268 on www.clinicaltrials.gov for additional details.

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 melanoma and renal cell carcinoma at the recommended Phase 2 dose. The Phase 2 clinical trial is designed to enroll up to approximately 70 patients in the United States and Europe. Please refer to NCT05052268 on www.clinicaltrials.gov for additional details.

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

The planned 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. The Phase 1 clinical trial is designed to enroll up to approximately 94 patients across all cohorts at multiple sites in the United States.

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

XTX101 is an investigational Fc-enhanced, tumor-activated anti-CTLA-4 monoclonal antibody designed to deplete regulatory T cells when activated (unmasked) in the 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. Please refer to NCT04896697 on www.clinicaltrials.gov for additional details.

About Xilio Therapeutics

Xilio Therapeutics is a clinical-stage biotechnology company discovering and developing tumor-activated immuno-oncology (I-O) therapies with the goal of significantly improving outcomes for people living with cancer without the systemic side effects of current I-O treatments. The company is using its proprietary platform to build a pipeline of novel, tumor-activated molecules, including cytokines and other biologics, which are designed to optimize their therapeutic index and localize anti-tumor activity within the tumor microenvironment. Xilio is currently advancing multiple programs for tumor-activated

I-O treatments in clinical development, as well as programs in preclinical development. Learn more by visiting www.xiliotx.com and follow us on Twitter (@xiliotx) and LinkedIn (Xilio Therapeutics, Inc.).

Cautionary Note Regarding Forward-Looking Statements

This press release contains forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995, as amended, including, without limitation, statements regarding plans, timing and expectations related to the initiation of patient enrollment in a monotherapy expansion cohort for the Phase 1 clinical trial for XTX202, the initiation of patient enrollment in a Phase 2 clinical trial for XTX202 and reporting data from the Phase 1/2 clinical trial for XTX202; plans, timing and expectations related to the initiation of patient enrollment in the planned Phase 1 clinical trial for XTX301 and reporting data from the Phase 1 clinical trial for XTX301; plans, timing and expectations related to completing monotherapy dose-escalation for the Phase 1 clinical trial for XTX101 and reporting data from the Phase 1 clinical trial for XTX101; plans, timing and expectations related to potential collaborations to advance XTX101; plans, timing and expectations related to progressing its next research-stage program; the potential benefits of any of Xilio's current or future product candidates in treating patients; Xilio's ability to fund its operating expenses and capital expenditure requirements with its existing cash and cash equivalents; and Xilio's strategy, goals and anticipated financial performance, milestones, business plans and focus. The words "aim," "may," "will," "could," "would," "should," "expect," "plan," "anticipate," "intend," "believe," "estimate," "predict," "project," "potential," "continue," "seek," "target" and similar expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words. Any forward-looking statements in this 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, including, without limitation, the preliminary intra-tumoral pharmacodynamic data reported for a single patient treated with XTX202 who had an optional on-treatment tumor biopsy and was the first patient for whom a tumor biopsy analysis was available as of the date hereof; Xilio's ability to successfully demonstrate the safety and efficacy of its product candidates and gain approval of its product candidates on a timely basis, if at all; results from preclinical studies or clinical trials for Xilio's product candidates, which may not support further development of such product candidates; actions of regulatory agencies, which may affect the initiation, timing and progress of current or future clinical trials; Xilio's ability to obtain, maintain and enforce patent and other intellectual property protection for current or future product candidates; Xilio's ability to obtain and maintain sufficient cash resources to fund current or future operating expenses and capital expenditure requirements; the impact of international trade policies on Xilio's business, including U.S. and China trade policies; and Xilio's ability to seek, establish and maintain a collaboration or partnership to develop XTX101 with a collaborator or partner. These and other risks and uncertainties are described in greater detail in the sections entitled "Risk Factor Summary" and "Risk Factors" in Xilio's filings with the U.S. Securities and Exchange Commission (SEC), including Xilio's most recent Quarterly Report on Form 10-Q and any other filings that Xilio has made or may make with the SEC in the future. Any forward-looking statements contained in this press release represent Xilio's views only as of the date hereof and should not be relied upon as representing its views as of any subsequent date. Except as required by law, Xilio explicitly disclaims any obligation to update any forward-looking statements.

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

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XILIO THERAPEUTICS, INC.
Condensed Consolidated Balance Sheets
(In thousands)
(Unaudited)

	September 30, 2022	December 31, 2021
Assets		
Cash and cash equivalents	\$ 139,143	\$ 198,053
Other assets	18,271	20,007
Total assets	<u>\$ 157,414</u>	<u>\$ 218,060</u>
Liabilities and Stockholders' Equity		
Liabilities	\$ 31,116	\$ 32,631
Stockholders' equity	126,298	185,429
Total liabilities and stockholders' equity	<u>\$ 157,414</u>	<u>\$ 218,060</u>

XILIO THERAPEUTICS, INC.

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

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2022	2021	2022	2021
Operating expenses ⁽¹⁾				
Research and development	\$ 13,038	\$ 10,470	\$ 44,204	\$ 39,836
General and administrative	7,168	5,491	21,778	15,652
Total operating expenses	20,206	15,961	65,982	55,488
Loss from operations	(20,206)	(15,961)	(65,982)	(55,488)
Other income (expense), net				
Other income (expense), net	416	(290)	226	(611)
Total other income (expense), net	416	(290)	226	(611)
Net loss and comprehensive loss	\$ (19,790)	\$ (16,251)	\$ (65,756)	\$ (56,099)
Net loss per share, basic and diluted	\$ (0.72)	\$ (21.27)	\$ (2.40)	\$ (76.18)
Weighted average common shares outstanding, basic and diluted	27,399,906	763,869	27,384,085	736,416

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

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2022	2021	2022	2021
Research and development expense	\$ 594	\$ 378	\$ 1,827	\$ 864
General and administrative expense	1,277	713	4,782	2,023
Total equity-based compensation expense	\$ 1,871	\$ 1,091	\$ 6,609	\$ 2,887

Unleashing the Potential of Immuno- Oncology Therapies

November 9, 2022

xilio
THERAPEUTICS

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Forward-Looking Statements

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The words "aim," "may," "will," "could," "would," "should," "expect," "plan," "anticipate," "intend," "believe," "estimate," "predict," "project," "potential," "continue," "seek," "target" and similar expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words. Any forward-looking statements in this presentation are based on management's current expectations and beliefs and are subject to a number of important risks, uncertainties and other factors that may cause actual events or results to differ materially from those expressed or implied by any forward-looking statements contained in this presentation, including, without limitation, risks and uncertainties related to ongoing and planned research and development activities, including initiating, conducting or completing preclinical studies and clinical trials and the timing and results of such preclinical studies or clinical trials; the delay of any current or planned preclinical studies or clinical trials or the development of Xilio's current or future product candidates; Xilio's ability to obtain and maintain sufficient preclinical and clinical supply of current or future product candidates; Xilio's advancement of multiple early-stage programs; there can be no assurance that interim or preliminary preclinical or clinical data or results will be predictive of future preclinical or clinical data or results, including, without limitation, the preliminary intra-tumoral pharmacodynamic data reported for a single patient treated with XTX202 who had an optional on-treatment tumor biopsy and was the first patient for whom a tumor biopsy analysis was available as of the date hereof; Xilio's ability to successfully demonstrate the safety and efficacy of its product candidates and gain approval of its product candidates on a timely basis, if at all; results from preclinical studies or clinical trials for Xilio's product candidates, which may not support further development of such product candidates; actions of regulatory agencies, which may affect the initiation, timing and progress of current or future clinical trials; Xilio's ability to obtain, maintain and enforce patent and other intellectual property protection for current or future product candidates; Xilio's ability to obtain and maintain sufficient cash resources to fund current or future operating expenses and capital expenditure requirements; the impact of international trade policies on Xilio's business, including U.S. and China trade policies; and Xilio's ability to seek, establish and maintain a collaboration or partnership to develop XTX101 with a collaborator or partner.

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

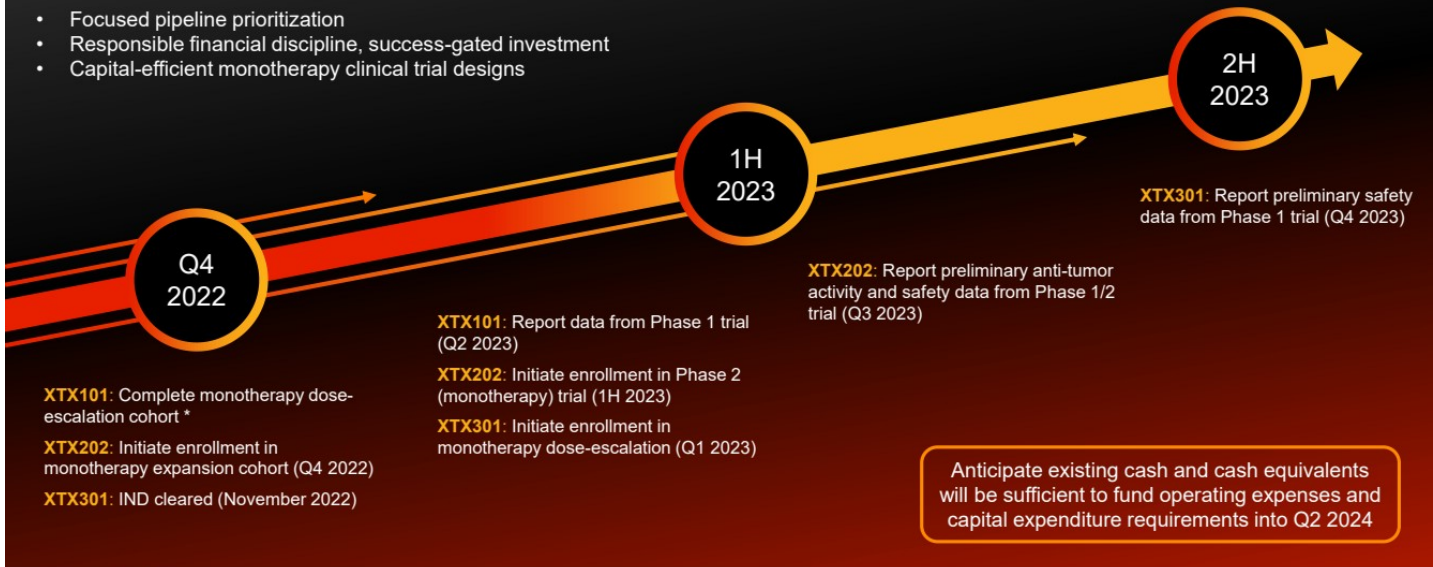
Certain information contained in this presentation relates to or is based on studies, publications, surveys and other data obtained from third-party sources and Xilio's own internal estimates and research. While Xilio believes these third-party studies, publications, surveys and other data to be reliable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

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



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

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



RP2D: recommended Phase 2 dose
* Plan to evaluate XTX101 as a monotherapy for the treatment of advanced solid tumors and explore opportunities for strategic collaborations to advance XTX101. Do not plan to initiate an anti-PD-1 combination cohort in the Phase 1 trial or initiate a Phase 2 trial without a development partner.

The Promise and Pitfalls of Immuno-Oncology Therapy

- **Immuno-oncology (IO) therapies have transformed the treatment landscape and long-term outlook for some patients with advanced cancer**

- IO treatments are primarily available for “hot” tumors, while “warm” and “cold” tumors continue to make up the majority of annual cancer deaths

- **IO therapies engage the immune system to recognize and destroy tumor cells**

- Potential to be curative
- Potential to address wide range of tumor types

- **But treatment potential for some of the most exciting IO targets has been impeded by dose-limiting systemic toxicity**

- Fatal multi-organ adverse events and peripheral side effects can occur with more potent IO agents
- Often results in dose reductions, interruptions or discontinuations for many patients
- Limits the ability to explore even more powerful targets or IO combinations that could have broad curative potential



Patient Portrayal

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

We are here to pursue that promise for patients

2016

Founded

XLO

NASDAQ

~100

Employees

3

Clinical Stage
Programs

xilio
THERAPEUTICS*

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

Mission

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

Vision

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

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

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



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



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



Uli Bialucha, Ph.D.
Chief Scientific Officer



Stacey Davis
Chief Business Officer



Chris Frankenfield
Chief Legal and
Administrative Officer

Xilio's Core Expertise



Cytokines



Protease Biology



Protein Engineering



Clinical Development

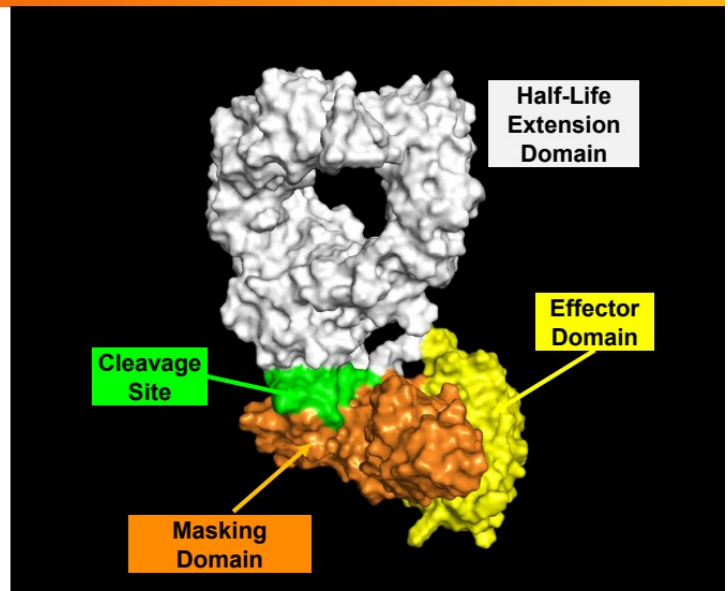


Data Science



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

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



Building a Transformative Immuno-Oncology Pipeline

Program	Disease Indication	Mechanism of Action	Discovery	IND-Enabling	Phase 1	Phase 2	Phase 3
Cytokine Programs							
XTX202 ⁽¹⁾	Oncology	IL-2					
XTX301 ⁽²⁾	Oncology	IL-12					IND Cleared
Discovery Stage	Oncology	Tumor-Activated Cytokine					
Antibody Program							
XTX101 ⁽³⁾	Oncology	Anti-CTLA-4					Plan to seek partnership for further investment



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

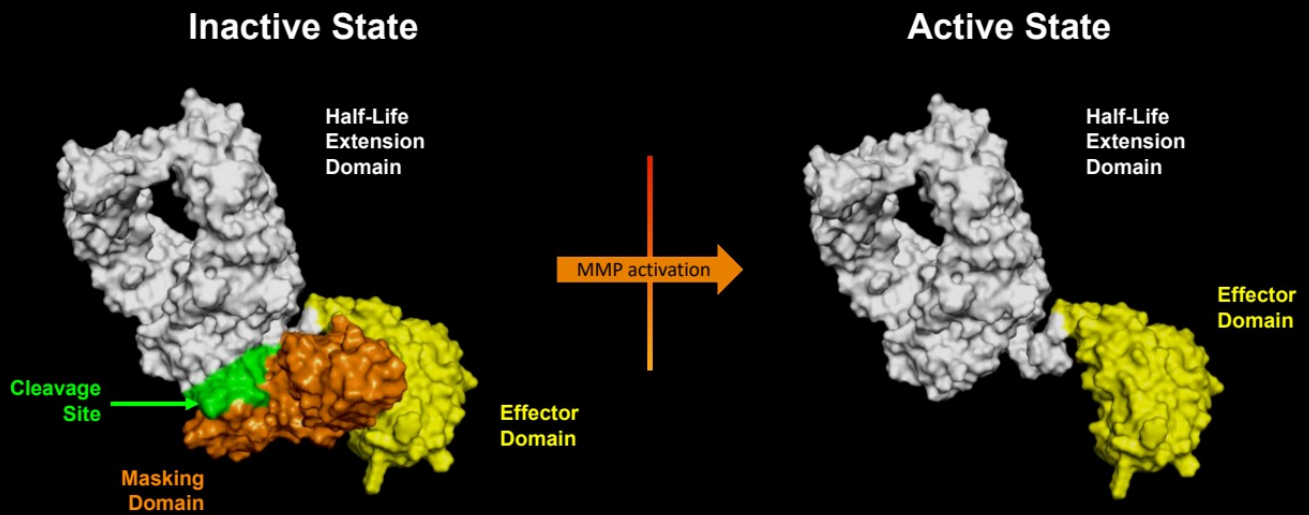


Xilio Designed, Tumor Activated

Seeking to Develop a Transformational IO Approach



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



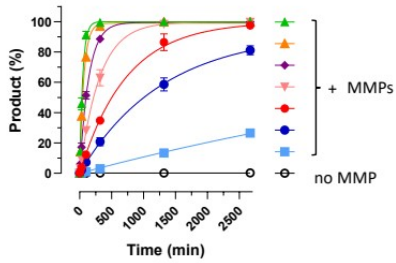
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MMP: matrix metalloproteases

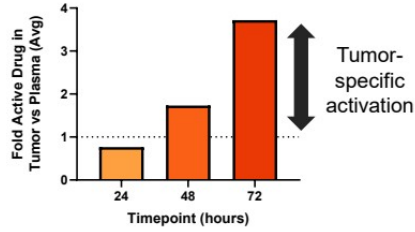
Xilio's Molecules are Activated by Dysregulated Tumor Proteases (MMPs)

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

In vitro recombinant MMP kinetic cleavage assay



Xilio molecules demonstrated tumor-specific activation *in vivo*



Presented at Cytokine Summit 2022 and SITC 2022

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

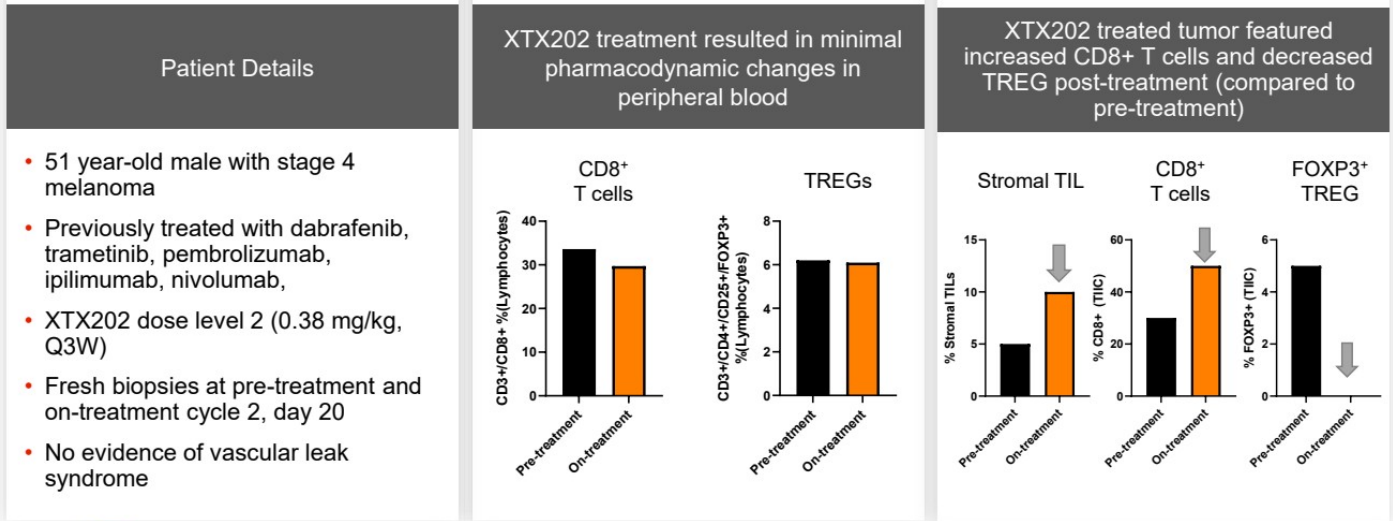
Tumor Type	Activation Efficiency	
	XTX202 (IL-2)	XTX301 (IL-12)
Colon	High	High
H&N	High	High
Prostate	High	High
RCC	High	High
Lung	High	High
Melanoma	Low	High
Plasma	Low	Low



- **Left panel:** Time-course of XTX301 activation by recombinant human matrix metalloproteinases (MMPs)
- **Middle panel:** Activation of XTX202 or XTX301 assessed in tumor biopsies *ex vivo*.
- **Right panel:** Mice bearing MC38 syngeneic colorectal carcinoma tumors were dosed with mXTX301 (murine surrogate for XTX301), and the percent activated molecule was measured over time in tumors and plasma. Fold difference in avg % active drug in tumor vs plasma shown.

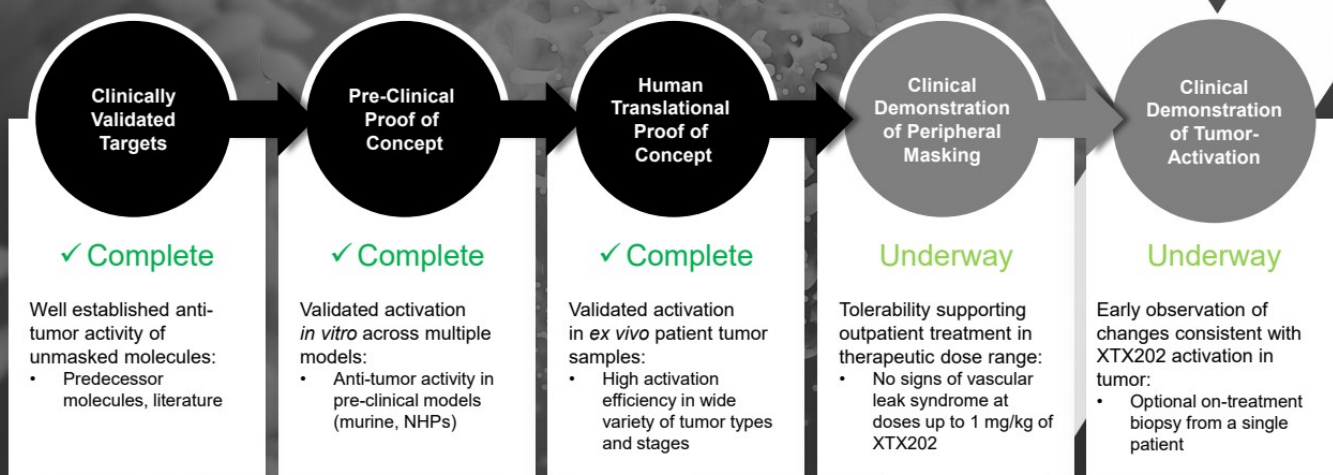
Xilio's First Demonstration of XTX202 Activation in a Patient Tumor

Preliminary Evidence of Intra-tumoral Pharmacodynamic Effects Consistent with Known IL-2 Biology



Patient had an optional on-treatment tumor biopsy and was the first patient for whom a tumor biopsy analysis was available as of November 7, 2022
 TREG: Regulatory T cell; TIL: Tumor infiltrating lymphocyte; TIIC: Tumor infiltrating immune cell

Executing on Our Vision to Deliver Tumor-Activated Immuno-Oncology Therapies Created through our Unique & Efficient Design Process



Xilio is positioned to demonstrate clinical platform validation in 2023

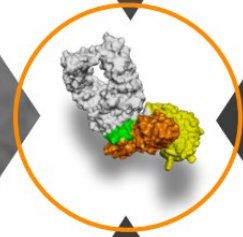


NHP: non-human primate

XTX202

Tumor-Activated IL-2

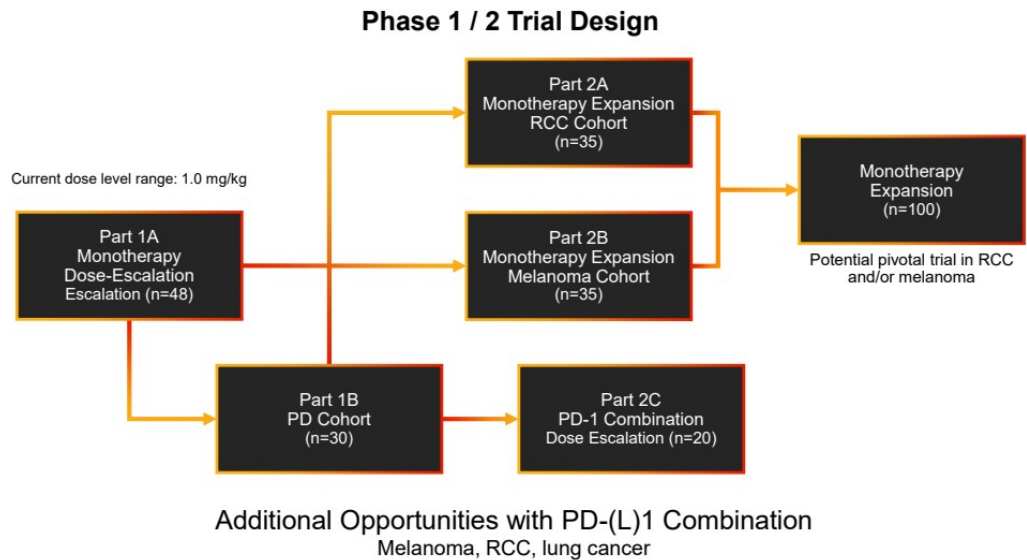
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XTX202 (IL-2) Phase 1/2 Trial Design Provides Efficient Path to Potential Monotherapy Proof-of-Concept

As of November 7, 2022:

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

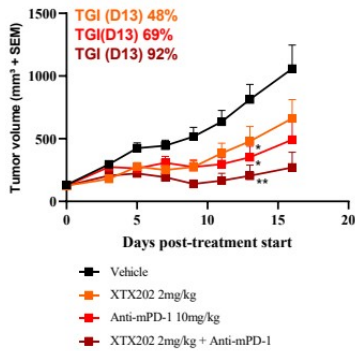


Data and trial updates reported as of November 7, 2022.

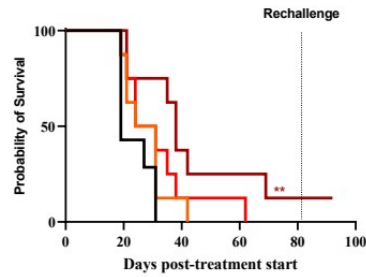
DLT: dose-limiting toxicity; MTD: maximum tolerated dose; NK: natural killer; PD: pharmacodynamic; RCC: renal cell carcinoma; TKI: tyrosine kinase inhibitor; VLS: vascular leak syndrome

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

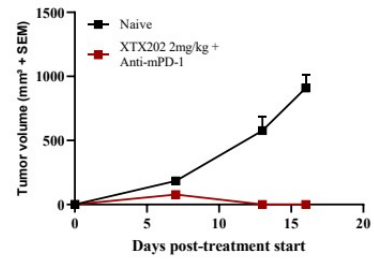
Enhanced *in vivo* activity with combination of XTX202 and anti-PD-1 mAb



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



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

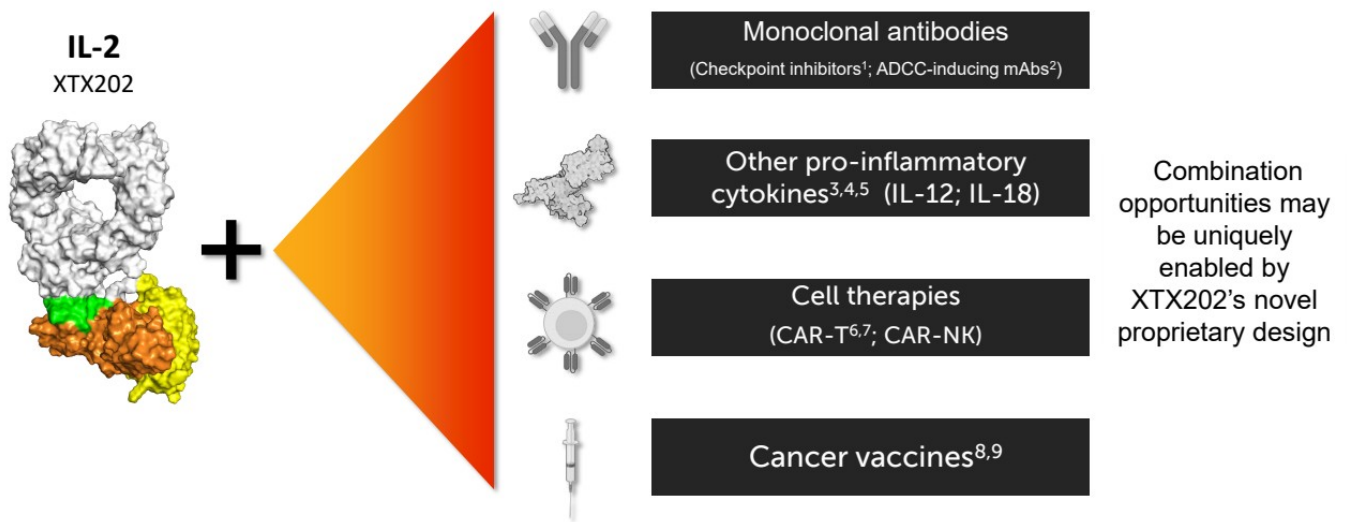


Data presented at Society for Immunotherapy of Cancer (SITC) in November 2022



Anti-tumor activity of XTX202 as a single agent and in combination with anti-mPD-1 was evaluated in hFcRn Tg32 transgenic mice bearing the murine MB49 bladder carcinoma model. The combination of XTX202 with anti-mPD-1 further improved anti-tumor activity with TGI 92% on Day 13 (Data presented as mean ± SEM, two-way ANOVA followed by post hoc Dunnett's test, *P < 0.05, **P < 0.005). The treatment with XTX202 alone or in combination with anti-mPD-1 improved animal survival from 19 days to 27.5 and 38 days, respectively (Gehan-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. SITC 2022

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



XTX202 (IL-2) Key Takeaways

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

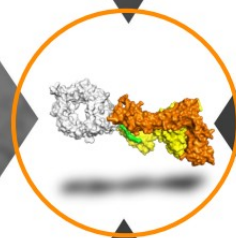


TREG: regulatory T cells.
Data and trial updates reported as of November 7, 2022.
* Patient had an optional on-treatment tumor biopsy and was the first patient for whom a tumor biopsy analysis was available as of November 7, 2022.

XTX301

Tumor-Activated IL-12

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

IL-12 Has Highly Compelling Biology for IO Applications



Exquisitely potent stimulator of NK and T cell cytotoxicity and INF γ production



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



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

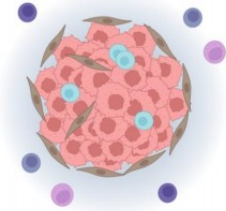


Demonstrated single agent objective responses in patients, but poorly tolerated (MTD <500 nanograms/kg on repeat dosing)

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

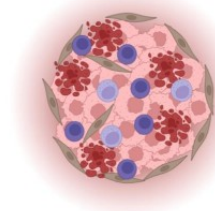
Cold Tumor

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



Hot Tumor

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

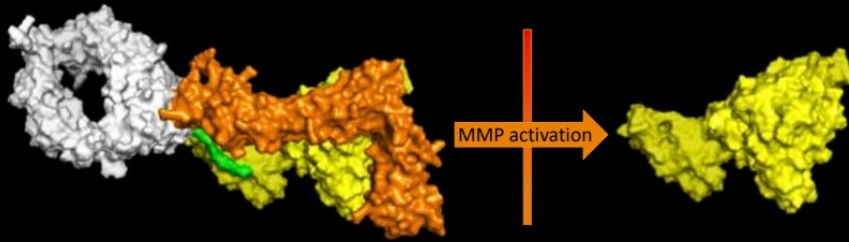


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Adapted from "Cold vs Hot Tumors", by BioRender.com (2022). Retrieved from <https://app.biorender.com/biorender-templates> Barraondo et al., Clin. Cancer Res., 2018; Nguyen et al., Front. Immunol., 2020

Inactive State

Active State



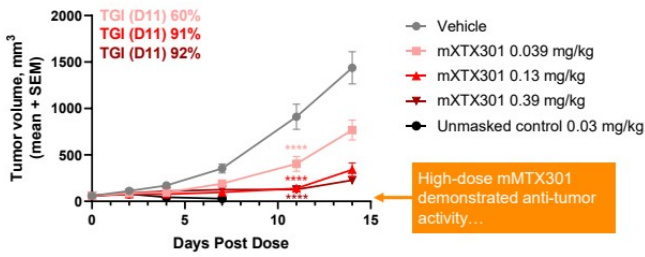
Designed to Outsmart Tumors

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

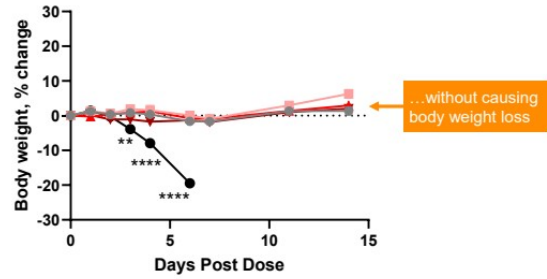
■ Half-Life Extension Domain ■ Cleavage Site ■ Masking Domain ■ Effector Domain

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

Tumor Growth



Body Weight



- mXTX301 demonstrated dose-dependent anti-tumor activity in MC38 murine model at all tested doses
- Dosing with mXTX301 at 0.13 and 0.39 mg/kg resulted in complete tumor regression in individual mice
- mXTX301 was well-tolerated in MC38 murine model with no significant body weight loss at all tested doses
- Unmasked control (mXTX302) not tolerated at 0.03 mg/kg dose; 75% (9/12) mice were euthanized by Day 11 due to body weight loss

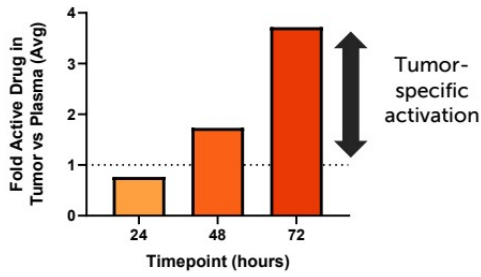
Data presented at New York Academy of Sciences' Frontiers in Cancer Immunotherapy in May 2022



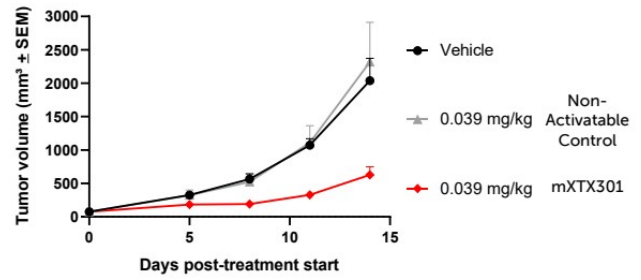
TGI: tumor growth inhibition.
 MC38 model: s.c. 0.5×10^6 cells; single IV dose of mXTX301 and mXTX302 on Day 0. Tumor growth data shown as mean \pm SEM. Tumor volume data was assessed by a two-way ANOVA followed by Bonferroni post hoc test on Day 11 compared to vehicle treated animals. **** $p < 0.0001$ for all mXTX301 treatment groups. Body weight data are shown as mean \pm SEM. A two-way ANOVA followed by Bonferroni post hoc test compared to vehicle treated animals was performed ** $p < 0.005$, **** $p < 0.0001$.

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

mXTX301 demonstrated tumor-specific activation *in vivo*



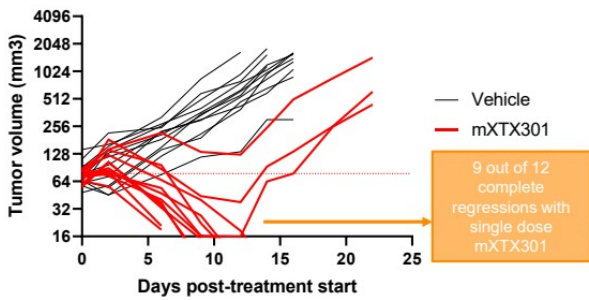
mXTX301 treatment resulted in cleavage-dependent enhancement in activity vs. non-activatable control



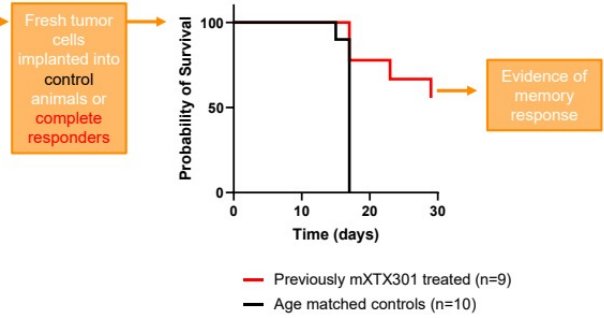
Left panel: Mice bearing MC38 syngeneic colorectal carcinoma tumors were dosed with mXTX301 (murine surrogate for XTX301) and the percent activated drug was measured over time in tumors and plasma.
Right panel: Mice bearing MC38 syngeneic colorectal carcinoma tumors were dosed once with mXTX301 or a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

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

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



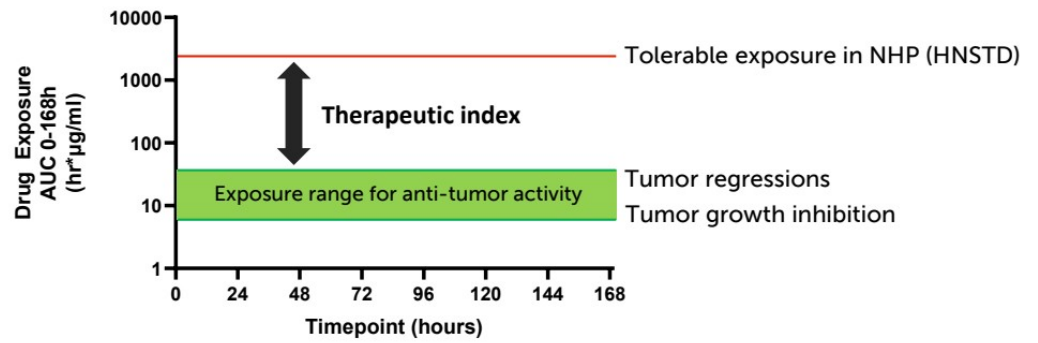
Majority of mXTX301 complete responders rejected tumors upon rechallenge



Left panel: Mice bearing MC38 syngeneic colorectal carcinoma tumors were dosed with mXTX301 (murine surrogate for XT301) or vehicle, and tumor growth was followed over time
Right panel: Mice having shown complete responses to mXTX301 were rechallenged with MC38 tumor cells on day 34 post initial treatment, while treatment-naïve, age-matched control animals were concurrently implanted with the same amount of MC38 tumor cells. Survival data are plotted over time; study was terminated once all animals on the control arm reached tumor size limits

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

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



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



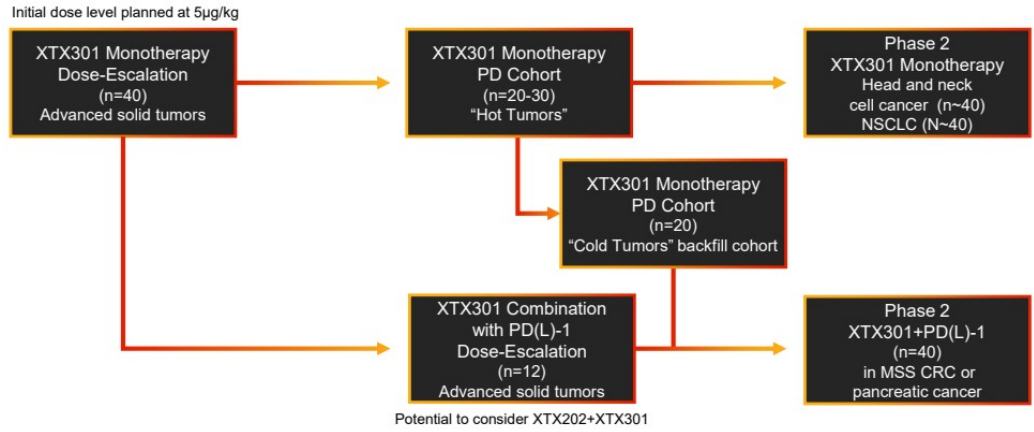
HNSTD: highest non-severely toxic dose; NHP: non-human primates; Q1W: once every week

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

As of November 7, 2022:

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

Planned Phase 1 / 2 Trial Design



Multiple Opportunities with Monotherapy and Combination Strategies
 NSCLC, head & neck, melanoma, TNBC, MSI high CRC, Prostate, Ovarian, Pancreas, Colorectal MSS



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

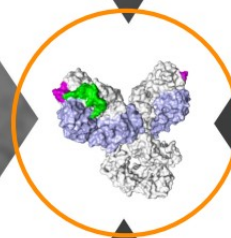
XTX301 (IL-12) Key Takeaways

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

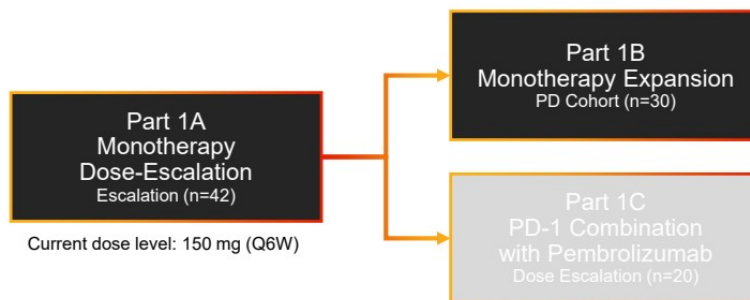
XTX101

Tumor-Activated aCTLA-4

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Phase 1 Trial Design



Additional Opportunities with PD-(L)1 Combination

Melanoma, renal cell carcinoma, MSS colorectal cancer

As of November 7, 2022:

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



PK: pharmacokinetic; Q6W: once every six weeks
Clinical trial collaboration and supply agreement established with Merck in May 2021 to evaluate XTX101 in combination with KEYTRUDA® (pembrolizumab)

XTX101 Anti-CTLA-4 Key Takeaways

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



Looking Ahead

**Xilio's Tumor-Activated Platform
Opportunities are Broad**

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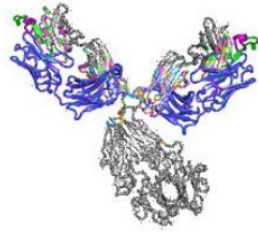
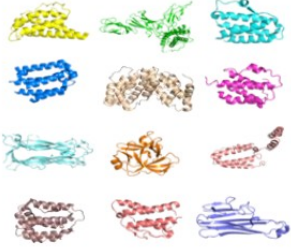
Looking Ahead: Potential to Deliver Highly Potent, Locally-Activated Immunotherapies Beyond Cancer

Masked Cytokines

Masked Antibodies

Pro- and Anti-Inflammatory Processes

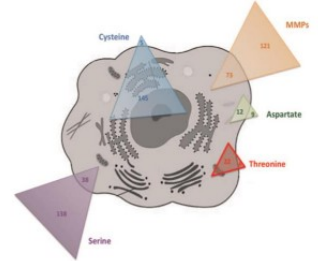
Proteases in Diseases of Immune Dysregulation



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



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



Actively pursuing the next generation of tumor-activated platform capabilities

Third Quarter 2022 Financial Results

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

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

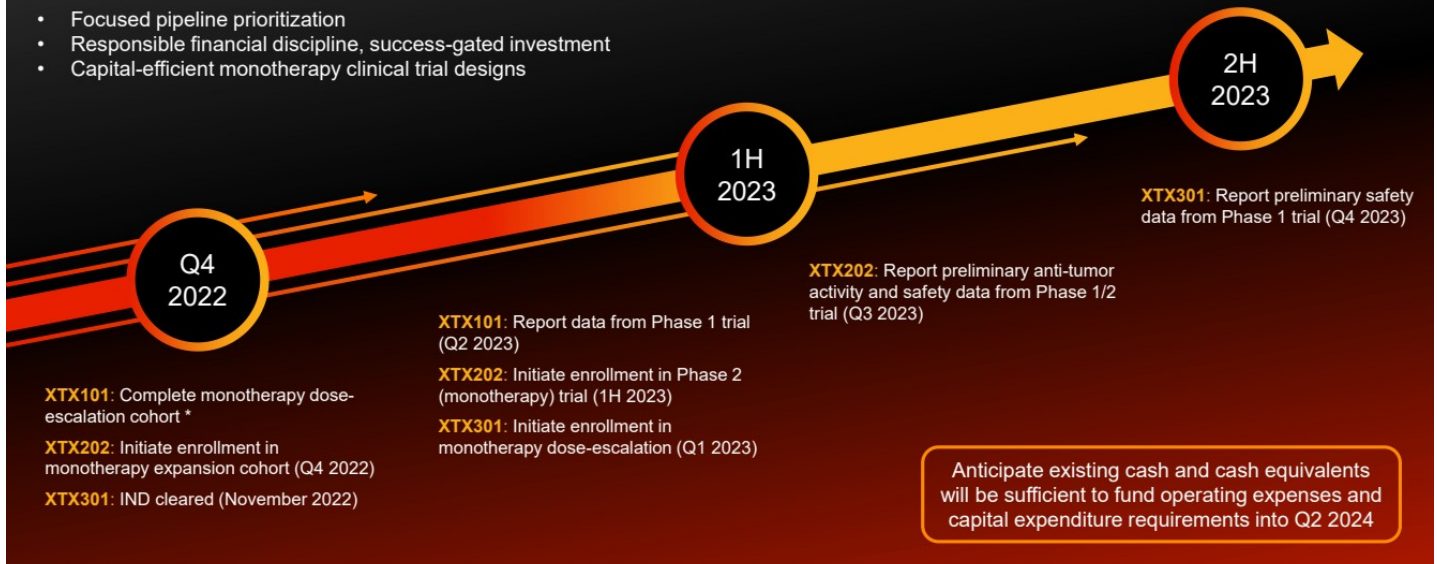
Anticipate existing cash and cash equivalents will be sufficient to fund operating expenses and capital expenditure requirements into Q2 2024



* Unaudited

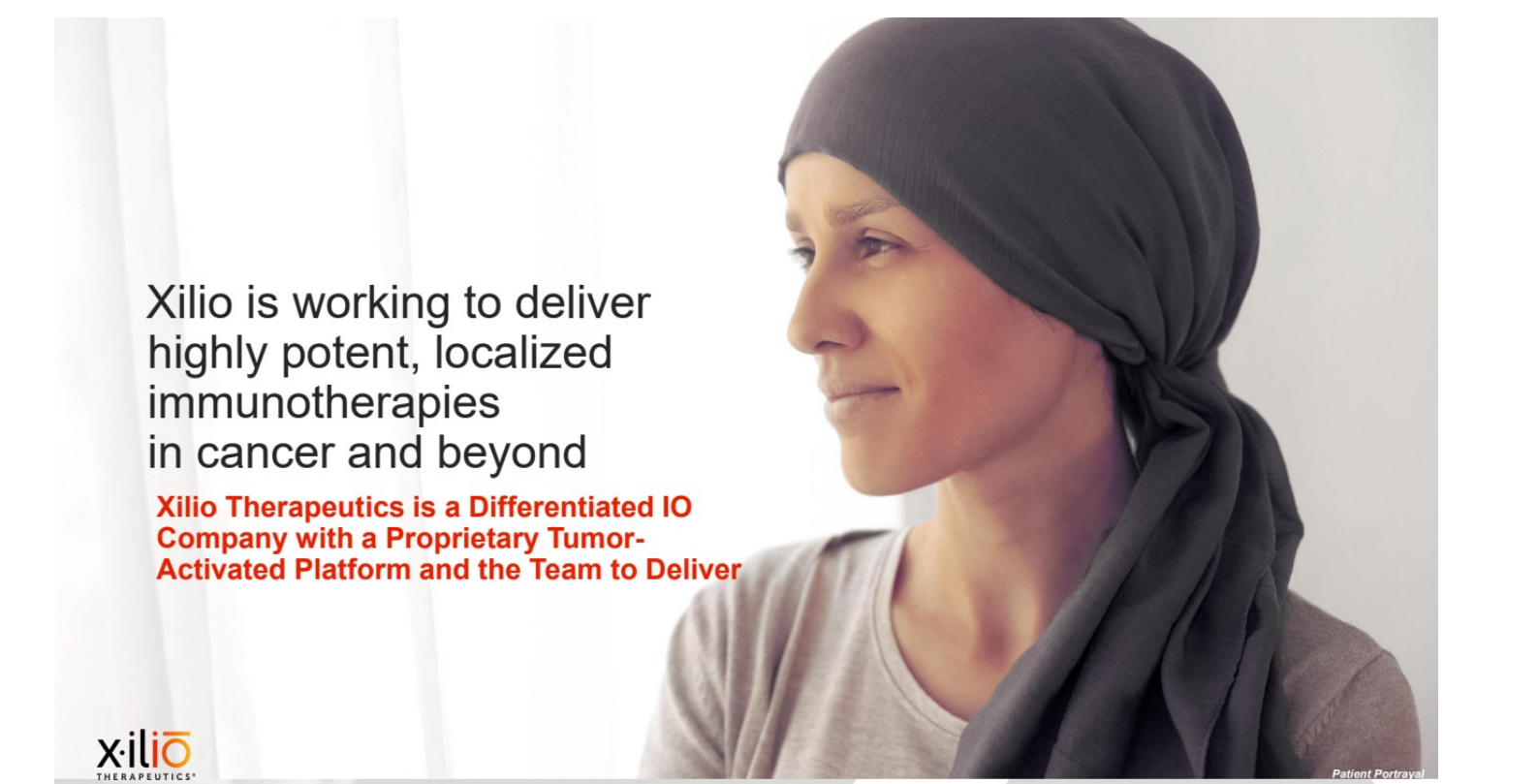
Xilio is Poised for a Dynamic 2023 and Multiple Anticipated Milestones

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



RP2D: recommended Phase 2 dose

* Plan to evaluate XTX101 as a monotherapy for the treatment of advanced solid tumors and explore opportunities for strategic collaborations to advance XTX101. Do not plan to initiate an anti-PD-1 combination cohort in the Phase 1 trial or initiate a Phase 2 trial without a development partner.



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

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



Patient Portrayal
